Journal of Medical Sciences

Vol. 15, No. 1 January 2007

Online version:
http://jms.netfirms.com

Khyber Medical College, Peshawar, Pakistan

Editorial Board

PATRON
Fazal Ahmad
Principal

CHIEF EDITOR
Nadeem Khawar

ASSOCIATE EDITOR
Nayyar Raza Kazmi

MANAGING EDITOR
Jamil ur Rehman

EDITORS
Abdul Wadood
Changez Khan
Sultan Mehmood
Azer Rashid
Zafar Iqbal
Amber Ashraf

Journal of Medical Sciences

Khyber Medical College,
Peshawar – Pakistan.

Vol. 15, No. 1 January 2007

Online version:
http://jms.netfirms.com

EDITORIAL

Social Health Insurance – Need of the Day in Pakistan
Nadeem Khawar

REVIEW ARTICLE

1) An Overview of Economic Evaluation of Health Care Programs – A Primer for Physicians 1
Nayyar Raza Kazmi, Rubina Bangash, Omar Farooq, Mohammad Imranullah

ORIGINAL ARTICLES

1) Erythrocyte Glucose 6 Phosphate Dehydrogenase Deficiency (G6PD) and Neonatal Hyperbilirubinemia 8
Irshad Ahmad, Iqbal Hussain, Sabir Khan, Abdul Hameed

2) Early Complications of Thyroid Surgery 13
Ijaz Ahmad, Abid Haleem Khattak, Nasrullah, Atta Ullah Jan

3) Age, Sex and Regional Distribution of Obese Ischemic Heart Disease in Tertiary Care Hospitals of Peshawar 18
Muhammad Fazal Zeeshan, Usman Ahmad Raza, Ghulam Sarwar

4) Frequency of the Symptoms with Colonoscopic Extent of Ulcerative Colitis 22
Abbas Khan, Ijaz Muhammad Khan, Muhammad Ali Khan, Aamir Ghafoor Khan

5) A Histological Study of the Liver of Mice Exposed to Cypermethrin 27
Qaiser Inayat, Jehanzeb Khan, Maqbool Ilahi, Rehana Azeem

6) Vitamin K Corrected Prothrombin Time as a Predictor of Survival in Severe Liver Disease 32
Noor-Ul-Iman, Humera Khan, Shabir Ahmad

7) Cystoscopic Procedures Under Local Anaesthesia 35
Mazhar Khan, Wasim Yar Khan, Riaz A. Khan, Abid Haleem, Fazal Ghani

8) Comparative Study of Visual Acuity in Phacoemulsification Vs Conventional Extracapsular Cataract Extraction with Posterior Chamber Intraocular Lens Implantation in Age-Related Cataract 39
Mohammad Alam, Zafar Iqbal, Amir Mohammad, Mian Ihsanullah

Journal of Medical Sciences is a peer reviewed journal. This means it submits most of its published articles for review by experts who are not part of the editorial board.

Editorial correspondence should be addressed to:

Dr. Nadeem Khawar
Professor of Paediatrics
Khyber Teaching Hospital
Peshawar, Pakistan.
Tel: +92-91 9216337
Fax: +92-91 9216337
E-mail: nkhawar@hotmail.com

Copyright: Material printed in this Journal of Medical Sciences may not be reproduced without the permission of the editors or publishers. Instructions to authors appear on the last page of each issue. Prospective authors should consult them before sending their articles and other material for publication with the understanding that except for abstracts, no part of the data has been published or will be submitted for publication elsewhere before appearing in this journal.

The Editorial Board makes every effort to ensure the accuracy and authenticity of material printed in the journal. However, conclusions and statements expressed are views of the authors and do not necessarily reflect the opinions of the Editorial Board or the Khyber Medical College. Publishing of advertising material does not imply an endorsement by the Khyber Medical College.

Printed at:
Khyber Printers
Small Industrial Estate,
Kohat Road, Peshawar.
Tel: (091) 2325196 / 5272407
E-mail: khyberprinters@yahoo.com

9) Incidence of Deep Vein Thrombosis in Cancer Patients in Northern Pakistan 44
Abid Jameel, Shahid Jamil

10) Prognostic Factors in Unilateral Idiopathic Sudden Sensorineural Hearing Loss 49
Amjad Khan, Waqaruddin, Altaf Hussain, Saeedullah

11) Frequency of Asymptomatic Hypocalcemia in Multiparous Women 53
Parveen Azim, M. Amjad Taqweem, Saima Gilani, Zafar Ali Amjad Mahboob

12) Complications of the Nasal Septal Corrective Surgery 56
Inayat Ullah, Sharafat Ali, Naseer Ahmad, Muhammad Yousaf, Arif Raza Khan

13) Case Based Series, of Percutaneous Antegrade Stenting for Lower Ureteric Obstruction Secondary to Pelvic Malignancy 59
Asif Malik, Sabina Aziz Asif, Hamid Hussain, JS Gellister

14) Frequency of Placental Attachment on Scarred Uterus 63
Nighat Shaheen, Abida Nasreen

15) A Critical Appraisal of the Obstetrical Correlates of Cesarean Section Rate at a Teaching Hospital 66
Gulrukh Qazi, Shahnaz Akhtar

16) Clinical, Biological and Radiological Profile of TB in Children Under 5 Years of Age 72
Amin Jan Gandapur, Nayyar Raza Kazmi, Fazlur Rahim, Nadeem Khawar

17) The Outcome of Total Abdominal Hysterectomy by General Surgeons. A Prospective Study of 100 Cases 77
Ata Ur Rehman Khalil, Muhammad Yunas, Amir Amanullah, Mukhtiar Ali, Wasim Yar Khan, Muhammad Janisar

18) Consultation Liaison Psychiatry in a Multi-Disciplinary Teaching Hospital 81
Sayed Mohammad Sultan, Mohammad Riaz

Global Research Updates 85

Instructions for Authors 90

EDITORIAL

SOCIAL HEALTH INSURANCE — NEED OF THE DAY IN PAKISTAN

Nadeem Khawar

In Pakistan, public health care provision has not been successful in creating health security for the poor. The sector remains grossly under-funded, with public expenditure on health accounting for barely 0.5 per cent of the GDP of which close to 75 per cent is spent on salaries[1]. There are only two countries in the world — Nigeria and Sudan — that spend less than this proportion on health.

It is around one per cent for India, two per cent for Bangladesh and Nepal and three per cent for China, while for most developed countries it ranges from five to seven per cent[2].

More than 80 per cent of the total health care expenditure is spent by the private sector and almost all of this represents private out-of-pocket expenditure on curative care — consultations and in-patient diagnostic care, laboratory tests and medicines. It is noteworthy that between 1990-2001, three countries — Bangladesh, Nepal and Bhutan — which recorded the maximum increase in public expenditure on health, also recorded the maximum reductions in infant mortality rates (IMR). The average annual reduction in IMR for Bangladesh was 7.6, Bhutan 4.7, Nepal 5.8, Sri Lanka 3.9, Pakistan 1.96 and India 3.1[3].

The health sector has acquired a notorious reputation for inefficiency and corruption at all levels. Most of the government-operated outlets for primary healthcare, except perhaps in Punjab, are on the verge of total collapse.

Quality standards are practically non-existent as are performance assessments, with little accountability in both public and private sectors. Very few norms and standards are adhered to. There is little performance monitoring in health centers.

There are some forms of social welfare protection instruments in many countries like unemployment benefits or social security for the needy, driven by the belief that it is the primary responsibility of the state to look after its citizens. Free or subsidized healthcare is also one such instrument.

The poor and aged are forced to sell their assets or take massive loans to cover the costs of medical treatment and care. They are also exploited by indifferent health professionals in the public sector.

Those hardest hit by lack of health coverage are the poor, who suffer from higher levels of mortality and malnutrition than the rich. A World Bank study on India shows that the poor-rich risk ratio is 2:5 for infant mortality and 1:7 for children underweight and that 24 per cent of the poorest quintile do not seek medical care when ill mainly because of poverty compared to nine per cent in the richest 20 per cent[4].

Furthermore, according to the World Bank, hospitalized Indians spend more than 58 per cent of their total annual expenditure on healthcare and almost 25 per cent of them fall into poverty every year as a direct result of medical expenses they pay on hospitalization.

The point is that low levels of expenditure, poor quality of services, and inefficiencies have failed to provide decent health cover for the poor. This has raised the need for alternative financing mechanisms and instruments to achieve this objective, that is, health insurance to improve the access of the poor to health services — an instrument now being developed by insurance companies in the private sector for the more affluent households and for employees of corporate entities. The poor can also make small, periodic contributions that could go towards meeting their healthcare needs. Hence, the need for setting up a health insurance scheme for low-income groups.

The government of India introduced the Universal Health Insurance scheme targeting the poor in 2003. The premium was set at Rs. 365 per annum for an individual and Rs. 548 for a family of five[5].

The government gives a subsidy of Rs. 100 per family below the poverty line. The benefits include reimbursement of expenditure of up to Rs. 30,000 and illness compensation of Rs. 50 per day for the period of hospitalization of the earning head of the family. There is a provision of coverage for Rs. 25,000 in case of death of an earning head of family in an accident.

The problem with the scheme is that the premium is too low for the insurance companies to offer good coverage and too high for the poor to pay upfront. Thus so far only two per cent of the policies have been sold to the people living below the poverty line. Pakistan, by learning from the experiences of India and other developing countries, can introduce its own scheme that addresses the kind of weaknesses identified here.

To make the scheme financially viable, the transaction costs for the insurance companies can be lowered by starting a Social Health Insurance for the masses. The compulsory nature of SHI will ensure universal coverage and risk pooling which will give ultimate benefit for the poor. However there is a need for acute advocacy drive in this regard to make people understand the benefits of Social Health Insurance. It will also help to improve the quality of standards in health care as both public and private sector will compete for adopting quality standards, which is a pre-requisite under the SHI for payments to the health care providers.

For the poorest of the poor who cannot make any contribution, health insurance will not be relevant. However there insurance will be done by the government under SHI scheme, and under the risk pooling mechanisms, the costs of illness treatments would be minimized.

REFERENCES

1. Government of Pakistan, Ministry of Finance Annual Financial Report 2005.
2. Word Bank Report 2005: 78-81.
3. State of the World Children 2006, Unicef: 103.
4. Yazbeck AS, Kwon SM. Challenges in Poverty reduction in India: A World Bank Report 2004: 203-210.
5. Health Insurance in India, a way forward or backward. Editorial, The Hindustan Times,dated 23.12.2003.

REVIEW ARTICLE

AN OVERVIEW OF ECONOMIC EVALUATION OF HEALTH CARE PROGRAMS – A PRIMER FOR PHYSICIANS

***Nayyar Raza Kazmi, Rubina Bangash, Omar Farooq, Mohammad Imranullah**

* Epidemiologist, Department of Child Health, Khyber Teaching Hospital, Peshawar
Email: nrazakazmi@gmail.com

ABSTRACT

In the developed world, the health care technologies and interventions are assessed on basis of economic evaluation, to see if they are cost effective, specially in the scenario of rising medical care costs. In Pakistan, very few if any physicians, are familiar with the details of carrying out economic evaluations of new emerging health technologies, with the result that today we are trying to invest in, what is perhaps not needed for the bulk of population. This paper revisits the major Economic methods of evaluating health care technologies and briefly presents the subject for the Physicians and Clinicians to understand

1. INTRODUCTION

Healthcare is one of the most demanding and ill performing sector in the Pakistan economy. Fast and unchecked growing population, rampant illiteracy, poor management and market failures has left Pakistan in a state of health which is reflected by the indicators which are worse in the region second only to the war torn Afghanistan.

Domestic and International compulsions, coupled with heavy military spending have traditionally left Health sector on the back seat with only 0.6% of the GDP annually being allocated to the Health Sector[1]. Bureaucratic delays and managerial problems leave the actual health expenditure slightly less than 0.5% of the annual GDP[2].

The Public Health Sector in Pakistan is largely subsidized with major financing from the Tax payers money but still the burden of purchasing health care in mostly left on the end user with out of pocket expenditures soaring to 80-90% of the individual health care costs. Foreign donations and grants by international organizations and Consortia account for approximately 14% of the Health Budget annually[3]. Despite this, most of the health policy is shaped by donor agencies, based on ideas, mostly tested in culturally different world.

Since much of health care expenditure is funded collectively through government, and because the level of expenditure is so large, it is important that governments carefully evaluate how the money is spent to make sure the benefits are as large as possible for any level of expenditure. This is the primary purpose of the economic evaluation of health care programs.

Collectively, they provide an important guide to government in trying to allocate health care resources efficiently across the diverse range of health care goods and services. In the backdrop of a meager health resource allocation, it becomes more prudent to ensure a logical utilization of this money with the objective of gaining the best return for the level of investment made in health care. Ironically, it has been observed that in spite of more and more funding, the scarcity of health care resources continues to increase. Difficult decisions have to be made. Markets are often suppressed so decisions need to be made collectively, through government, on how to allocate scare health care Rupees. Increasingly, governments in third world countries are using the techniques of program evaluation rather than relying on historical precedents, political lobbyists and public pressure groups. Therefore there is a need for Pakistan to learn in this area and streamline its healthcare programs on the basis of allocative and technical efficiency.

2. Program Evaluation

Economists and health care planners have developed a set of widely used techniques to evaluate the cost and medical effectiveness of health care programs. Essentially, they try to answer questions such as 'Is this health care program worthwhile?' and 'Should this health care program be expanded or contracted?' The term 'program' can be applied to any type of health care intervention, curative or preventive. Programs may be narrow or broad based. Examples include:

- Starting a nation wide Hepatitis B and C Prevention and Control Program.
- New medical procedures (whether to adopt or not)
- Screening and prevention of tuberculosis[9] and
- Alternative ways of repairing hip fractures[12] .

Most types of program evaluation use similar methods to measure costs, although some studies are more inclusive than others. Generally, benefits are more difficult to measure than costs, and evaluations differ, often fundamentally, in the way in which they measure the benefits or outcomes of a program. The four most common types of program evaluation used in health care are

1. cost-minimization analysis,
2. cost-effectiveness analysis,
3. cost-utility analysis and
4. cost-benefit analysis.

I will explore each of these types of program evaluation in some detail. Each of the methods has advantages and disadvantages relative to the others and the selection of the most appropriate method of analysis depends on the nature of the program being evaluated and the purpose of the evaluation.

2.1 Cost-Minimization Analysis

Cost-minimization techniques are appropriate for those situations when the benefits of two or more methods of delivery are identical, or at least very similar. Their purpose is to determine which method is cheaper. There is no need to measure the benefits, as the outcomes of alternative programs are so similar. The major advantage of cost- minimization is that it is cheaper to apply than the other types of program evaluation. It does not require the estimation of benefits that are generally more difficult to estimate than costs. All the other methods of program evaluation require the investigator to measure benefits. The disadvantage of cost-minimization analysis is that it can only be used to compare programs or projects with very similar outcomes. A program of screening for Childhood TB cannot be compared with one that increases the availability of Tetanus Toxoid vaccine using cost-minimization analysis. And yet, this is the kind of choice that health authorities have to make. Furthermore, the outcomes of alternative methods of delivery are seldom exactly the same, even when they are broadly similar. Outcomes may differ in quantity or quality and the differences may be in terms of medical effectiveness or they may differ in non-medical ways such as convenience to the patient. In either case, the assumption of equal outcomes is unrealistic.

2.2 Cost-Effectiveness Analysis

Cost-effectiveness analysis measures the benefits of programs in physical units with immediate medical meaning. Typical examples of the units of measurement include lives saved, life- years saved, number of patients immunized, number of participants who quit smoking, number of deaths averted, and so forth. The advantages of cost-effectiveness analysis are that the benefits or outcomes of health care programs are explicitly measured and the units of measurement are easy to understand and readily accepted by the public and medical professionals[4].

One disadvantage of this approach is that a single physical measure (such as lives saved) is unlikely to capture all the dimensions of the benefits of the concerned intervention. Some interventions may not save many lives but may reduce pain or otherwise increase the quality of life. Another problem arises because units of measurement vary from program to program; it is difficult to compare the relative effectiveness of programs with different outcomes. For example, one program may cost Rs. 2000 per life- year saved while another costs Rs. 50 per child immunized. How can such programs be compared? A final disadvantage is that many of the concepts such as lives saved or life-years saved are not as simple as is commonly thought. This method of analysis implicitly assumes that all deaths averted are equally valued by society. This may not always be the case. Is saving the life of a 90 year old quadriplegic equally valued by society as the saving of the life of a healthy six year old? Similarly, all life- years saved are not homogeneous but vary substantially in quality. Cost-effectiveness analysis often makes no attempt to measure the quality of life; it only measures the quantity of life[5]. For example enabling blind persons to see may not increase their life expectancy but it will certainly increase the quality of their lives.

2.3 Cost-Utility Analysis

Cost-utility analysis is another type of economic evaluation method which attempts to overcome some of the problems of cost-effectiveness analysis but is more difficult to understand and is more expensive to apply[6]. It assumes that life- years must be treated as having different values when the quality of life differs. It tries to focus on a utility measure which can measure health across the board for all conditions alike. Such measures try to combine the morbidity and mortality in one indicator.

The first step in cost-utility analysis is to determine a utility index for various health states. Typical health states relevant to a particular program are described, evaluated using one of several techniques and a weight is then attached to measure the relative utility of each health state. 'Healthy' and 'Dead' are the two reference states and are arbitrarily given utility indices of one and zero respectively. Other health states are then located on this scale. The lower the index, the less desirable the state of health. For example, someone experiencing mild angina is estimated to have a utility index of 0.90, someone who is anxious or depressed and lonely much of the time is estimated to have a utility index of 0.45 and a blind person is estimated to have a utility index of 0.39[7]. Being confined to bed with severe pain or being unconscious may have utility indices which are less than zero, indicating a condition less satisfactory than death. Where do these indices come from? A variety of approaches has been adopted. I will briefly illustrate two approaches: time

trade-off and standard gamble. Suppose we are evaluating a program to require safety helmets when riding a motorcycle. In some circumstances helmets may reduce the likelihood of brain injury; we concentrate on brain injury that is permanent and results in no loss of mental capacity but does result in slurred speech. We need an index that compares the quality of life for a person in good health compared to one with slurred speech but otherwise good health.

The time trade-off approach[8] surveys individuals and asks them the following question. How long in the condition of slurred speech (followed by death) would you equate to 10 years of normal health (followed by death)? How would you answer this question? Assume that the average response is 12.5 years. That is, people on average equate living in normal health for 10 years to living with slurred speech for 12.5 years. The utility index is calculated as:

U(I) = Time (normal health)/Time (state I) So U(I) = 10/12.5 = 0.80.

Thus, using the time trade-off approach, the quality of life of someone with slurred speech is estimated to be 0.80. Another approach is the standard gamble[9]. The standard gamble approach surveys people and asks the following question. What value of P (a probability with possible values between zero and one) would make you indifferent between the two alternatives in Table 1?

Table 1: The Standard Gamble

	Probability	Outcome
Alternative 1	*P*	Normal health for 10 years followed by death
	$1 - P$	Immediate death
Alternative 2	1.0	Slurred speech for 10 years followed by death

Assume your answer is 0.85. This means you are indifferent between the certainty of living for 10 years with the condition of slurred speech and the uncertainty of living in normal health for 10 years (with a probability of 0.85) or immediate death (with a probability of 0.15). If this is the average response to the survey question, then using the standard gamble approach, the estimate of the utility index for slurred speech is 0.85.

U(I) = P = 0.85

Now for a moment if you compare the Time Trade off and the standard gamble approach, you probably had more difficulty answering the question in the standard gamble than for the time trade-off example. This is a problem with the standard gamble approach. Although economists, for theoretical reasons, prefer the standard gamble, survey participants are often confused and may not answer questions in a way that reflects their true feelings. The alternative, the time trade-off approach, is reasonably reliable, easy to administer and to understand, and is commonly used.

It is important to note that regardless of how the utility of a health state is estimated; the result is a cardinal measure. Health economists are used to working with ordinal measures; for example, a combination of goods on a higher indifference curve reflects a preference for any combination of goods on a lower indifference curve. However, the magnitude of the difference cannot be determined from the indifference map. A cardinal measure enables us not only to rank different health states but also to indicate the magnitude of people's preference. In the previous example, living with slurred speech is less desirable than being in normal health (an ordinal ranking). More precisely, it is 85 per cent as desirable (a cardinal difference).

The next step in cost-utility analysis is to estimate the number of QALYs associated with a program. QALY stands for 'quality-adjusted life-year'. QALYs attempt to measure the quantity and quality of health benefits that result from a health care intervention program. An illustration of how the benefits of a health care intervention generate QALYs is shown in Table 2. We assume that the introduction of motorcycle helmets eliminates accidents resulting in slurred speech. (In reality not all cases of slurred speech would be eliminated but there would be other health benefits.)

The gain in QALYs from the introduction of helmets is 105000 (70700000 – 70595000). This value is influenced by the number of people affected (10000), the number of years people are affected (we assume each person lives an additional 70 years), and the improvement in health (U(I) increased from 0.85 to 1.00). The number of QALYs is a measure of the health benefits resulting from the introduction of motorcycle helmets. It is equivalent to 105000 people living one year longer in normal health. Once the cost of the program to introduce motorcycle helmets is estimated we can estimate the cost per QALY. Assume that the net cost of introducing helmets is Rs. 20,000,000. The net cost would take into account costs such as those associated with the administration of the program, the cost of the helmets less the reduction in medical expenses and so forth. The cost per QALY is easily calculated:

Cost per QALY = Net cost of program/Increase in number of QALYs

= Rs. 20,000,000/105000

= Rs. 190.48

Although the above example of estimating the cost per QALY is only illustrative, actual programs have been carefully evaluated in Australia and overseas using similar techniques. Table 3 indicates some of the results for the United Kingdom. The cost per QALY has been calculated for 10 different programs[10]. The costs are measured in British pounds as of August 1990. Note the enormous range in the cost per QALY

Table 2: The effects of Motorcycle Helmets (A Hypothetical Example)

	Number of Individuals	Life Years affected	Health State	Utility Index	QALY's
Before the introduction of helmets	1000,000	70,000,000	Normal state	1.00	70,000,000
	10,000	700,000	Slurred Speech	0.85	595,000
Total					70,595,000
After the introduction of Helmets	1000,000	70,000,000	Normal	1.00	70,000,000
	10,000	700,000	Normal	1.00	700,000
Total					70,700,000

of the different programs. It is only £220 for cholesterol testing and diet therapy and more than £126000 for the treatment of anaemia in dialysis patients. That is, it requires more than 500 times the expenditure in the latter program to save a QALY as is required for cholesterol testing. Such differences are commonly observed when programs have been subjected to careful cost-utility analysis. These large differences suggest that program evaluation is important and can assist decision makers in determining how to allocate health care dollars. By shifting resources away from programs with high costs per QALY to those with low costs per QALY, total health benefits can be in- creased without increasing total health expenditure. By definition this would mean an increase in the efficiency of the health care system.

Table 3: Some Interventions and their Costs per QALY in British Pounds

Therapy	Cost per QALY
Cholesterol testing and Diet Therapy	220
Neurosurgical intervention for head injury	240
GP advice to stop smoking	270
Hip Replacement	1180
Breast Cancer Screening	5780
Heart Transplantation	7840
Home Hemodialysis	17260
Neurosurgical intervention for malignant intracranial tumors	107780
Erythropoietin treatment of anemia in dialysis patients	126290
Source Maynard (1991)	

The main advantage of cost-utility analysis is that it explicitly takes into account the quality of life as well as the quantity of life when measuring the benefits of a program. Another advantage of cost-utility analysis is that health professionals and the wider community generally accept the gain in QALYs as a measure of benefits. The main difficulty of cost-utility analysis is that it requires the calculation of a utility index for every health state relevant to a particular program. This can be expensive and time consuming. One approach to overcome this problem is to construct a multiattribute health status classification system (Drummond et al.[6] 1997, pp 157–65). Regardless of the techniques used, the construction of cardinal utility indices is inherently subjective and has numerous theoretical limitations. Estimates can vary depending on the method used to construct the utility indices and the type of people included in the survey. Should the survey panel be representative of the population, include only those who have been affected by the medical condition, or represent the medical professions who treat these conditions? These and other questions have no easy answers[11].

2.4 Cost-Benefit Analysis

The final method of program evaluation is cost-benefit analysis. In many ways it is the most complicated of the four types of evaluation. It also has the potential to be the most useful. All of the methods measure the costs of programs in dollars or some other monetary unit such as Ruppees or British pounds. Cost-benefit analysis measures the benefits as well as the costs in monetary units. This makes it easier to determine whether or not a program is worth continuing. If the dollar value of the benefits exceeds the costs, the program is generally deemed to be worthwhile.

Cost-benefit techniques were first developed to assist military decision makers and have been applied

with success to public projects such as the construction of a dam or the development of a port facility. More recently these techniques have been applied in the health sector. Cost-benefit analysis differs from the other types of program evaluation in that it attempts to measure the value of life, the value of a life-year or the value of a QALY. At first, the concept of putting a dollar value on human lives is shocking and even offensive to some people. Nevertheless, we all make decisions that reveal the dollar value we place on small increments in the length of our own lives[12].

There are two basic approaches that have been used to estimate the value of human life. The first is referred to as the human capital approach and is based on estimates of a person's lifetime productivity. That is, the value of a life is equated with the value of goods and services that a person will produce over their lifetime. This, in turn, is measured by the wages that a person can be expected to earn. There are two problems with this approach. First, only output in the market economy is generally valued. This results in several anomalies. Home production such as cooking and childcare are usually not included. This tends to reduce the value of a woman's life as she spends less time, on average, in the paid labour force than her male counterpart. Because well-educated men and women generally earn more than those with less education, their lives are given a higher value. The value of the lives of people who have retired may be assumed to be zero as they are no longer employed. To overcome these problems, the average wage for all individuals is sometimes used to calculate the value of a life, regardless of whose life is saved.

Another problem of the human capital approach is determining whether the value of a life should be determined by the gross value of production or the net value of production after subtraction of the individual's consumption. Those who suggest using the net value approach argue that the contribution an individual makes to society is determined by the difference between what they produce and what they consume.

Because of these and other problems many economists favour the willingness-to-pay approach to the valuing of life. This approach observes human behaviour and uses this information to impute a value for small increases in life expectancy. We can illustrate this approach with a hypothetical example. People in hazardous employment are often paid extra to compensate them for the extra risks they incur in their work. Say there are two categories of welders. They have similar training, skill and experience but one group works on high-rise buildings where the risk of accidental death is higher. To compensate them for the greater risk they are paid a higher salary. Assume that ordinary welders earn Rs. 30,000 per year while those who work on high-rise buildings earn Rs. 31,000. Also assume that the probability of accidental death is 0.02 per year for ordinary welders and 0.06 for those working on high-rise buildings. Those who work on high-rise buildings are willing to increase their risk of accidental death by 0.04 per year in return for extra income of Rs. 1000. They are implicitly valuing 0.04 life-years at Rs. 1000. This in turn implies that they value one life-year as Rs. 25 000.

0.06 life-years – 0.02 life-years = Rs. 1000

0.04 life-years = Rs. 1000

0.04 life-years/0.04 = Rs. 1000/0.04

1.0 life-year = Rs. 25 000

The major advantage of cost-benefit analysis is that costs and benefits are measured using the same monetary index. As a result individual programs can be evaluated in isolation and decisions can be made about the desirability of continuing or expanding a program. It is not necessary to calculate the benefit to cost ratio for all programs to make such a decision.

The disadvantage of cost-benefit analysis is that it is difficult to measure the value of human life or even to estimate the value of marginal extensions of human life. Different approaches yield estimates that are widely divergent and cannot be easily reconciled.

3. Principles Affecting All Types of Program Evaluation

There are several broad principles that are important to take into account regardless of the type of program evaluation that is conducted. The first is the concept of opportunity costs. The second is the usefulness and often necessity of evaluating policies or programs from a societal perspective rather than merely from the perspective of a single individual or organisation. Other important concepts are marginal costs and marginal benefits and the need to clearly distinguish marginal, average and total when estimating costs and benefits. Finally, the concept of discounting is important in program evaluation as many health care programs have very long time horizons.

3.1 The Importance of Opportunity Costs

When estimating the costs of a health care program it is important to include all relevant economic costs. They include private expenditure on medical goods and services such as doctors' bills and pharmaceutical drugs. They also include non-medical expenses such as patients' expenditures on petrol or train fares when traveling to receive medical care. Expenditures that occur in the public health care system and other government departments should also be included[13].

It is also important to identify opportunity costs. These are generally not so obvious and are also more

difficult to estimate. For example, in a preventative health care program a dietitian may be employed to provide advice to patients who are in hospital. The cost of the dietitian (including all oncosts) represents a direct financial outlay that results from the program and obviously needs to be included. The dietitian may also be provided with an office free of charge by the hospital. There is no financial outlay associated with the use of the office. Nevertheless, an estimate of the opportunity costs of the office space needs to be made. If the preventative care program did not use the office, it could have been used for some other purpose. The value of the office needs to be included. An estimate might be made based on the floor space of the office and the rental value of office space in the region.

Another opportunity cost that is common in program evaluation is the value of participants' time. This includes the time participants spend traveling, waiting for treatment and receiving treatment. The opportunity cost of time is the value of the alternative forgone. The alternatives may be leisure time or paid employment. The value of this time is not easy to estimate but it is common to use average weekly wages by age and gender for the people affected.

3.2 Taking a Societal Perspective

One of the distinguishing traits of an economist is the ability to analyze policies and programs from a societal perspective rather than perspective of an individual firm or group. This applies to program evaluation in health care. Unless directed otherwise by the organization paying for the study (such as a pharmaceutical company), an economist should try to estimate all the costs and benefits resulting from a health care intervention and not merely those of the public or private health care system[14]. Practical and funding constraints sometimes make it impossible to estimate all costs and benefits but such limitations need to be recognized and acknowledged.

3.3 Total, Average and Marginal Costs and Benefits counted to determine their present value

Discounting is necessary because people have a time preference; that is, they prefer current consumption over future consumption. Future costs and benefits are not as valuable as current costs and benefits and need to be discounted to determine their present value so that useful comparisons can be made. A future cost or benefit will be discounted by a greater amount the more distant the time period and the higher the discount rate that is applied.

Although total and average costs are usually easier to calculate and are more likely to be available, marginal costs and benefits are often more relevant for decision making. It is especially important to estimate marginal costs and marginal benefits when deciding whether or not a program should be expanded or curtailed. Optimality conditions generally require that marginal social costs equal marginal social benefits and these concepts should be estimated whenever possible.

The importance of marginal analysis is highlighted in a classic study on cancer detection[11]. It was common practice for doctors to request six different stools be tested in screening for colon cancer. Economic analysis revealed that while the average cost of the fifth test was only $2268 per case detected the marginal cost was $4,472,695 and the marginal cost of the sixth test was $47,107,214. It turns out that while the cost of undertaking a fifth or sixth test is rather modest, such tests hardly ever detect cancers that have not been revealed in the first four tests. As a consequence of economic analysis, hospital protocols were changed.

4. Concluding Remarks

There has been a substantial increase in the use of program evaluation techniques throughout the Australian health care system and they are of great assistance in providing relevant information in a useful framework for decision makers. Program evaluation is also an important and growing area of employment for economists.

Carefully conducted health care program evaluations can provide important and useful information. However, we will never be in a position of having evaluations of all, or even a significant proportion of, health care programs. Decision makers need to combine sound judgment with the best quantitative and qualitative information available in making difficult health care choices.

REFERENCES

1. Federal Budget of Pakistan 2006-07, Ministry of Finance, Government of Pakistan.
2. Economic Survey of Pakistan 2005, State Bank of Pakistan: 145.
3. Khattak FH, Chugtai AA. Donor Contribution in Health Sector of Pakistan- Consultant Report 2006: 70-75.
4. Abelson P. 'The value of life and health for public policy', *Economic Record*, 2003 vol. 79: 2-13.
5. Australian Institute of Health and Welfare, *Health Expenditure Australia 2001-02*, Health and Welfare Expenditure Series No. 17, AIHW Cat. No. HWE 24, 2003 AIHW, Canberra.
6. Drummond M, O'Brien B, Stoddart G, Torrance G. *Methods for the Economic Evaluation of Health Care Programmes*, 2nd edn, 1997 Oxford University Press, Oxford.
7. Ippolito P, Ippolito R. Measuring the value of life saving from consumer reaction to new information,

Journal of Public Economics, 1984: vol. 25, pp. 53-81.

8. Kingston G. Cost benefit analysis in theory and practice, *Australian Economic Review*, 2001 vol. 34, pp. 479-87.

9. Macintyre C, Plant A, Hendrie D. The cost-effectiveness of evidence-based guidelines and practice for screening and prevention of tuberculosis, *Health Economics*, 2000: vol. 9, pp. 411-21.

10. Maynard A. Developing the health care market, *Economic Journal*, 1991: vol. 101, pp. 277-86.

11. Neuhauser D, Lewicki A. What do we gain from the sixth stool guaiac?, *New England Journal of Medicine*, 1975: vol. 293, pp. 226-8.

12. Polder J, van Balen R., Steyerberg E, Cools H, Habbema J. A cost-minimization study of alternative discharge policies after hip fracture repair, *Health Economics*, 2003: vol. 12, pp. 87-100.

13. Torrance G, Feeny D. Utilities and quality-adjusted life years, *International Journal of Technological Assessment in Health Care*, 1989: vol. 5, pp. 559-75.

14. Viney R. Cost benefit analysis of non- drug treatment of hypertension, in *Economics and Health: 1989*, ed. C. Selby Smith, Public Sector Management Institute, Monash University, Clayton, Victoria.

ORIGINAL ARTICLE

ERYTHROCYTE GLUCOSE 6 PHOSPHATE DEHYDROGENASE DEFICIENCY (G6PD) AND NEONATAL HYPERBILIRUBINEMIA

***Irshad Ahmad, Iqbal Hussain, Sabir Khan, Abdul Hameed**

*Assistant Professor, Department of Child Health
Khyber Teaching Hospital, Peshawar

ABSTRACT

Background: This study was conducted with the objectives to determine the relative frequency and common age of presentation of babies with jaundice due to G6PD deficiency during the 1st two weeks of life. We believe that G6PD deficiency leading to severe hyperbilirubinemia is very common in neonatal period. The jaundice appears early in these babies but somehow they are brought to the hospital very late. By the time they reach the hospital the bilirubinemia reaches to significantly dangerous levels. These are the babies who then need single and double phototherapy and even multiple exchange transfusions, thus increasing the workload and adding to the morbidity and mortality.

Research Methodology: This was a Hospital based descriptive study. The study was conducted at the Department of Pediatrics, Khyber Teaching Hospital Peshawar from March 2005 to August 2005. The data from a total 200 healthy full term babies of age 2 to 14 days with jaundice was collected on a structured pro forma. Their clinical and laboratory profile was documented. The results were analyzed using descriptive statistics and were compared with national and international studies.

Results: In this study, out of total 200 babies with jaundice, 24 (12%) cases were found to be deficient in G6PD enzyme. The sex ratio (M:F) was 7:1 The admission age varied from 2 to 14 days with a mean of 6.29 (±2.69) days. The age of appearance of jaundice varied from 1 to 3.5 days with a mean of 1.85(±0.74) days. The mean delay period was 4.44±2.47 days and the range varied from 0 to 10.5 days. The total serum bilirubin varied from 11 to 30.5 mg% with a mean value of 19.34 (±6.25) mg%. The G6PD discoloration time at the time of admission varied from 60 to 120 minutes with a mean of 92.9 (±23) minutes. All G6PD deficient babies received phototherapy. Eleven babies (46%) developed severe hyperbilirubinemia. Six of them required exchange transfusion. More than one exchange transfusion was performed in three babies. Two (8.3%) babies developed kemicterus.

Conclusion: G6PD deficiency is the second common cause of neonatal jaundice in the first two weeks. Mostly the babies present late leading to severe hyperbilirubinemia requiring phototherapy and exchange transfusion. These are the babies who need early admission to prevent significant hyperbilirubinemia and thus to avoid serious sequelae.

Keywords: Glucose 6 Phosphate Dehydrogenase, Neonatal Jaundice, Hyperbilirubinemia, Phototherapy, Exchange Transfusion.

INTRODUCTION

Worldwide deficiency of G6PD is the most common red cell enzyme defect that causes hemolytic anemia[1]. G6PD deficiency is present in over 400 million people all over the world and is especially prevalent throughout tropical and sub-tropical regions of the world[2]. This X-linked hereditary deficiency was discovered more than 50 years ago as an outgrowth of studies of the unique sensitivity of some persons to the hemolytic action of certain drugs[3]. Diseases which involve this enzyme occur more frequently in males than in females. Italians, Greeks and other Mediterranean, middle Eastern, African and Asian ethnic groups also have a high incidence, ranging from 5 -40% of a variant designated G6PD B^- $G6PD^{Mediterranean}$. In Pakistan, G6PD B-($G6PD^{Mediterranean}$) variant accounts for more than 75% of G6PD deficiency[4].

G6PD enzyme plays an important role in the Pentose pathway of glucose metabolism and its deficiency results in the instability of reduced Glutathione in red blood cells leading to hemolysis. G6PD deficiency is one of the important causes of neonatal hyperbilirubinemia. Because of the hemolytic nature of the jaundice, the hyperbilirubinemia is only indirect and the serum bilirubin level is often high, requiring phototherapy and sometime exchange transfusions[5].

Neonatal jaundice is particularly associated with the Mediterranean and oriental types of G6PD deficiency. The jaundice seldom appears within first 24 hours of life, and more often develops in second day of life. Often there is no exposure to an offending agent. Another group is seen where jaundice develops later. In this group there has often been exposure to naphthalene, aniline dyes or vitamin K analogues[6]. It is

also one of the common etiologic factors for neonatal hyperbilirubinemia in our country. However the data is limited[7]. In Pakistani children G6PD deficiency is the second most common cause of hemolytic anemia (after Thelassemia)[8].

We conducted this study to determine the relative frequency of G6PD deficiency in neonatal jaundice in our hospital. We were also interested to determine the common age of presentation and the age of appearance of jaundice. We were also interested to determine the average delay period in presentation in our babies. We believe that majority of babies with jaundice are brought late to our hospital. This delayed presentation is more serious in cases of G6PD deficiency. These are the babies who present with severe hyperbilirubinemia. They need intense phototherapy and repeated exchange transfusions during hospital stay. Some of them present even with kemicterus. Both repeated exchange transfusions and kemicterus poses significant risk to short term and long term morbidity and mortality to our babies. If we could decrease the mean delay period in presentation in babies with jaundice by public awareness we will be able to reduce morbidity and mortality related to severe hyperbilirubinemia due to G6PD deficiency.

PURPOSE OF THE STUDY

The main objectives of our study were to:

1) To determine the relative frequency and laboratory profile of G6PD deficiency in full term healthy neonates presenting with jaundice in the initial two weeks of life.
2) To determine the mean delay period in days in presentation in babies with Jaundice during 1st two weeks of life.

RESEARCH METHODOLOGY

This study was carried out in Special Care Baby Unit (SCBU) at the Department of child health, Khyber Teaching Hospital, Peshawar from 04-03-2005 to 10-09-2005. It was a descriptive study. Full term, healthy jaundiced babies having postnatal age between 2 to 14 days were included in our study. Babies who were Premature (born before 37 completed weeks of gestation), Low birth weight jaundiced babies (less than 2500 grams), with neonatal sepsis and jaundice, jaundiced babies having congenital anomalies/syndrome, like Down syndrome, cleft lip, neonatal hepatitis syndrome, hypothyroidism were excluded from our study. **Full term babies** were defined as having gestational age between 37 weeks and 42 completed weeks. Gestational age was assessed by standard "New Ballard Score". **Healthy babies** were those having no signs/symptoms of sepsis or had no risk factors for sepsis like prolonged rupture of membranes for more than 18 hours, maternal peripartum fever or infection, resuscitation at birth, multiple gestations, premature and low birth weight. **Age of appearance** was the age at which the mother or any other attendant noticed the jaundice first time at home. **Delay period** was calculated by subtracting age of appearance from the admission age. **Significant hyperbilirubinemia** was defined as serum total bilirubin >16mg% and **Severe hyperbilirubinemia** as serum total bilirubin > 20mg%[9].

Complete history, detailed examination and investigations of every neonate were recorded on prepared proforma including sex, address, age at the time of admission and age of appearance of jaundice. All the babies with jaundice were investigated for serum total bilirubin level and G6PD enzyme estimation time in minutes, using "Sigma Diagnostic G6PD reagent" for the semi-quantitative, visual and calorimetric determination of G6PD deficiency in red cells. The patient was diagnosed as G6PD deficient when the test result was more than 60 minutes. Other investigations life Hemoglobin %, reticulocyte count, baby and mother blood group were also done in all patients.

As this was a descriptive study, frequency, mean, standard deviation and range was calculated for numerical variables using statistical package for social sciences.

RESULTS

During the study period, a total of 750 babies were admitted in SCBU, of whom 200 were admitted for jaundice. Out of the 200 jaundice babies, 24 (12%) were found to be G6PD deficient. Out of these 24 G6PD deficient babies 21 (87.5%) were males while 3 (12.5%) were females. The overall male to female ration was 7: 1. Rests of the cases are shown in figure 1. In a large majority of cases i.e. 125 (62.5%) we could not determine any cause.

The mean age of appearance of jaundice in G6PD deficient babies was 1.85 (±0.74) days, while the range was 1 to 3.5 days. The mean age of admission was 6.29±2.69 days, while the range was 2 to 14 days. The mean delay period in presentation was 4.44 (±2.47) days, while the range was 0 (the baby presented on the day of appearance) to 10.5 days.

The mean values of biochemical parameters are shown in Table 1. All G6PD deficient babies eventually received phototherapy. Out of 24 babies, 16 (66.6%) babies developed severe hyperbilirubinemia (serum bilirubin level more than 20 mg%). Out of these 16 babies with severe hyperbilirubinemia, 4 responded to double phototherapy, while in rest of the 12 cases exchange transfusion was done. Among these 12 babies, 3 required more than one exchange transfusion. Two (8.3%) babies had signs of kemicterus at the time of admission.

Out of 24 G6PD deficient babies, 6 (25%) were having history of neonatal jaundice in other siblings.

5 (20.8%) babies had history of G6PD deficiency in other close family members. There were 3 (12.5%) babies who had history of exchange transfusion and 1 (4.1%) having history of kemicterus in other siblings as well.

DISCUSSION

Neonatal jaundice is one of the most common causes of admission to neonatal care unit all over the world. There are many causes of neonatal jaundice including G6PD deficiency, ABO incompatibility, Rh incompatibility, breast milk jaundice, sepsis, hereditary spherocytosis and undetermined causes[10]. G6PD deficiency is the second most common cause of hyperbilirubinemia and hemolytic anemia in our country[7]. The children who are G6PD deficient may present in the later life with chronic hemolytic anemia or acute hemolytic crisis if they are exposed to certain oxidant drugs or chemicals. To prevent all these complications G6PD status of the person must be known[11]. The presence of concomitant hemolytic disorders like ABO and Rh incompatibility and other risk factors for jaundice may lead to the early development ofkemicterus[12].

The male predominance in this study is exactly similar to that reported nationally and internationally. This observation supports the X-linked recessive mode of inheritance of this enzymopathy. However, the occurrence in females is possible due to being homozygous for G6PD deficiency[10].

The frequency of G6PD deficiency (12%) in this series is almost similar as reported in the past by Imran M et al in 1984[13] and Parveen A et al in 1986[14] (Table No.2). But this figure is relatively higher than reports from international studies by Iranpur et al 2003[15] (7.5%) and Reclose G J et al 2000[16] (5.5%). On the other hand, this frequency is quite lower than the frequency mentioned by Thaitumyanon et al 2002[17] who reported 25.5%. These variations may be due to demographic difference (frequency varies from 1.5% to 51% in different parts of the globe[18]), difference in the genetic make up of societies, sociocultural differences, frequency of carrier individuals, sample size, method used for G6PD enzyme estimation and detection rate.

The age of appearance of jaundice in this study is somewhat earlier in this study than reported nationally and internationally by workers like Imran M et al 1984[13] (Table No. 3). Perveen A et al 1986[14],, Rehman G et al 2004[19], Khan A et al 2002[20]. Rehman H, et al 1995[21], Ding G et al 2001[22] and Kaplan M et al 2001[23]. However in all these studies, it was not clearly mentioned regarding the delay in presentation, so that we could make any comparison.

Severe hyperbilirubinemia is a high risk for development of kernicterus[12] and in this series 2 (8.3%) of G6PD deficient babies presented with kernicterus. The reason was delay in seeking medical advice, though exchange blood transfusion was tried in the hope of reversing the hyperbilirubinemia. Kernicterus due to G6PD Deficiency has also been reported by Khan A et al in 2002[20]. In rest of the cases phototherapy and exchange transfusion were very effective in reducing the serum bilirubin level in preventing kernicterus in all the babies with severe hyperbilirubinemia. Screening is mandatory for the detection of G6PD deficiency in all neonatal jaundice babies to initiate early treatment for jaundice and to prevent chronic hemolytic anemia and acute hemolytic crisis later on by avoiding different oxidant chemicals and drugs.

CONCLUSION

It is concluded that:

1) G6PD deficiency is the second common cause of neonatal jaundice in our hospital.

2) Neonatal jaundice due to G6PD deficiency appears early but the babies present late leading to severe hyperbilirubinemia requiring phototherapy and exchange transfusion.

3) Delay in presentation is at times associated with development of kemicterus.

RECOMMENDATIONS

Public awareness should be created so that the moment the parents notice the jaundice, the baby should be taken to the nearest hospital for in time investigations and management. Early presentation and early management will significantly reduce the work load and will also help in reducing the morbidity and mortality related to severe hyperbilirubinemia due to G6PD deficiency.

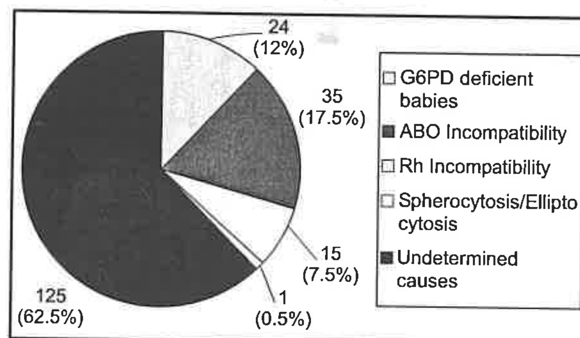

Fig. 1: Spectrum of causes of Neonatal Jaundice
Total cases (n) = 200

Table No. 1: Laboratory Profile

Test (Unit)	Mean (±Standard Deviation)	Range
Hemoglobin (mg%)	16.53 (±4.25)	12-18.5
Reticulocyte count (%)	4.50 (±1.25)	2-8.5
Sernm total Bilirubin (mg%)	19.15 (±6.54)	7.5-30.5
G6PD discoloration time (seconds)	92.92 (±23.07)	60-120

Table No. 2: Comparison of Frequency of G6PD deficiency

Name of author	Frequency of G6PD (%)
IMRAN M et al 1984[13]	12%
PERVEEN A et al 1986[14]	12.1%
REHMAN H et al 1995[21]	8.2%
KHAN A et al 2002[20]	13%
REHMAN G et al 2004[19]	14%
RECLOSE G J et al 2000[16]	5.5%
IRANPOURR et al 2003[15]	7.5%
THAITUMYANON et al 2002[17]	35.5%

Table No. 3: Comparison of age of onset of jaundice in G6PD deficiency neonates

Name of author	Age of onset of Jaundice
Imran M et al 1984[13]	1-7 days (most common 2nd day)
Perveen A et al 1986[14]	1-7 days (most common 2nd day)
Rehman H et al 1995[21]	1-7 days (most common 1st 48 hours)
Kaplan M et al 2001[23]	Immediate perinatal life
Ding G et al 2001[22]	1st 2-3 days
Khan A et al 2002[20]	1-7 days (2nd day)
Rehman G et al 2004[19]	1-7 days (1st 48 hours)

REFERENCES

1. Lane PA, Nuss R, Ambrouso DR, Hematologic disorders. In: Hay WW Jr, Hayward AR, Levin MJ, Sondheimer JM (editors). Current pediatric diagnosis & treatment, 16th Ed. New York: McGraw Hill, 2003: 836-90.
2. Yercuchimovich M, Shapira B, Mimoumi FB, Dollberg S. Neonatal nucleated red blood cells in G6PD deficiency. AmJ Perinatal 2002; 19: 215.
3. Beutler E. The hemolytic effect of Primaquine and related compounds: a review. Blood 1959; 14: 103.
4. Saha N, Ramazan M, Tay JS, Low PS, Bassair JB, Khan FM. Molecular characterization of red cell G6PD deficiency in North-West. Hum Hered 1994; 44(2): 85.
5. Khan A, Khawar N. Neonatal hyperbilirubinemia secondary to erythrocyte glucose 6 phosphate dehydrogenase deficiency. J Postgrad Med Inst 2002; 16: 33-38.
6. Mehta A, Mason PJ, Valliamy TJ. Glucose 6 phosphate dehydrogenase deficiency. Beillieres Best Res Clin Haematol 2000; 13: 121.
7. Rehman G, Shah S, Khan K, Ziaullah, Talaat A. Erythrocyte glucose 6 phosphate dehydrogenase deficiency: a cause of neonatal jaundice. J Postgrad Med Inst 2004; 18: 70-75.
8. Haneef SM, Maqbool S, Arif MA. Blood. Text book of pediatrics, Pakistan pediatric association. 3rd ed. PPA, 2004: 545: 545-588.
9. Joseph R. Mass newborn screenin in Singapore position and projection. Ann Acad Med Singapore. 2003 May; 32 (3): 318-27.
10. WHO working group. Glucose 6 phosphate dehydrogenase deficiency. Bull WHO. 1989, 67: 601-11.
11. Segel GB. Enzymatic defects. In Behrman RE, Kliegman RM, Jenson HB (editors). Nelson Text book of pediatircs. 17th ed. Philadelphia: W. B. Saunders, 2004:1635-38.
12. Hansen T W. Kemicterus: an international perspective. Semin Neonatol. 2002 Apr; 7(2): 103-9.
13. Imran M, Rashid, Akbar A. Neonatal jaundice due to G6PD deficiency. Pak paediatr Jr 1984 VIII (3): 126-8.
14. Parveen A, Azra A, Ahmad K. G6PD status and neonatal hyperbilirubinemia. Pak Paediatr Jr 1986: Vol-x (4): 241-44.
15. Iranpour R, Akbar M R, Haghshenas I. G6PD deficiency in neonates. Indian J Pediatr. 2003 Nov; 70(11): 855-7.

16. Reclose G J, Hatzidakis C J, Sehulpis K H. G6PD deficiency neonatal screening: preliminary evidence that a high percentage of partially deficient female neonates are missed during routine screening. J Med Screen. 2000; 7(1): 46-51.

17. Thaithumyanon P, Visutiratmanee C. Double phototherapy in jaundiced term infants with hemolysis. J Med Assoc Thai. 2002 Nov; 85(11): 1176-81.

18. Ali S, Khan S J. G6PD deficiency in new borns. Pak Ped. J. 1985; IX: 151-63.

19. Rehman G, Shah S, Khan K, Ziaullah, Talaat A. Erythrocyte G6PD deficiency: A cause of neonatal jaundice. JPMI 2004; 18:70-5.

20. Khan A, Khawar N. Neonatal hyperbilirubinemia secondary to erythrocyte G6PD deficiency. JPMI 2002; 16: 33-8.

21. Reman H, Khan M A, Hameed A, Roghani M T, Ahmad A. Erythrocyte G6PD deficiency and neonatal jaundice. JPMA 1995 45: 269.

22. Ding G, Zhang S, Yao D, Na Q, Wang H, Li L et al. An epidemiological survey on neonatal jaundice in China. Chin Med J (Engl). 2001 Apr; 114(4): 344-7.

23. Kaplan M, Algur N, Hammerman C. Onset of jaundice in G6PD deficient neonates. Pediatrics 2001 Oct; 108(4): 956-9.

ORIGINAL ARTICLE

EARLY COMPLICATIONS OF THYROID SURGERY

*Ijaz Ahmad, Abid Haleem Khattak, Nasrullah, Atta Ullah Jan

*Assistant Professor, Surgical 'C' Unit, Department of Surgery,
Khyber Teaching Hospital, Peshawar

ABSTRACT

Background: Thyroidectomy is a common surgical procedure performed by both general surgeons and ENT surgeons. This procedure has got certain specific short term and sometimes life-threatening complications. Some of the complications are life-long. The objective of our study was to find out the frequency of short term morbidity and mortality of thyroid surgery in recent years in our unit.

Research Methodology: The data of 248 patients undergoing thyroid surgery in the past three years in Surgical (D) Unit of Khyber Teaching Hospital was reviewed for complications during their hospital stay.

Results: 248 patients were included in the study, with a male to female ratio of 1:5.2. The mean age of the patients was (39.9 years). Total morbidity was 28.6% with 7.26% of them developing serious complications. The serious complications were reactionary haemorrhage and respiratory distress. 2.01% partial recurrent laryngeal nerve damage. Mortality of thyroid surgery during this period was 0%.

Conclusion: Overall morbidity of thyroid surgery was quite high but serious complications were relatively less. This high morbidity can be reduced by better knowledge of thyroid anatomy and its associated structures, identification of recurrent laryngeal nerve and its dissection, ligation of individual branches of inferior and superior thyroid artery over the capsule and identification and preservation of parathyroids.

Keywords: Operative complications, thyroidectomy, recurrent laryngeal nerve, hypocalcemia.

INTRODUCTION

Thyroid surgery began in early 19th century. Guillaume Dupuytren in Paris performed the first well-documented 'anatomical' total thyroidectomy in 1808. By 1850 14 successful partial or total thyroidectomies were performed across Europe[1]. Theodore Billroth began the era of modern thyroid surgery in Zurich with a 40% mortality initially. By 1877 in Vienna he was able to report thyroidectomy with a mortality of only 5%. Billroth performed conservative subtotal thyroidectomy but still having a significant morbidity with 36% recurrent laryngeal nerve damage[2].

Theodore Kocher is regarded as the father of modem thyroid surgery. By l878 he had, reported; 200 thyroid procedures with a mortality of 4.5%[3].

Over the past several-decades, better awareness regarding thyroid anatomy and function has decreased operative complications of thyroid surgery. The mortality has been reduced to less than 1% and morbidity 13%[4]. The complications of thyroid surgery accounts for about 5% of general surgical claims[3]. Complications are more frequent with more radical surgery, invasive pathologies and large or toxic goiters.

Knowing the detailed anatomy and its variations, the preoperative pathology, preoperative preparation of the patient and meticulous operative technique can however reduce morbidity of thyroid surgery.

Thyroid surgery has got its specific complications that can be divided into short term and long-term complications. The short-term complications include reactionary hemorrhage, respiratory distress, transient hypocalcemia, thyroid crises and transient recurrent laryngeal nerve (RLN) damage. The long-term complications are permanent nerve damage, hypothyroidism, permanent hypoparathyroidism, recurrence and keloid scar formation.

This study was desgined to document relative frequencies of early complications of thyroid surgery observed during the hospital stay of the patients after thyroid surgery.

RESEACH METHODOLOGY

This study was conducted at Surgical (D) unit of Khyber Teaching Hospital Peshawar. The retrospective data of 248 patients who underwent thyroid surgery during Jan 2003 to Dec 2005 was evaluated with main emphasis on complications during hospital stay after surgery.

The patients included in the study had a thyroid swelling due to a sjmple benign multinodular goiter, isolated nodule, toxic adenomas or toxic multinodidar goiter that were controlled with drugs and carcinoma thyroid. All these patients were evaluated for anaesthesia and surgery. All the patients had indirect larryngoscopy done before surgery. Only those patients developing specific complications of thyroid

surgery were included in the study. All those patients unfit otherwise or poor risk patients for anaesthesia were excluded from the study. Those developing complications due to anaesthesia or drugs were excluded from the study.

The surgical procedures performed were subtotal thyroidectomy (leaving behind a gland equal to thumb size), near total thyroidectomy (leaving behind small amount of thyroid tissue with superior vessels and posterior capsule). Lobectomy with asthmesectomy was performed in cases of isolated nodule only.

RESULTS

The study included 248 patients in a period of three years. The year wise distribution according to gender is given in Table 1. The ratio between male and female patients was 1:5.2.

Table 1: Year wise sex distribution

Sex	2003	2004	2005	Total
Male	11	16	13	40 (20.25%)
Female	59	61	88	208 (79.75%)
Total	70	77	101	248

The age of patients ranged from 16 to 65. The age distribution of the patients is given in Table 2. Thyroid pathologies were most frequent between 3rd and 5th decades. The mean age of patients was (39.9 years).

Table 2: Year wise age distribution

Age range	2003	2004	2005	Total
10-19	2	2	3	7
20-29	11	14	12	37
30-39	34	28	28	90
40-49	12	23	47	82
50-59	9	7	7	23
60-69	2	3	4	9
Total	70	77	101	248

The most common disease for which thyroid surgery was performed was simple MNG in 190 (76.65%) patients. Solitary nodule was found in 27(10.92%). Toxic MNG in 15(6.05%). There were 16(6.5%) with carcinoma thyroid. The year wise details are given in Table 3.

Table 3: Year-wise distribution of thyroid pathology

Disease	2003	2004	2005	Total
Simple MNG	50	60	80	190 (76.65%)
Solitary nodule	8	8	11	27 (10.92%)
Toxic MNG	6	4	5	15 (6.05%)
Carcinoma thyroid	6	5	5	16 (6.5%)
Total	70	77	101	248

The commonly performed operation for MNG was subtotal thyroidectomy although the trend in recent years has changed towards near total thyroidectomy. For benign solitary nodules Lobectomy with asthemesectomy was done. In case of malignancy total thyroidectomy was performed. The detailed account of operations performed is given in Table 4. In all the cases a readyvac drain was used deep to the muscles. Truncal ligation of the inferior thyroid artery was done only in 15% cases. In 85% cases the individual branches of inferior thyroid artery were ligated. The recurrent laryngeal was identified but not dissected in 75% of the cases. The superior pole vessels were ligated in bulk close to the gland and not individually isolated. The superior laryngeal nerve was not looked for.

Table 4: Type of operation performed year wise

Type of operation	2003	2004	2005	Total
Subtotal Thyroidectomy	54	43	54	151
Near Total/Total Thyroidectomy	10	30	43	83
Lobectomy With Asthemesectomy	6	4	4	14
Total	70	77	101	248

The commonest complications that followed thyroid surgery within 48 hours were reactionary hemorrhage, respiratory distress, transient hypocalcemia and voice changes. Reactionary hemorrhage occurred in 24 (9.67%) cases. Out of these only 5 cases had a major collection with 3 of them requiring re-exploration. In the rest of them it was just a minor subcutaneous collection requiring needle aspiration only. Transient hypocalcemic tetany occurred in 21(8.4%) cases of total or near total thyroidectomy. All these cases responded to oral or injectable calcium and vitamin D preparations given from 1 week to 6

weeks. Minor voice changes occurred in 12(4.83) cases. 5 of these cases had sluggish movement of the unilateral vocal cord on direct laryngoscopy on recovery from anaesthesia. 13(5.24%) patients developed respiratory problems. Three of them had very huge long-standing goiters they developed severe distress and required tracheostomy. The rest of them responded to conservative treatment. The overall complication rate was 28.6%. The details are given in Table 5.

Table 5: Post operative complications year wise

	2003	2004	2005	Total
Reactionary Hemorrhage	6	8	10	24 (9.67%)
Hypocalcemia	6	7	8	21 (8.4%)
Respiratory Distress	4	4	5	13 (5.24%)
Voice Changes	2	4	6	12 (4.83%)
Total	18	15	29	71

There was no mortality due to specific complications of thyroid surgery during the study period of three years.

DISCUSSION

Enlarged thyroid gland or goiter is endemic in some parts of Pakistan. A high prevalence of 74% has been reported in the northern areas of the country[5]. Most of these cases are referred to one of the three major hospitals of the province at Peshawar, KTH being one of them. Thyroid surgery is a common procedure performed in all of these major hospitals.

Surgical treatment of thyroid has become very much safe in recent years with little morbidity and mortality in most of the series. Detailed anatomic and technical knowledge and experience are essential to perform careful thyroid surgery[6].

Thyroid pathologies are most common in females as shown by a study in Pakistan by Butt et al (77.8%)[7]. In our study it is 79.75% females. Thyroid diseases are most common in 3rd and 4th decades of life. The mean age being (39.9 years). Which is similar to other studies[8,9] 41 to 45 years. The most common disease requiring thyroid surgery was simple MNG in 76.65%. This figure is higher than other studies which is 57.5%[10,6]. The reason for MNG being so common in our study is the endemic goiter in our northern areas. In a study in Hong Kong[11] only 20% had MNG. In a study in Kenya[12] showed a 16% malignancy rate while we had 6.9% cases having malignancy.

All the patients with solitary nodule on ultrasound or thyroid scan or clinical suspicion of malignancy had an FNAC done before surgery. Reports of FNAC correlated with post operative biopsy reports in 94% of the cases which is similar to other studies of 94.9%[8].

All the patients who underwent surgery had an indirect laryngoscopy done to confirm mobility of the vocal folds. Internationally it is a routine preoperative examination for thyroid surgery[13]. Postoperative all the patient had direct laryngoscopy on the table. Sluggish movement of unilateral vocal cord was reported in five cases.

The commonest surgical procedure in our study was subtotal thyroidectomy in (60.88%) cases. The trend in our unit and internationally is changing towards near total and total thyroidectomy[9,2] Near total thyroidectomy was performed in (33.8%) cases. Lobectomy with asthmesectomy was done in (5.32%). This was preferred in solitary benign nodules as is done elsewhere[14,15].

71 out of 248 patients' developed postoperative complications. Out of 71 patients only 18 (7.26%) had relatively serious complications. The rest of them had minor self-limiting and easily manageable complications. The patients operated upon by junior consultants had relatively more complications as compared to the once operated upon by senior consultants.

The frequency of heamatoma was (9.67%) in our study; most of these were superficial haematomas or seromas.5 (2.01%) of our patients had major collection and 3 of them requiring re-exploration. In other study a lower incidence had been reported by Adam D Rubin et al[16] 0.3% and Batacharya et al 1%[11]. An incidence of 5% was reported in a study in Pakistan[9]. The reason for higher incidence in our study being; not ligating the inferior thyroid and the superior pole in bulk and not isolating the superior pole vessels.

Voice changes were noted in 12(4.83%) cases. Hoarseness can be due to recurrent laryngeal nerve (RLN) or superior laryngeal nerve damage. 5(2.01%) of our patients had sluggish movement of unilateral vocal fold on direct laryngoscopy on the table. In the rest of them voice changes were noted on the first postoperative day, the cause being superior laryngeal nerve damage probably. In the literature frequency of RLN damage is reported from 0 to 9.52%[11,12,17,18,19]. Deliberate identification and dissection of the RLN can decrease the incidence of nerve damage[19,20]. Intra-operative stimulation of the RLN with a nerve stimulating device can minimize the risk of nerve damage to 0%[21]. Conversely when the nerve is not clearly identified the reported injury rate is 4 to 6.6%[22].

Temporary hypocalcemia indicated by tingling sensations around the lips and in the hand or full fledge tetani was noted in 8.46% cases. A low serum calcium

level on investigation confirmed it. The rate of temporary hypocalcemia is reported from 2 to 53%[23]. In another study by Eitizaz[24] out of 72 patients 30% developed transient hypocalcemia. Avoiding truncal ligation of inferior thyroid artery thus avoiding devascularisation of parathyroid glands can minimize this complication.

A serious and life threatening complication is post operative respiratory distress which occurs as a result of large heamatoma behind the muscles compressing the airway[25] as occurred in 3 cases in our study. It can also occur due to tracheal collapse from chodromalasia of long-standing huge goiters[25] as occurred in three of our cases who required tracheostomy. Laryngeal edema is another common cause of respiratory distress, which is due to the very lax mucosa of the relatively narrow sub-glottic area of the larynx, injudicious use of cautry and un-necessary dissection near the larynx[6].

Most of our patients stayed in the hospital for 2 days post operatively. The stitches and the drain were removed with in 48 hours. In only 10% cases hospital stay was more than 48 hours. In another study also the mean hospital stay was 2.5 days[11].

There was no mortality in our study. In most of the published studies recently the mortality rate of thyroid surgery is less than 1%[23].

CONCLUSION

Thyroid surgery has become very safe with little risk of mortality and long-term complications in the recent years. For safe surgery better understanding of anatomy of the thyroid gland itself and its associated structures is of paramount importance. The course and the relationship of RLN in the neck with surrounding structures is not constant. For preservation of the nerve identification of its whole in the neck is a fundamental step in thyroid surgery. Capsular dissection, ligation of individual branches of inferior thyroid artery and isolation of the superior thyroid vessels and then ligation results in lower complication rate. If facility of nerve stimulator is available the nerve can be minimized to 0%. Identification of parathyroids and there re-implantation can reduce permanent hypoparathyroidism in cases of total thyroidectomy.

REFERENCES

1. Welboum RB. The Thyroid. The history of endocrine surgery. New York: Praeger.1990; 19-8.
2. Delbridge L. Total thyroidectomy: The evaluation of surgical technique. ANZ. J. Surg 2003; 73. 761-768
3. Kaplan EL. Thyroid and the parathyroid. In: Schwartz SI, Slives GT, Spencer FC, Storer EH, Editors. Principles of Surgery. 4th ed. Singapore; McGraw-Hill, 1986; 1545-1557.
4. Gimm O, Brauckhoff M, ThanhPN, Sekulla C, Dralle H. An update on thyroid surgery. Eur-J-Nucl-Med-Mol- Imaging. 2002 Aug; 29 Suppl 2: 447-52.
5. Malik AZ, Latif S, Anwar I, Syed R, Alvi I. Giant Multinodular Goiters: surgical experience in northern Pakistan. Pak-J-Surg (Int). 1999 Sep; 27(3): 225-9.
6. Collin, Thomas Jr. Nodular goiter and benign and malignant neoplasms of the thyroid. In: Christopher D, editor. Textbook of surgery. 12th ed. London: Sanders WB, 1998: 690-712.
7. Sippel RS, Gauger PG, Agelos P, Thompson NW, Mack E, Chen H. palliative thyroidectomy for malignant lymphoma of the thyroid. Ann-Surg-Oncol. 2002 Nov; 9(9): 907-11.
8. Folk SA. The management of hyperthyroidism. Clin-Otolaryngol- North-Am. June; 23(3): 361-377.
9. Shaik SA. Thyroidectomy. A new approach. JCPSP. 2002; 12(8): 1757-9.
10. Spinelli C, Bertochini A, Lima M, Miccoli P. Grave-Basedau's disease in children and adolescents: Total vs Subtotal Thyroidectomy. Pediatr-Med-Chir. 2002 Sep-Oct; 24(5): 383-6.
11. Bhattacharyya N, Fried MP. Assessment of the morbidity and complications of total thyroidectomy. Arch Otolaryngol Head Neck Surg. 2002; 128: 389-392.
12. Chow TL, Chi TW, Lim BH, Kwok SPY. Outcomes and complications of thyroid surgery: retrospective study. HKMJ. 2001; 7: 261-5.
13. Hawasli A, Rizzo P, Khoury H, Mc Caffrey JL. Can fine needle aspiration biopsy of thyroid nodule help in determining the extent of surgery in follicular and Hurthle cell neoplasm at a community teaching institution? Am-Surg. 2002,Oct; 68(10): 907-10.
14. Delbridge L. Solitary thyroid nodule: current management. ANZ J Surg. 2006 May; 76(5): 381-6.
15. Yeh MW, Siddhu SB, Sywk M, Edhouse P,Delbridge LW. Complition thyroidectomy for malignancy after initial minima access thyroid surgery. ANZ J Surg. 2006 May; 76(5); 332-4.
16. Rubin AD, Pramod KS. Complications of thyroid surgery. Head and Neck Oncology. 2003 Dec;74(3) 230-35.
17. Iqbal J, Zubair M. Anatomical considerations regarding recurrent laryngeal nerve in relation with thyroid surgery. JCPSP. 2002; 8(6): 276-7.
18. Sajid MA, Maqbool M, Anwar M, Muhammad Y, Chaudhry AM. Anatomical variations of recurrent laryngeal nerve as seen in thyroid surgery. Annals KE. 2002 Jan-Mar; 6(1): 14-15.
19. Arif M, Ahmad I, Recurrent laryngeal nerve palsy during thyroidectomies. Pak J Surg(Int). 2001, Jul-Sept; 6(3): 12-14.
20. Hisham AN, Lukman MR. Recurrent laryngeal nerve in thyroid surgery: a critical appraisal. ANZ-J-Surg. 2002, Dec; 72(12): 887-9.

21. Tomoda C, Hirokawa Y. Urunno T. Sensitivity and Specificity of Intraoperative Recurrent Laryngeal Nerve Stimulation Test for Predicting Vocal Cord Palsy after Thyroid Surgery. World J Surg. 2006 Jun 13; 24(10) 415-20.

22. Marcus B, Edwards B, Yoo S, Byme A et al. Recurrent laryngial nerve in thyroid and parathyroid surgery the university of Michigan experience. Laryngoscope. 2003, Feb; 113(2): 356-61.

23. Thomusch O, Macheus A, Sekulla C,Ukkat J, Braukhoff M, Dralle H. The impact of surgical technique on post operative hypo-parathyroidism in bilateral thyroid surgery: a multivariate analysis of 5846 consecutive patients. Surgery. 2003, Feb; 133(2): 180-5.

24. Bashir EA, Khan FA, Javed M. Ligation of inferior thyroid arteries in subtotal thyroidectomy and postoperative parathyroid function. JCPSP. 1999; 8(1): 17-19.

25. Wade JSH. Respiratory obstruction in thyroid surgery. Ann RC Surgeons of England. 1980; 62: 15-35.

ORIGINAL ARTICLE

AGE, SEX AND REGIONAL DISTRIBUTION OF OBESE ISCHEMIC HEART DISEASE IN TERTIARY CARE HOSPITALS OF PESHAWAR

***Muhammad Fazal Zeeshan, Usman Ahmad Raza, Ghulam Sarwar**

*General Medical Practitioner, Peshawar

ABSTRACT

Background: Ischemic Heart Disease is the commonest disorder of heartland a major case of death. Obesity is one of the recognized, modifiable risk factors for ischemic heart disease. The current study aims to determine the distribution of obesity in known ischemic heart disease patients with regard to age, sex and region. There have been very few studies of this kind in N.W.F.P.

Research Methodology: It was an observational, cross-sectional study. Systematic random sampling was employed. Physical observations including height and weight were made by calibrated instruments and Body Mass Index (BMI) was calculated and used as an index of obesity.

Results: 61% (122/200) patients with IHD were found to be obese. The frequency of obesity was 100% in IHD patients aged <20 years and 84% in those aged >60 years. In females with IHD, 81.08% were obese while in males 49.21% were obese. Of the IHD patients of urban origin, 62.71% were obese while those of rural origin 60.28% were obese.

Conclusions: Obesity in association with IHD was found in high frequency at extremes of ages and in females while there was little difference amongst the rural and urban population.

Keywords: Ischemic heart disease, obesity, body mass index.

INTRODUCTION

Ischemic heart disease (coronary heart disease) is the commonest form of heart disease and the single most important cause of early deaths in developed world. With the highest incidence in South Asia, heart diseases claim 17 million lives world-wide annually[1]. While the disease is mostly due to formation of an atheroma and its complications, particularly thrombosis, the factors that lead to atheromas are the real culprits that need to be addressed[2]. Fixed risk factors include age, male sex, family history and modifiable ones are smoking, hypertension, lipid disorders, diabetes mellitus, sedentary lifestyle, poly-unsaturated fatty acids deficiencies and obesity[3]. Risk multiplies in presence of more than one risk factor[4].

Obesity being a common and familiar risk factor is frequently overlooked and therefore becomes a more serious contributor. It is an independent risk factor and is not only responsible for ischemic heart disease but is also with diabetes mellitus, hyperlipidemia, hypertension etc. The World Health Report 2002 states that approximately 58% of diabetes mellitus globally, 21% of ischemic heart disease and 8-42% of certain cancers were attributable to BMI above 21 kg/m^2.

Obesity is a common nutritional disorder and may be defined as a condition in which there is excessive amount of body fat[1]. Generally it follows long term caloric intake in excess of what is required for the maintenance of body functions[5]. A number of factors are also associated with its development, which include age, family history, lipid disorders, sedentary lifestyle, lack of exercise, drugs, endocrine disorders and dietary factors like excess fat intake. Interestingly, some of the key factors like family history, sedentary lifestyle, lack of exercise, lipid disorders and dietary factors that lead to obesity are also the risk factors causing ischemic heart disease[1].

The current study aims to determine the age, sex and regional (urban/rural) distribution of obese IHD patients visiting tertiary care hospitals of Peshawar (Pakistan) in an effort to identify important areas of concern in the context of N.W.F. Province. The results may be used to target healthcare measures towards identified risk groups in order to maximize the efficient use of limited resources.

RESEARCH METHODOLOGY

The basic design of this survey based study was descriptive in nature. A questionnaire was developed with the consultation of two renowned cardiologists. The group members were instructed in detail regarding the method of questioning and obtaining consent. They were also made to acquire reasonable skill at

use of weight machine, skin fold calipers, and other related equipment. The study was then conducted as an Interviewed Questionnaire by group members after a trial for language and comprehension in Khyber Teaching Hospital.

To ensure inclusion of patients from various backgrounds and with diverse variables, four largest tertiary care hospitals of Peshawar were selected, namely, Khyber Teaching Hospital (KTH), Lady Reading Hospital (LRH), Hayatabad Medical Complex (HMC) and Rehman Medical Institute (RMI). The selection criteria for patients included in the study was defined as all those cases who had been already diagnosed (on basis of symptoms, ECG and angiography) as suffering from Ischemic Heart Disease by the relevant hospital physician and also cases who were waiting for (or undergone) coronary artery bypass or some other form of treatment for the disease. Patients who only had symptoms but without confirmed diagnosis were excluded from the study. Systematic Random Sampling was used to select cases in each ward of each hospital included in the study, every second patient being interviewed. The teams visited the four hospitals every 3rd day waiting for arrival of fresh cases. The final sample size obtained was 200 patients, after excluding 20 incomplete questionnaires (90.91% response rate). The study was conducted from 15th June 2004 to 15th August 2004.

Interview questionnaires were coded and entered into Microsoft Excel and frequency of obese patients (defined as BMI>23 for Asian countries) with IHD was computed in regard to the variables selected for study.

All the 200 patients were weighed with a weighing machine and their Body Mass Indices calculated according to the formula: BMI = Weight in kg / Height in meters squared. The cut off limit for normal BMI was the recommended[6,7] standard for Asians i.e. 23 kg/m . Mildly obese were classified as having BMI 23-25 kg/m^2 and moderately obese as having BMI 25-30 kg/m^2, while severe obese were defined as having BMI >30 kg/m^2.

RESULTS

Our sample included 126 (63%) male and 74 (37%) female patients. Of the 200 cases, 3 (1.5%) were below age 20 years, 28 (9.3%) were in 20-40 years age group, 105 (52.5%) were in 40-60 years age group, while 64 (32%) were above 60 years of age. 195 (97.5%) of the patients were married. The sample was largely of rural origin with 141 (70.5%) patients of rural origin and 59 (29.5%) or urban origin. Majority of the subjects, 120 (60%) were illiterate. 35 (17.5%) had primary education, 23 (11.5%) had secondary education, 3 (1.5%) had higher secondary education and 19 (9.5%) were graduates.

In our study, 122 (61%) subjects were obese, 73 (36.5%) had a normal BMI, while 5 (2.5%) were underweight. Of the obese subjects, 37 (30.3%) were mildly obese, 45 (36.9%) were moderately obese and 40 (32.8%) were severe obese.

The overall and hospital-wise frequency distribution of obese IHD patients into various BMI categories is shown in Table 1.

The sample was divided into four age groups (<20, 20-39, 40-59, >60). The age distribution of obese IHD cases is shown in Table 2 in each BMI category as well as the total obese cases.

Of the 200 cases of IHD studied, 62 (49.21%) of the male and 60 (81.08%) of the females were found to be obese. The frequency of obesity in male and female according to individual BMI categories is shown in Table 3.

The distribution of obese IHD cases in subjects of urban and rural origin based on individual BMI categories as well as overall distribution is shown in Table 4.

Table 1: Distribution of Obese IHD cases in hospitals

Obese Cases with IHD				
Hospital	**Mild**	**Moderate**	**Severe**	**Total**
LRH	21/80 (26.25%)	32/80 (40%)	27/80 (33.75%)	80/98 (81%)
KTH	5/11 (45.45%)	3/11 (27.27%)	3/11 (27.27%)	11/35 (31.43%)
RMI	10/28 (35.71%)	8/28 (28.57%	10/28 (35.71%)	28/38 (73.68%)
HMC	1/3 (33.33%)	2/3 (66.67%)	0/3	3/29 (10.34%)
Total	37/122 (30.33%)	45/122 (36.88%)	40/122 (32.79%)	

Table 2: Age distribution of Obese IHD cases

	Obese Cases with IHD *n (%)*			
Age group (years)	**Mild**	**Moderate**	**Severe**	**Total**
<20	0/3	1/3 (33.33%)	2/3 (66.67%)	3/3 (100%)
20-39	4/20 (20%)	4/20 (20%)	12/20 (60%)	20/28 (71.43%)
40-59	12/45 (26.67%)	18/45 (40%)	15/45 (33.33%)	45/105 (42.86%)
>60	21/54 (38.89%)	22/54 (40.74%)	11/54 (20.37%)	54/64 (84.38%)

Table 3: Sex distribution of Obese IHD cases

	Obese Cases with IHD *n (%)*			
Sex	**Mild**	**Moderate**	**Severe**	**Total**
Male	21/62 (33.87%)	24/62 (38.71%)	17/62 (27.42%)	62/126 (49.21%)
Female	16/60 (26.67%)	21/60 (35%)	23/60 (38.33%)	60/74 (81.08%)

Table 4: Regional (Rural/Urban) distribution of Obese IHD cases

	Obese Cases with IHD *n (%)*			
Region	**Mild**	**Moderate**	**Severe**	**Total**
Urban	13/37 (35.14%)	12/37 (32.43%)	12/37 (32.43%)	37/59 (62.71%)
Rural	24/85 (28.24%)	33/85 (38.82%)	28/85 (32.94%)	85/141 (60.28%)

DISCUSSION

The most obvious result shown by this study is a high frequency (61%) of obesity in patients with IHD. This is a reconfirmation of the large number of studies conducted world-wide as mentioned earlier in the introduction. Study has shown that risk of IHD is greater at a higher BMI but is not significantly greater at a BMI of 23-29.9.[8] However, a migrant study has shown that mortality from IHD in South Asian people is higher than in Europeans with the same BMI.[9] Thus we cannot discard the mild and moderate obese classes of patients from the high risk group.

Concerning the distribution of obese IHD cases in various hospitals, Lady Reading Hospital was found to be catering for majority of the patients and therefore any specific healthcare programme for IHD must be commenced in this hospital for most efficient results.

Age distribution in this study shows obese IHD patients distributed at the extremes of ages with a dip in the middle age population. Interestingly, severe obesity with IHD was seen more commonly in younger age group but with a small sample size, and mild obesity with IHD was more prevalent in older age group. This may perhaps be an effect of high mortality associated with severe obesity. Similar results have been obtained in some other studies. One analysis of Framingham Heart Study showed that the association of obesity with IHD is stronger in men and women below 50 years of age.[10] In another study, higher BMI at a younger age was associated with an increased risk of IHD mortality, whereas this did not apply in older ages.[11] This clearly signifies obesity as a high risk factor in younger age groups.

Our study shows a high frequency of obesity in female IHD patients as compared to male (81% versus 49%) and more so in the severely obese. However the sample size of female patients was much smaller and therefore it cannot be said with certainty whether this result is truly significant. Further research is therefore needed in this area to answer the question. It might be worthwhile to quote a 44 year follow-up of Framingham Heart Study showing that milder grades of obesity in females are not significantly associated with IHD risk.[12]

Another interesting outcome of the present study is the almost equal frequency of obese IHD patients with rural and urban back grounds. This is more true for the severely obese group. There is large amount of data available on effects of socio-economic factors

on obesity, showing a positive relation in the developing countries and a negative one in the developed countries. The current study is limited in that it assesses only the rural and urban status rather than complete socio-economic details, which requires a dedicated study in itself. However, it indicates the importance of promoting weight reduction programmes in rural areas as equally as the urban areas.

The current study has underlined some important similarities and differences with currently available data regarding IHD in obese patients. However, the study has the typical limitations of any cross-sectional study including lack of data on duration of IHD and such other time-related factors, as well as the small sample size available. Nevertheless it does highlight some key areas where further research needs to be conducted for a comprehensive analysis of the situation.

REFERENCES

1. WHO. Reducing Risks, Promoting Healthy Life, Overview. World Health Report. 2002; p. 7-10.
2. Cotran RS, Kumar V, Robbin SL. Ischemic Heart Disease, The Heart. In: Pathological Basis of Disease: 6th ed. WB Saunders Company; 1997. p. 311.
3. Summerton C, Shetty P, Sandle LN, Watt S. Nutritional and Metabolic Disorders. In: Haslett C, Chilvers ER, Boon NA, Colledge NR, Hunter JAA. Davidson's Principles and Practice of Medicine: 19th ed. Churchill Livingstone; 2002. p. 301-306
4. Park K, Epidemiology of Chronic Non-communicable Diseases and Condition. In: Park's Textbook of Preventive and Social Medicine: 21st ed. M/S Banarsidas Bhanot Publishers; 2001.p.273.
5. Chandrasoma P, Taylor CR. Abrnormalities of blood vessels. In: Concise Pathology: 3rd ed. Appleton & Lange; 1998. p. 148.
6. WHO expert consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. The Lancet, 2004; 157-163.
7. Chamukuttan S, Vijay V, Ambady R. Cutoff Values for Normal Anthropometric Variables in Asian Indian Adults. Diabetes Care 2003; 26: 1380-1384.
8. Shaper, AG. Epidemiology of Ischemic Heart Disease. Medicine International 1997; 40(2): 38-43.
9. Paul M. McKeigue. Metabolic consequences of obesity and body fat pattern: lessons from migrant studies. The Ciba Foundation; 1997.
10. Hubert H, Feinleib M, McNamara P et al. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation. 1983; 67(5): 968-77.
11. Singh P, Lindsted K. Body mass and 26-year risk of mortality from specific diseases among women who never smoked. Epidemiology. 1998; 9: 246-54.
12. Wilson P, D'Agnostino R, Sullivan L et al. Overweight and obesity as determinants of cardiovascular risk. The Framingham experience. Archives of Internal Medicine 2002; 162:1867-72.

ORIGINAL ARTICLE

FREQUENCY OF THE SYMPTOMS WITH COLONOSCOPIC EXTENT OF ULCERATIVE COLITIS

***Abbas Khan, Ijaz Muhammad Khan, Muhammad Ali Khan, Aamir Ghafoor Khan**

*Senior Registrar, Department of Gastroenterology, Hayatabad Medical Complex, Peshawar
E-mail: drabkhattak@yahoo.com

ABSTRACT

Background: Ulcerative colitis is a non specific inflammation of the colonic mucosa which usually presents with diarrhea with or without mucus and bleeding per rectum. The inflammatory process involves a part or whole of the colon. We decided to see the correlation between the clinical presentation and colonoscopic extent of ulcerative colitis.

Research Methodology: This study was carried out in Gastroenterology department PGMI/ Hayatabad Medical Complex Peshawar from 1st July 2002 until 30th June 2005. Colonoscopy was performed (after pre colonoscopic preparation) in 200 patients who presented with clinical features of ulcerative colitis. The disease was graded as mild, moderate, or severe on the bases of True love & Witt criteria and the colonoscopic extent was graded as distal colitis, left sided, and total colitis.

Results: The colonoscopic extent of the disease was total colitis in 96 patients (48%), left sided colitis in 80 patients (40%) and distal colitis in 24 patients (12%). The ulcerative colitis was of mild severity in 56 patients (28%), moderately severe in 84 patients (42%) and severe in 60 patients (30%). The majority of patients were male with a mean age of 33.28 years.

Conclusion: There was no correlation between the clinical features and colonoscopic extent in this study. Therefore total colonoscopy should be performed in all patients with ulcerative colitis to determine the extent of the disease.

INTRODUCTION

Ulcerative colitis is a non-specific inflammatory condition of the large intestine of the alimentary tract. It involves the mucosal surface of the colon resulting in diffuse friability, erosions, inflammation and ulceration with bleeding[1,2,3]. The disease almost always involves the rectum and may also involve part or the entire colon as well as terminal ileum (backwash ileitis)[4]. The symptoms of ulcerative colitis occur in any age group and the peak age incidence is between 20 and 40 years[1,5]. The sex distribution is about equal[1,5]. The clinical manifestation of ulcerative colitis may be intestinal and extra intestinal. The common presenting symptoms of ulcerative colitis are diarrhoea with mucous and blood. Some times there is lower abdominal pain and tenesmus during defecation. Exacerbation and remission of the symptoms is usual characteristic of the disease[1'5'6]. Some patients have minimal or no constitutional symptoms and only present with chronic diarrhoea. Therefore colonoscopy and biopsy is useful and essential for the diagnosis of ulcerative colitis[7].

Ulcerative colitis in NWFP is not uncommon, however because of lack of awareness on the part of patients and doctors and inadequate facilities, diagnosis of ulcerative colitis is considerably delayed. Another reason is that Amoebic and bacillary dysentery is also a common problem in our community and the clinical presentation is like ulcerative colitis and there are no clinical tools to differentiate between these two and Ulcerative colitis[8-10]. Therefore referral to tertiary care level center is delayed. It is usually considered a problem of developed countries, however; latest reports suggest that the incidence of ulcerative colitis may be equal or slightly higher in the developing world. The rising trend in incidence in the developing world could very well be attributed to some extent, to the increasing awareness on the part of the doctors and better diagnostic facilities at tertiary care level hospital[8-12].

Therefore we carried out this study to determine the correlation of clinical features with colonoscopic extent of ulcerative colitis.

RESEARCH METHODOLOGY

This study was completed in Gastroenterology Department at Postgraduate Medical Institute, Hayatabad Medical Complex Peshawar. 200 patients with Ulcerative colitis were enrolled from 1st July 2002 to 30th June 2005. All these 200 patients were new cases. Informed consents from all patients (200 cases) were taken.

Inclusion criteria:

The patients of adult age group (16 years to 60 years) both male and female presenting with features suggestive of ulcerative colitis for more than 03 weeks duration were included in the study.

Exclusion Criteria:

Patients with infectious diarrhea on the basis of stool microscopy and culture, patients with Irritable Bowel Syndrome, on the basis of clinical features and patients with age <16 and >60 years were excluded from the study.

The necessary lab investigations were done and all patients were classified into mild, moderate and severe on the basis of True love and Witt criteria, which is as follows.

	Mild	Moderate	Severe
1. Stool Frequency/day	< 4	4-6	> 6 mostly bloody
2. Pulse (beat/ minute)	< 90	90-100	>100
3. Temperature F°	Normal	90-100	>100
4. Haematocrit %	Normal	30-40	< 30
5. Weight loss %	Normal	1-10	> 10
6. ESR	<20	20-30	>30
7. Albumin gm/dL	Normal	3-3.5	<3

A detailed history of the clinical presentation and duration of disease was taken. The patients were examined for signs of disease and also for the extra intestinal manifestations of the disease.

The following investigations were done in the Pathology Department PGMI/HMC.

i) Blood Complete, Hb%, TLC, DLC, Platelet, ESR.

ii) Stool naked eye examination, Stool Routine Examination (Microscopy and Culture).

iii) Blood Urea, creatinine, and serum Electrolytes.

(iv) LFTs (bilirubin, Alanine Ammo Transferase, Alkaline Phosphatase.

(v) Total Lower protein and A/G (Albumin / Globulin) ratio.

(vi) Blood Group.

(vii) GI endoscopy (colonoscopy).

During the procedure multiple biopsies from different sites were taken to confirm the histological diagnosis of ulcerative colitis. All the biopsies were reported from Shifa International Hospital Islamabad.

The colonic extent of disease involvement on the basis of colonmoscopic findings was recorded as follow:

Distal colitis: (Proctosigmoiditis)

When the colonic involvement of the disease was limited to rectum, sigmoid and junction of descending colon and sigmoid.

Total colitis: When the disease involved the whole colon or proximal to hepatic flexure.

Left sided colitis: When the involvement of colon in ulcerative colitis was from rectum to splenic flexure or was intermediate between the above two (distal and total colitis).

RESULTS

Data of the 200 collected cases of ulcerative colitis was analyzed for clinical features and colonoscopic extent of the disease. The most common presenting features are shown in Table 1.

Out of 200 patients 60 patients (30%) had severe ulcerative colitis. Among these 60 patients 8 patients (13.33%) had total colitis, 40 patients (66.6%) had left sided colitis and 12 patients (20%) had distal colitis.

84 patients (42%) had moderate disease on True love and Witt criteria. Among these 84 patients 48 patients (57.14%) were having total colitis. 28 patients (33.33%) had left sided colitis and 8 patients (9.52%) had distal colitis. The rest 56 (28%) patients were having mild disease. Among these 4 patient (7.14%) had distal disease, 12 patients (21.43%) were with left sided colitis and 40 patients (71.42%) had total colitis. Extra Extra colonic manifestations are shown in Table 2.

Laboratory investigations were also done and the disease was classified into mild, moderate and severe on the basis of True love & Witt criteria which is shown in Table 3.

The major bulk of the patients were from the various districts of NWFP. The larger number 56 patients (28%) were from Peshawar district and only 16 patients (8%) were Afghan Refugees.

Out of 200 patients total colitis was noted in 96 patients (48%). Majority were female. Left sided colitis was seen in 80 patients (40%) and distal colitis in 24 patients (12%) Table No. 4.

Table No. 1: Clinical Features of patients with Ulcerative Colitis

	No. of Pts.	%age
Bloody diarrhoea with mucous	172	86%
Diarrhoea with/ without mucous	20	10%
Bleeding per rectum only	8	4%
Fever	132	66%
Abdominal pain (cramps)	156	78%
Weight loss	60	30%
Vomiting	20	10%
Nausea anorexia	68	34%

Table No. 2: Extra Intestinal Manifestation in patients with Ulcerative Colitis

	No. of Pts.	%age
Clubbing	4	2%
Sacroileitis	8	4%
Fatty Liver	4	2%

Table No. 3: Clinical Grading of Ulcerative Colitis (True love and Witt criteria)

	No. of Pts.	%age
Mild	56	28%
Moderate	84	42%
Severe	60	30%

Table No. 4: Colonoscopic Extent of Ulcerative Colitis

Extent	No. of Pts.	%age
Total colitis	96	48%
Left sided colitis	80	40%
Distal colitis	24	12%

DISCUSSION

In this study of 200 patients with ulcerative colitis, the majority of patients were male, which is in contrast to the Western Literature in which the sex distribution is about equal[2,13,14,15,16,32]. The reason being reluctance on the part of female patients to present theirselves for colonoscopy. It was also noted that the majority of patients having total colitis were female. The reason may be due to delay in consulting a doctor and colonoscopic procedure. Most of the patients were between 20 and 40 years of age, which correspond to the International Literature[33]. Majority of the patients were from urban area and were non-smokers. The results are similar to International studies[2,13,14,15,16,32].

Extra colonic manifestations were few. Only four patients had clubbing eight patients had sacroileitis and only four patient were noted to have fatty liver, which may be due to malnutrition. These findings were in contrast to the Western Literature where the extracolonic manifestations are more commonly prevalent[1,2,13-16,19,34]. Pseudo polyps were noted in twenty patients. No other complications of ulcerative colitis were noted in this study. It has been stated that the disease is often less complicated by intestinal and extraintestinal manifestations in developing countries[8,9,11,17,18,20-24,34].

In ulcerative colitis, distinguishing distal disease from proximal disease, or left sided disease by symptoms alone is unreliable[25]. In evaluating the ulcerative colitis activity and extent, the significance of clinical features varies with the anatomical extent of the disease[26]. Therefore it has been suggested that the anatomical involvement in ulcerative colitis should be considered when assessing the clinical features and severity of the disease[27].

Previous studies have been done for the correlation of clinical presentation and degree of colonoscopic findings without grouping the patients into the extent of colonoscopic involvement[28,29].

There was no correlation between the clinical presentation and extent of ulcerative colitis in this study. Among patients with severe disease on clinical parameters about 21% had only distal colitis while in patients with clinically mild disease majority (around 71%) had total colitis. These finding are in marked contrast to Western Literature[29-31]. Both H., et al report that the symptoms complex tend to differ according to the extent of disease but in general the severity of symptoms correlates with the severity of disease[35].

In our patients with ulcerative colitis there was a discrepancy between the clinical presentation and anatomic extent of ulcerative colitis. However Hameed K. et al report correlation between clinical features and anatomic extent in ulcerative colitis similar to our result.[9,12]. In this study a $P<0.02$ was observed which was significant.

The discrepancy, in the clinical features and extent of the disease may be due to possible differences in the aetiology of the disease in the west and east especially the diet. As our diet contain more vegetables and is rich in fibers as compared to the west. The laxative effects of fiber rich diet decreases the transit time of the gut and help in expulsion of the toxins from the gastrointestinal tract. Furthermore protozoal and bacterial infections of gut are more common in our setup, which may contribute to an immunoprotective effect against the disease. Snuff addiction is more common in our society and may have a protective effect[9,12].

CONCLUSION

There was a poor correlation between the clinical features and colonoscopic extent in this study. In majority of patient's with mild ulcerative colitis total colitis was noted. A significant number of patients with severe symptoms were having only distal colitis. The present study also suggests that clinical features alone are not reliable markers and colonoscopy should be performed in all patients with ulcerative colitis to determine the extent of disease.

REFERENCES

1. Jewell DP. Ulcerative colitis. In: Sleisenger and Fordtran's Gastrointestinal and liver disease. 6th ed. Philadelphia: WB Saunders. 1998: 17-35-61.

2. Me Quaic KR. Alimentary tract (inflammatory bowel disease). Tierney Jr, Lawrence M, McPher Stephen J, Papadela MA, and editor; In: Current medical diagnosis and treatment. 41st ed. Philadelphia: McGraw Hill; 2002: 653-7.

3. Howerth GF, Robinson MHE, Jenkins JD, Longan RFA. High prevalence of undetected ulcerative colitis: data from Nottingham faecal occult blood screening trial. Am J Gastroenterol 2002; 97 (3); 690-4.

4. Heuschen UA, Hinz U, Allemeyer EH, Stern J, Lucas M, Autschbach F, et al. Backwash ileitis is strongly associated with colorectal carcinoma in ulcerative colitis. Gastroenterology 2001; 120: 841-7.

5. Simon T. Ulcerative colitis. Med int. 1998; 12 (44): 81-6.

6. Sheavman DJC. Disease of the alimentary tract and pancreas. In: Christopher RWE, Bouchioc IANA D, Edwin C, editors, Principles and practice of medicine. 17th ed. Baltimore: Churchill Livingstone. 1995: 456-64.

7. Shah RJ, Fenoglio-Preiser C, Bleau B.L, Gainnella RA. Usefulness of colonoscopy with biopsy in the evaluation of patients with chronic diarrhoea. Am J Clin Gastroenterol 2001; 96: 1091-5.

8. Shafi MS - Ulcerative Colitis A Northern Pakistan experience Pak J Gastroenterol 1992:6 12-15.

9. Hamid K, Khan IU. Spectrum of Ulcerative Colitis in North West Frontier Province of Pakistan. J Coll Phy Surg Pak 2002; 8: 458-460.

10. Provenzale D, Onken J. Surveillance issues in IBD.- UC. Clin Gastroenterol 2001; 32: 99-105.

11. Iman NU, Burkee GJ. Cyclosporin in inflammatory bowel disease. J Med Sci 1999; 9 (I): 41-3.

12. Hameed K, Khan IU, Farooqi JI, Shah S. Correlation of endoscopic extent and severity with the clinical presentation of ulcerative colitis. J Coll Phy Surg Pak. 2001; 11: 551-3.

13. Waye JD, William CB, Colonoscopy & flexible sigmoidoscopy chap 122. 3rd edition. Text Book of Gastroenterology volume II Publisher Lippon Cott, Williams & Wilkins A. Walter Klieuwer Company; 1999: 2701-2717.

14. Kumar P, Clark M, Kumar & Clark Medicine 4th edition W.B. Saunder; 1999: 261-268.

15. Glickman RM, Inflammatory bowel disease in Harrison's Principles of internal medicine volume II 14th edition; McGraw Hill Company; 1998: 1633-1645.

16. Francis J, Berry M, Rhodes J, Willium GT, Ulcerative Colitis in Gastroenterology Medicine International Pakistan edition 1994: 314-320.

17. Malik MN, Masud G, Rana K, Ulcerative colitis an experience in a medical unit of a teaching hospital at Lahore. Pak J Gasteroenterol 1995; 1: 18-22.

18. Hassnain AS. Ulcerative colitis a histopathological study comprising Western and Pakistani idiopathic ulcerative colitis. Jour Pak Med Ass 1991 (2) (50) 23-7.

19. Bornstein CN, Blanchard JF, Rawsthovne P, Yun NR. The prevalence of extra intestinal diseases in IBD. A population based study Am J Gastroenterol 2001; 4: 1116-22.

20. Rankin GB, Gastrointestinal & Systemic manifestation of IBD Medical Clinics of North America 1994; 1: 1994.

21. Khan AQ, ulcerative colitis in Pakistan a retrospective analysis of 256 patients, biomedica. 7; 1991: 1.

22. Naqui AB, Inayattullah M, Arshad M. Features of ulcerative colitis a study of 30 cases from a Multan region, Pak J Gasteroenterol 1994: 5-9.

23. Gafri SMW. Dysplasia & Surveillance in Ulcerative Colitis review article. Jour Pak Med Assoc 1994: 223-24.

24. Shah SHA. Lyraphoma complicating Ulcerative Colitis, a case report. Jour Pak Med Assoc, vol. 43; 1993: 37-39.

25. Rex .DK. Editorials, sigmoidoscopy or colonoscopy: which way are we headed? Am J Gasteroenterol 2000; 5: 116-118.

26. Floren CH, Benoni C, willen R. Histologic and colonoscopic assessment of disease extension in ulcerative colitis. Scand j Gasteroenterol 1987; 22: 459-62.

27. Farmer RG, Easley KA, Rankin GB. Clinical patterns, natural history and progression of ulcerative colitis: a long term follow up of 1118 patients. Dig Dis Sci (1993); 38: 1137-46.

28. Powell J, Day DW, Buckell Na.Cellier C. Correlation between defined sigmoidoscopic appearance and other measures of disease activity in ulcerative colitis Dig Dis Sci (1982); 27: 533-7.

29. Gomes P, Boulay CD, Smith CL, hold stock G. Relationship between disease indices and colonoscopic findings in patients with chronic inflammatory bowel disease. Gut (1986); 27: 92-5.

30. Holmquist L, Ahren C, Fall Strom SP. Relationship between results of laboratory tests and inflammatory activity assessed by colonoscopy in children

and adolescents with ulcerative colitis. J Pediatr Gastroenterol 1989; 9: 187-93.

31. Holmquist L, Ahren C, Fall Strom SP. Clinical disease activity and inflammatory activity in the rectum in relation to mucosal inflammation assessed by colonoscopy: a study of children and adolescent with chronic inflammatory bowel disease. Acta Pediatr Scand 1990; 79: 527-34.

32. Stowe SP, Redmond SR, Stormont JM. An epidemiologic study of inflammatory bowel disease in Rochester, New York, hospital incidence. Gastroenterology (1990); 98: 104-10.

33. Langhol ZE, Munkholm P, Davidson M, Binder V. Course of ulcerative colitis, analysis of change in disease activity over years. Gasteroenterology (1994); 107:3-11.

34. Solonbel JF. Inflammatory bowel disease in spouses and their offspring. Gasteroenterology (2001); 120: 816-9.

35. Both H, Torp-Pederson K, Kriener-S. Clinical manifestation of ulcerative colitis and Crohn's disease in a regional patient group. Scand J Gastroenterol 1983: 18: 987.

ORIGINAL ARTICLE

A HISTOLOGICAL STUDY OF THE LIVER OF MICE EXPOSED TO CYPERMETHRIN

***Qaiser Inayat, Jehanzeb Khan, Maqbool Ilahi, Rehana Azeem**

*Assistant Professor, Department of Anatomy, Khyber Medical University, Peshawar.
E-mail: qaisarinayat@hotmail.com

ABSTRACT

Background: Synthetic Pyrethroid insecticides are being widely used nowadays in the agricultural sector and as a household insecticide. It is advocated that these insecticides have a high insecticidal activity but low toxicity to birds and mammals. The present study was designed to highlight the toxic effects of Cypermethrin, a new synthetic pyrethroid insecticide, on the liver of mammals.

Research Methodology: The study was conducted on adult albino mice. The insecticide solution was administered to mice through the oral route in doses of 15mg / kg body weight and 30 mg / kg bodyweight for a period of 6 weeks. At the end of the experimental period all the animals were sacrificed and their livers were dissected out and fixed in 10% neutral buffered formalin and processed for histological studies.

Results: At both the doses, there was increase in the relative tissue weight of liver of the experimental animals. Histological changes in the liver included increase in the size of hepatocytes, congestion of blood vessels, lymphocytic infiltration and isolated foci of necrotic hepatocytes.

Conclusions: Cypermethrin is toxic to mammals. It is hepato-toxic, causing dilatation of the central veins and the sinusoids and necrosis of hepatocytes. Therefore, the persons who handle the insecticide (farmers, industrial workers) should compulsarily take precautionary measures to avoid toxicity.

Key words: Insecticides, liver, Cypermethrin.

INTRODUCTION

The advent of pesticides after the world war two ushered a new era of increased agricultural production[1]. The injudicious use of these insecticides posed a serious threat to non-target organisms including man. The present study is an attempt to assess and evaluate the effects of one of the newly marketed synthetic pyrethroid insecticide, Cypermethrin on non-target organisms. It is widely used in the agricultural sector and as a household insecticide. It is also used as an animal ectoparasiticide[2,3,4].

Cypermethrin is a neurotoxin. It acts by increasing the open time of sodium channels leading to prolonged membrane depolarization, enhanced neurotransmitter release and repetitive neuronal activity, eventually resulting in the depletion of the neurotransmitter and block of excitation in the nerve[5]. Poisoning is always due to accidental spillage during spray operations. The oral LD 50 for Cypermethrin in mice varies from 82 to 779 mg/kg body weight. It is widely claimed that pyrethroids have low toxicity to mammals[6,7].

Several studies have been conducted to evaluate the residues of pyrethroids in the environment. The presence of pyrethroid insecticides flumethrin, deltamethrin, Cypermethrin and cyhalothrin in milk and blood of cows was detected after a single dermal application of the recommended doseses upto four weeks after the application[8]. Cyfluthrin, Cypermethrin or permethrin were detected in the Blood and urine samples of thirty pest control operators, 24 hours after exposure[9]. In Germany, environmental surveys were conducted in 1985/86, 1990/91 and 1991/92. Dust samples were collected from 1600 randomly selected houses. An analysis of these samples was performed in respect of their content of 8 different pyrethroids. 90% of the samples contained permethrin while 8% of the samples contained other pyrethriods (Cyfluthrin, lambda Chyalothrin, Cypermethrin, alpha Cypermethrin, Deltamethrin, Epenthrin, d-Phenothrin)[10]. A study was conducted in 1999 to evaluate the residues of pyrethroids in grains, fruits and vegetables. Fourteen laboratories in six countries participated in this study. Residues of eight different pyrethroids were recovered in wheat, oranges, and tomatoes[11].

RESEARCH METHODOLOGY

In this study, 24 adult albino Swiss mice weighing 27.8-33.5 gm were procured from the Veterinary Research Institute, Lahore and were kept at the animal house of Postgraduate Medical Institute, Lahore. They were fed on commercial diet and water ad libitum. The animals were provided optimal light and temperature.

After two weeks of acclimatisation, animals were randomly divided into two groups A and B. Group A was the experimental group while group B was the control group. Groups A and B were further subdivided into subgroups A1, A2, B1 and B2 respectively. Each sub group comprised of six animals. The animals were weighed at the start of the experiment and then weekly till the end of the experiment. The animals of the experimental group A1 received Cypermethrin in 50% ethanol in a dose of 30 mg/kg body weight, as a single daily oral dose, the animals of the experimental group A2 received Cypermethrin in 50% ethanol in a dose of 15 mg/kg body weight, as a single daily oral dose. The animals of the control group B1 received .08 ml of the solvent (50% ethanol) as a single daily oral dose while the animals of the control group B2 did not receive any treatment (Table 1).

At the end of the experimental period (six weeks) all the animals were sacrificed and liver was dissected out, examined macroscopically and weighed. The liver of all the animals was washed in normal saline and fixed in 10% formalin. After histological processing the histological sections were stained with haematoxylin and eosin. The slides were then examined under the light microscope.

Table 1: The experimental plan

Groups	Dosage of Drug
Experimental group A1	30 mg/kg Cypermethrin in 50% ethanol
Experimental group A2	15 mg/kg Cypermethrin in 50% ethanol
Control group B1	0.08 ml of 50% ethanol
Control group B2	No treatment

RESULTS

General Physical Condition

Mice in the control group "B" remained healthy and active throughout the experimental period. No morbidity or mortality was seen in this group. The animals in the experimental group "A", in about 15-20 minutes after receiving the drug, became irritable. They started pawing and burrowing. After a while the animals of subgroup A2 calmed down and became lethargic. While the animals of the subgroup A1 exhibited abnormal movements of the head (side to side movements). The abnormal movements improved 2-3 hours after administration of the drug. In about a week's time all the animals were lethargic and less active as compared to the control group. No mortality was seen in this group.

Body Weight

Animals in both the experimental groups A1 and A2 showed insignificant weight gain as compared to the control groups (Table 2).

Histological Observations Of The Liver

No abnormality was detected in the control groups. The experimental groups showed increase in the size of hepatocytes, congestion of sinusoids and central veins, isolated foci of necrotic hepatocytes and lymphocytic infiltration (Table: 4, fig: 1, 2, 3, 4)

DISCUSSION

General Physical Condition

The animals in the experimental group A, in about 15-20 minutes after receiving the drug, became irritable. They started pawing and burrowing. After a while, the animals of subgroup A2 calmed down and became lethargic. While the animals of the subgroup A1 exhibited abnormal movements of the head (side to side movements). The abnormal movements improved 2-3 hours after administration of the drug. In

Table 2: Mean values of the changes in the body weight of Albino mice of the control and the experimental groups

Group/Dose	Weight At The Start (in gms)	Weight At The End (in gms)	% Weight Gain
A1 30 mg/kg orally	30.35 ±2.27	30.68± 1.97	X1.09
A2 15 mg/kg orally	30.49 ± 1.83	31.56±2.31	X3.51
B1 0.08ml of ethanol orally	30.03 ± 1.79	33.1 ±1.31	**10.2
B2No treatment	30.15 ± 1.69	33.23 ± 1.27	**10.2

Values are expressed as mean ± standard deviation.

X P > .05 difference insignificant. * P < .05 difference significant.

** P <. 01 difference considerably significant. *** P < .001 difference very significant.

Table 3: Comparison of changes in the liver weight of albino mice of the control and the experimental groups

Group/Dose	Mean Body Weight	Mean Liver Weight	Relative Liver Weight
A1 30mg/kg orally	30.68 ± 1.95gm	2.098 ± 0.303 gm	***6.84 ± 0.84%
A2 15mg/kg orally	31.56 ± 2.31gm	2.12 ± 0.21gm	***6072 ± 0.56
B1 .08 ml of ethanol orally	33.1 ± 1.31gm	1.79 ± 0.24gm	X543 ± 0.91
B2 No treatment	33.23 ± 1.27gm	1.94 ± 0.41gm	5.82 ± 1.05

Values are expressed as mean ± standard deviation.

X P > .05 difference insignificant.

* P < .05 difference significant.

** P < .01 difference considerably significant.

*** P <. 001 difference very significant.

Table 4: Comparison of the mean values of histological observations of the liver of mice of the experimental group A with the control group B2

Parameters	Control Group B1	Control Group B2	Experimental group A1	Experimental group A2
Size of Hepatocytes (in (μm)	18.26 ± 0.85	x17.93 ± 0.427	*21.37 ± 0.674	*19.82 ± 1.02
Size of Nucleus (in μm)	7.925 ± .279	X7.633 ± 0.225	**8.67 ± 0.427	*8.083 ± 0.538
Number of nuclei per Cell	1.05 ±.08	1.07 ± 0.08	1.1 ± 0.13	1.15 ± 0.21
Number of nucleoli Per Cell	1.85 ± 0.26	1.67 ± 0.18	3.58 ± 0.13	2.95 ± 0.48
Number of Hepatocytes per HPF	163.8 ± 9.35	X168.83 ± 3.6	**148.3 ± 5.75	*150.7 ± 6.02
Size of Central Vein (in μm)	76.4 ± 3.528	*77.6 ± 1.99	**85.28 ± 3.48	*79.83 ± 1.65
Size of Sinusoids (in μm)	6.9 ± 0.237	x6.6 ± 0.374	***7.77 ± 0.39	**7.63 ± 0.528
Number of Necrotic Cells per HPF	2.333 ± 1.37	x167 ±1.367	***12.67 ± 3.78	***13.83 ± 2.64
Thickness of Capsule (in μm)	1.75 ± 0.164	x1.95 ± 0.138	xl.917 ± 0.349	x1.797 ± 0.177
Infiltration	+	+	+++	++

Values are expressed as mean ± standard deviation.

X P > .05 difference insignificant.

* P < .05 difference significant.

** P < .01 difference considerably significant.

*** P <. 001 difference very significant.

\+ Slight

++ Moderate

+++ Profuse

about a week's time, all the animals were lethargic and less active as compared to the control group. These changes in behavior resulted probably due to the neurotoxicity of Cypermethrin. Vijeverberg and Berkin[12] and McDaniel and Moser[13] have reported similar observations of Cypermethrin toxicity. The signs were less severe in animals receiving lower dose. This is because the toxicity of Cypermethrin is dose dependent[14].

Body Weight

In the experimental group A, weight gain was observed in both the subgroups A1 and A2. However the weight gain was statistically insignificant as compared to the control group B2 (Table 2). This is consistent with the findings of Shakoori et al[15], Luty et al[16] and Elbeticha et al[17].

Gross Appearance Of Liver

The increase in liver weight observed in the subgroups A1 and A2 (Table 3) could be due to hypertrophy and congestion of liver. The pale areas observed in the livers of subgroups A1 probably correspond to areas of hepatic necrosis. Increase in the liver weight is consistent with the findings of Shakoori et al[15], Beilschimidt[3], Hemming et al[6] and Instit'oris et al[18].

Histological Observations Of The Liver

The changes observed in the experimental groups A1 and A2 were dilatation and congestion of vessels (central veins and hepatic sinusoids), necrosis of hepatocytes and lymphocytic infiltration

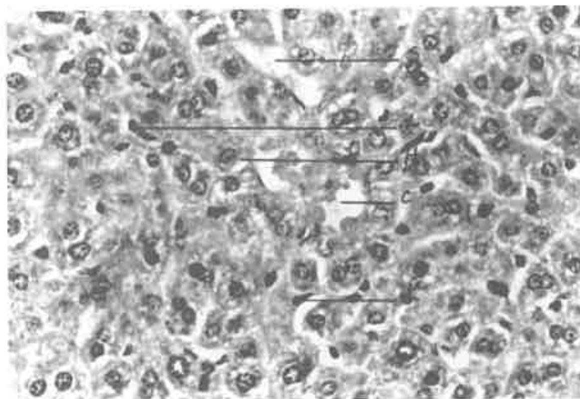

Fig. 1: A photomicrograph of the histological of the mouse liver of the control group B1. Showing C: central vein, S: sinusoid, H: Kupffer cell, L: lymphocyte. H & E, X 588.

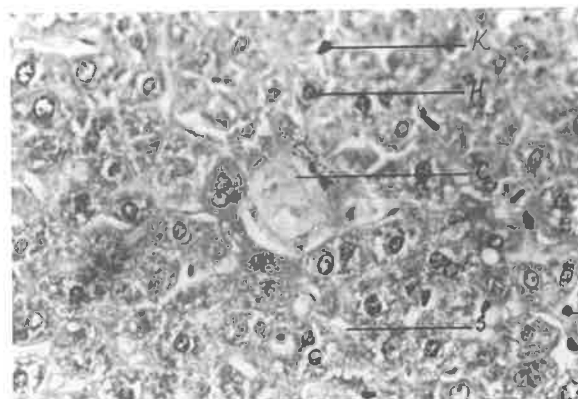

Fig. 2: A photomicrograph of the histological section of the mouse liver of the control group B2. Showing C: central vein, S: sinusoid, H: hepatocyte, K: Kupffer cell. H & E, X 588.

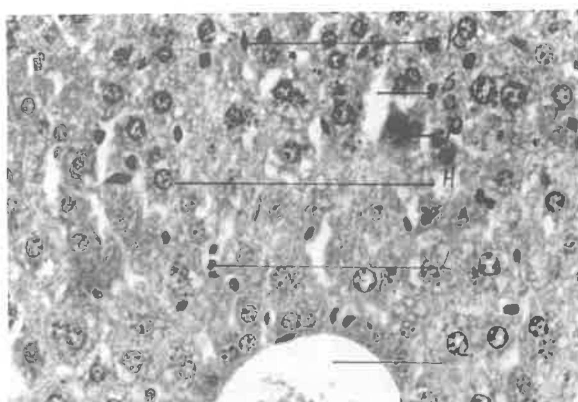

Fig. 3: A photomicrograph of the histological section of the mouse liver of the experimental group. A1. Showing C: central vein, S: sinusoid, H: hepatocyte, L: lymphocyte, N: cell at early stage of necrosis, K: Kupffer cell. H & E, X 588.

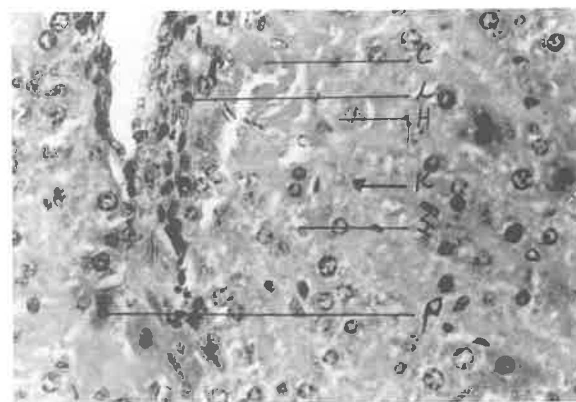

Fig. 4: A photomicrograph of the histological section of the mouse liver of the experimental group A2. Showing C: central vein, S: sinusoid, H: hepatocyte, L: lymphocyte, K: Kupffer cell, N: cell at early stage of necrosis. H & E, X 588.

(Table 4). Shakoori et al[15], Tamang et al[19] and Luty et al[16] have reported similar changes.

The increase in size of cells and necrosis of hepatocytes probably resulted from the direct toxic effect of Cypermethrin on these cells. It has been reported by El-Tawil et al[20] that Cypermethrin irreversibly damages the plasma membranes of hepatocytes leading to cellular death. Furthermore, el-Toukhy and Girgis[21] reported that Cypermethrin inhibits the ATPase system in the hepatocytes leading to histopathological changes in the liver.

The congestion and dilatation of vessels may probably be due to impaired venous drainage resulting from obstruction in venous pathway caused by cellular swelling and injury.

Cypermethrin is known to cause mobilization of leukocytes and increase their phagocytic activity[16]. The lymphocytic infiltration may partly be due to the effect of Cypermethrin and partly as a response of injury to hepatocytes. Tamang et al[19] has also reported lymphocytic infiltration in the portal triads in the animals exposed to Cypermethrin.

CONCLUSION

Cypermethrin is toxic to mammals. It inhibits growth of mammals exhibited by reduced weight gain. It is hepato-toxic, causing dilatation of the central veins and the sinusoids and necrosis of hepatocytes. It is also potentially toxic to the kidneys causing lymphocytic infiltration and congestion of vessels that can lead to necrotic changes.

Since Cypermethrin is an essential insecticide for routine use in agriculture, studies are required to find an agent that could counteract its toxicity.

REFERENCES

1. Busvine JR, ed. Insects and hygiene. Third Ed. London, Chapman and Hall. 1980, 61-66.

2. Fuchs RA, Schroder R. Agents for control of animal pests. In, Chemistry of pesticides. KH Buchel ed. New York, John Whilley and sons. 1983, 9-27.

3. Beilschmidt DM. Toxicology and environmental fate of synthetic pyrethroids. J. Pesticide Reform. 1990, 10, 32-37.

4. Tomlin CDS., ed. The pesticide manual. 12th Ed. Surrey UK, British Crop protection Council. 2000, 230-231.

5. Narahashi T. Nerve membrane sodium channels as the major site of pyrethroids and D.D.T. J. pesticide. Chemistry. 1983, 3, 109-121.

6. Hemming H, Flodstrom S, Warngrad L. Enhancement of altered foci in rat liver and inhibition of intercellular communication in vitro by the pyrethroid insecticides fenevalerate, flucythrinate and cypermethrin. J. Carcinogenesis. 1993, 14(12), 2531-2535.

7. Johri AK, Saxena DM, Lal R. Interaction of synthetic pyrethroids with microorganisms, a review. J. Micro. Bio. 1997, 89, 360-361.

8. Bissacot DZ, Vassilieff I. HPLC determination of flumethrin, deltamethrin, cypermethrin and chylothrin residues in the milk and blood of lactating dairy cows. J Anal Toxicol. 1997, 21(5), 397-402.

9. Leng G, Lewalter J, Rohrig B, Idel H. The influence of individual susceptibility in pyrethroid exposure. J Toxicol Lett (VXN). 1999, 107, 123-130.

10. Friedrich C, Becker K, Hoffmann K, Hoffmann G, Krause C, Noike P. Pyrethroids in house dust of the German housing population results of 2 nationwide crossectional studies. J Gesundheitswesen. 1998, 60 (2), 95-101.

11. Pang GF, Cao YZ, Fan CL, Zhang J J. Multi-residue gas chromatographic method for determining synthetic pyrethroid. Pesticides in agricultural products. J-AOAC-Int. 1999, 82(1), 186-212.

12. Vijverberg H. P, Van den Bercken J. Neuro toxicological effects and mode of action of pyrethroid insecticides. J. Crit. Rev. Toxicol. 1990, 21(2), 105-26.

13. McDaniel K. I, Moser V.C. Utility of a neurobehavioral screening battery for differentiating the effects of two pyrethroids, permethrin and cypermethrin. J. Neurotoxicol. Teratol. 1993, 15, 71-83.

14. Gupta PK. Toxicity of Cypermethrin in Mice, Rats and Rabbits. J. Environ. Biol. 1990, 11(3), 331-334.

15. Shakoori AR, Ali SS, Saleem MA. Effects of six months feeding of cypermethrin on the blood and liver of albino rats. J. Biochem. Toxicol. 1988, 3, 59-71.

16. Luty S, Latuszynska J, Obuchowska Przebirowska D, Tokarska M, Haratym Maj A. Sub acute toxicity of orally applied alpha cypermethrin in Swiss mice. J. Ann. Agric. Environ. Med. 2000, 7, 33-41.

17. Elbeticha A, Da'as S. I, Khamas W, Darmani H. Evaluation of the toxic potentials of cypermethrin pesticide on some reproductive and fertility parameters in the male rats. J. Arch. Environ. Contam. Toxicol. 2001, 41(4), 522-8.

18. Instit'Oris L, Undeger U, Siroki O, Nehez M, Desi I. Comparison of detection sensitivity of immuno- and genotoxicological effects of sub acute Cypermethrin and permethrin exposure in rats. J. Toxicology. 1999, 137(1), 47-55.

19. Tamang RK, Jha GJ, Singh KK. Clinicopathology of acute cypermethrin toxicity in goats. Indian Journal of Animal Sciences. 1989, 61(5), 493-494.

20. El-Tawil OS, Mohamed S, Rahman A. Effect of Cypermethrin on isolated male and female rat hepatocytes. J. Toxicology and Environmental Health. 1997, 52, 461-474.

21. El-Toukhy M A, Girgis R S. In vivo and in vitro studies on the effect of Larvin and Cypermethrin on adenosine triphosphate activity of male rats. J. Environ. Sci. Health. 1993, 28(5), 599-619.

ORIGINAL ARTICLE

VITAMIN K CORRECTED PROTHROMBIN TIME AS A PREDICTOR OF SURVIVAL IN SEVERE LIVER DISEASE

***Noor-Ul Iman, Humera Khan, Shabir Ahmad**

*Associate Professor, Medical 'C' Unit, Department of Medicine,
Khyber Teaching Hospital, Peshawar. E-mail: druliman@yahoo.com

ABSTRACT

Background: The aim of this study was to evaluate the effect of vitamin K on prolonged prothrombin time in severe liver disease (both acute and chronic) and its impact on short-term survival.

Research Methodology: All patients with severe liver disease were included. Vitamin K 10 mg was administered daily for three days in all patients. Prothrombin time (PT) pre- and post-vitamin K therapy were checked. Patients were grouped into two according to whether the PT was corrected by more than 50% or not. Supportive therapy was given in all cases.

Results: 34 patients (22 male and 12 female) were included in the study. Mean age was 44.7 years. 26 patients corrected their PT by more than 50% after Vitamin K therapy. Of these, 25 survived and were sent home. The second group had 08 patients who did not correct their PT by more than 50% and of these, only 02 survived. The overall probability of survival for cases of severe liver disease after administration of intravenous Vitamin K was approximately 77% (0.77).

Conclusion: Prolongation of PT unresponsive to intravenous vitamin K therapy is an ominous prognostic test. PT corrected by more than 50% after Vitamin K therapy predicts survival by a probability of 0.72 (72%).

Key words: Liver disease. Vitamin K, Prothrombin time (PT).

INTRODUCTION

Prothrombin time was originally described by Quick in 1935[1] and is an excellent gauge of hepatic protein synthetic ability[2]. Normal PT is 12-16 seconds in adults[3] and is more sensitive to deficiencies of factors VII, X, and V[4]. These procoagulant factors are synthesized by the liver. When the liver is severely damaged either by acute or chronic insult, there is alteration in hepatocyte perfusion, decrease in number of hepatocytes and seriously impaired synthetic function of the liver[5] which is reflected in prolongation of prothrombin time. PT > 5 seconds above control, not corrected by parenteral vitamin K suggests poor prognosis[6].

RESEARCH METHODOLOGY

All patients with severe liver disease (acute fulminant hepatic failure or Child-Pugh class C cirrhosis) and prolonged PT admitted to Medical C Unit, Khyber Teaching Hospital, Peshawar between September 1999 and February 2001 were included in the study. Vitamin K was given intravenously at a dose of 10 mg/ day for three consecutive days. PT was checked at the end of vitamin K therapy and was compared with the one at admission. Patients who corrected their PT by more than 50% were grouped together and those who failed to do so were put in a separate group. Survivals/deaths were recorded. All patients were allowed to receive supportive treatment including fresh frozen plasma and blood transfusion. Probability of survival was calculated for both groups post administration of Vitamin K. (Table 1).

RESULTS

Total number of patients included in the study was 34. Male patients were 22 and female patients were 12 (Fig. I). The youngest patient was 12 years old and the eldest was 70 years old, with the mean age of 44.7 years. Twenty-six patients corrected their PT by more than 50% after parenteral vitamin K therapy (Fig. 2). All but one survived. One patient received two bags of fresh frozen plasma and three pints of blood while another received three pints of blood. Eight patients did not correct their PT by more than 50%. Six of them died and only two survived (Fig. 3). Four of the six deceased received multiple bags of fresh frozen plasma and blood transfusion. The propability of survival after Vitamin K administrators is shown in Table 1.

Table 1:

	SURVIVABILITY		
	Survived	Expired	Total
PTc	25	1	26
PTnc	02	06	08
	27	07	34

PTc PT corrected by > 50%

PTnc PT not corrected by > 50%

P (survivability) = {25/34 x 25/26} + {8/34 x 2/8} = 0.72+0.058 = 0.778.

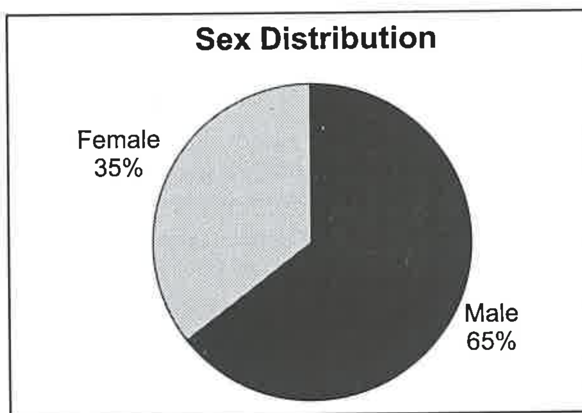

Fig. 1:

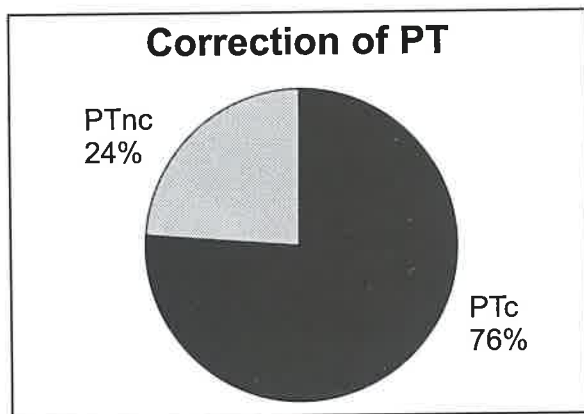

Fig. 2:

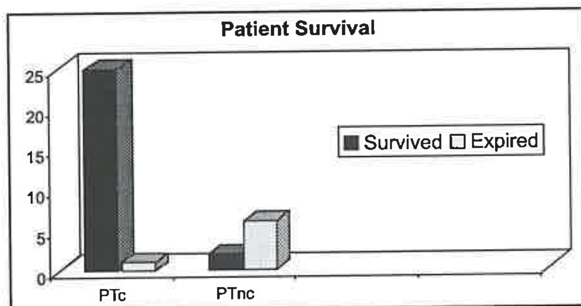

Fig. 3:

DISCUSSION

Prothrombin time is very sensitive to severe liver injury due to any cause[7]. Both clinical and biochemical factors have been evaluated to predict prognosis in severe liver disease. It has been observed that APACHE III score can correctly predict death in 82.3% vs 72.7 % for Child system but when combined with information of ascites and prolonged PT, death can be correctly predicted in 88.2% patients[8]. Patients with cirrhosis suffer from a complex haemostatic disturbance due to abnormalities in clotting and fibrinolytic system activation and in primary haemostasis[9]. The deterioration in coagulation function and increased fibrinolytic activity parallels the severity of liver cirrhosis. Adequate treatment for cirrhotic bleeding should not only correct the coagulation defect but should also lower the increasing fibrinolytic activity[10]. Mba E.T et al confirmed that PT remained prolonged after vitamin K therapy in patients with cirrhosis while it got corrected in obstructive jaundice, thus helping to differentiate between the two[11]. Prolongation of PT which is unresponsive to parenteral vitamin K administration is an ominous prognostic sign in acute viral hepatitis [12].

Our results are in concordance with the current literature on this subject. Instead of predicting mortality we tried to predict survival in patients with severe liver disease. As shown in Table 1, a prolonged prothrombin time which is corrected by more than 50% by intravenous vitamin K therapy would help predict survival in short-term with a probability of 0.72 i.e. 72%. Overall short term survival probability for severe liver disease with administration of Vitamin K is 0.77 (77%).

We hypothesize that partial or complete correction of PT by parenteral vitamin K therapy suggests that fully functioning hepatocytes have survived the insult in adequate numbers, so that vitamin K is utilized efficiently to synthesize vitamin K dependent procoagulants to correct PT and also to perform other functions to sustain life. Fresh frozen plasma is commonly administered to patients with coagulopathy due to advanced liver disease[13-17]. We also did not refrain from administering fresh frozen plasma or transfusing blood if the situation would demand. Factor VII is an important early marker of significant parenchymal liver disease and is often the first vitamin K dependant factor which levels are reduced[18]. Synthetic factor VII has been reported to largely correct PT in patients with chronic liver disease[19-20], indicating that factor VII deficiency is the main determinant of the prolonged PT. The failure of fresh frozen plasma to correct the coagulopathy by providing factor VII is due to lower number of units employed in clinical practice that probably would not contain enough quantity of factor VII. Higher volumes (six or more units) of fresh frozen plasma may be more effective but are rarely employed[21].

REFERENCES

1. James NG., Kolodziej MA; Evaluation of haemostasis and thrombosis. Chapter 76, Internal Medicine, JH Stein, 4th edition, 1994: 744-747.
2. Scheig R., Evaluation of tests used to screen patients with liver disorders; Primary Care; Clinics in office Practice. Sep 1996; 23(3); 551-60.
3. Weatherall DJ; Disorders of the Blood, Oxford Text Book of Medicine; Weatherall, Ledingham and Warrell, Chapter 22.1, 3rd edition, 1996: 3379.

4. Machin SJ, Mackie IJ; Introduction to disorder of haemostasis; chapter 22. 62; Oxford Text Book of Medicine; Weatherall, Ledingham and Warrell, 3rd edition; 1996: 3628.

5. Gogov B, Bratovic I, Vukobrat-Bijedic Z, Lacevic N; Relation of laboratory parameters to complications of liver cirrhosis; Med Arch 1999; 53(4); 211-40.

6. Kaplan MM; evaluation of hepatobiliary disease; chapter 53; Internal Medicine; JH Stein, 4th edition; 1994: 544-551.

7. Payen C, Dachraoui A, Puice C, Descotes J; Prothrombin time prolongation in paracetamol poisoning: a relevant marker of hepatic failure?; Hum Exp Toxicol 2003 Nov; 22(11); 617-621.

8. Wang H, Liu S; Predicting mortality for 205 cirrhotic patients by APACHE III score system; Zhonghua Gan Zang Bing Za Zhi 2000 Dec; 8(6); 348-349.

9. Violi F, Leo R, Vezza E, Basili S, Cordova C, Balsano F; Bleeding time in patients with cirrhosis: relation with degree of liver failure and clotting abnormalities; J Hepatol 1994 Apr; 20(4); 531-536.

10. Ho CH, Hou MC, Lin HC, Lee FY, Wu JC, Lee SD; Haemostatic changes in patients with liver cirrhosis. Zhonghua Yi Xue Za Zhi (Taipei) China 1999 Jun; 62(6); 376-382.

11. Mba ET, Adeoye FA, Jaiyesimi AE; Use of haemostatic parameters as a diagnostic and prognostic index in persistent jaundice: a Zambia experience; Cent Afr J Med 1990 Nov; 36(11); 283-287.

12. LaBrecque DR; Acute and chronic hepatitis, chapter 57; Internal Medicine; JH Stein, 4th edition, 1994: 586-601.

13. Spector L, Corn M, Ticktin HE; Effect of plasma transfusion on the prothrombin time and clotting factors in liver disease; N Eng J Med 1966; 275; 1032-7.

14. Amitrano L, Guardascion MA, Brancaccio V, Balzano A; Coagulation disorders in liver disease; Semin Liver Dis 2002; 22; 83-9.

15. Kaul V, Munoz SJ; Coagulopathy of liver disease; Curr Treat Options gastrenterolo 2000; 3; 433-8.

16. Gazzard BG, Henderson JM, Williams R; The use of fresh frozen plasma or a concentrate of factor IX as replacement before liver biopsy; Gut 1975; 16; 621-5.

17. Williamson LM, Llewelyn CA, Fisher NC et al; A randomized trial of solvent/Detergent-treated and standard fresh frozen plasma in the coagulopathy of liver disease and liver transplantation; Transfusion 1999; 39; 1227-34.

18. Salah S, Bobzien W; Bleeding problems in patients with liver disease: ways to manage the many hepatic effects on coagulation. Post grad Med 1999; 106(4); 187-95.

19. Bernstein D; Effectiveness of the recombinant factor VIIa in patients with Coagulopathy of advanced Child B and C cirrhosis; Semin Thromb Hemost 2000; 26; 437-8.

20. Bernstein DE, Jeffers L, Erhardtsen E et al; Recombinant factor VIIa corrects Prothrombin time in cirrhotic patients; A preliminary study; Gastroenterology 1997; 113; 1930-7.

21. Wael I, Fernando Salazar et al; Role of Fresh Frozen Plasma Infusion In Correction of Coagulopathy of Chronic Liver Disease; A Dual Phase Study; The American J of Gastroenterology; Vol 98;6;1391-94.

ORIGINAL ARTICLE

CYSTOSCOPIC PROCEDURES UNDER LOCAL ANAESTHESIA

***Mazhar Khan, Wasim Yar Khan, Riaz A. Khan, Abid Haleem, Fazal Ghani**

*Associate Professor of Surgery, Surgical 'C' Unit, Khyber Teaching Hospital, Peshawar

ABSTRACT

Background: Cystourethroscopy is a common urological procedure used for both diagnostic and therapeutic purposes. Usually it is done under general anesthesia (GA) especially in males in our set up. This study was aimed to evaluate the feasibility and effectiveness of rigid cystourethroscopic procedures under local anesthesia (LA) as day case.

Research Methodology: This descriptive study was conducted in Surgical C Unit of Khyber Teaching Hospital and Khyber Medical Centre by a single surgeon from Feb 2002 to Dec 2005. A total of 330 male patients were included in the study. 11ml of 2% lignocaine jelly was used for LA and patient response to pain was assessed by visual analogue scoring system.

Results: Among 330 patients, 312 patients completed the protocol. All the patients were cooperative and the procedure went smooth with no major complications. Slight transient hematuria occurred in 107 (33.1%) while 210(65%) had less then 4 pain score.

Conclusion: Rigid cystoscopic procedures can safely be performed with good patient tolerance as day case under LA.

Keywords: Cystourethroscopy, litholopaxy, ureteric stent, hematuria, lignocaine jelly.

INTRODUCTION

The role of cystourethroscopy whether flexible or rigid is not only limited to the diagnosis but several therapeutic procedures can also be done like bladder biopsies, retrograde catheterization, ureteric stenting and its removal, extraction of small bladder stones etc.

It is a common practice to perform rigid cystoscopy under GA[1] and flexible cystoscopy under LA[2,3,4] in our set up. Flexible cystoscopy is a good diagnostic tool but has limited therapeutic use. Also the flexible cystoscope is very expensive and has short working life. In a poor developing country like ours with a very busy operation list and limited number of hospital bed availability, the rigid cystoscopy under LA as day case is a preferable choice to cope with the work load.

The aim of this study was to find out the feasibility and effectiveness of rigid cystourethroscopic procedures under LA as day case.

RESEARCH METHODOLOGY

Total of 330 patients were enrolled in the study 312 patients completed the protocol while in 11 patients the procedure was abandoned due to pain. 7 patients were reluctant to expose themselves on OT table and were excluded from the study.

Inclusion Criteria:

1. Male patients aged 20 years and above.
2. Cooperative and mentally alert patients.

Exclusion Criteria:

1. Patients who had prior cystoscopy under LA.
2. Patients suffering from urological diseases like meatal stenosis, urethral strictures, stone in the urethra, hip deformity, urinary tract infection.
3. Patients requiring bladder biopsy.

Informed consent was taken from every patient. The procedure was done by single surgeon. Intravenous line was secured before procedure and single dose of 500 mg Amikacin was given. Patients with deranged renal function were given 1gm Ceftriaxone. Local anesthesia was achieved with 11ml of 2% lignocaine jelly (instella gell) about 20 minutes prior to procedure. Patients had to empty their bladder before instillation of local anesthesia.

Cystoscopies were done by 21Fr Olympus scope while litholopaxy was done with 24Fr sheath. Normal saline at room temp was used for irrigation and every patient was instructed to relax external sphincter as the scope approached membranous urethra. At the end of procedure bladder was left optimally filled and patients were kept in recovery room for one hour. They had to empty their bladder in transparent jar to assess the extent of hematuria if present. Pain during the procedure was assessed by visual analogue scoring system.

RESULTS

Out of 330 patients, 11 couldn't tolerate the procedure due to pain and the procedure was abandoned. These cases were considered failure. 7 patients were reluctant to expose themselves on O.T table and were excluded from the study. Success rate = 312 out of 323 = 96.6% Failure rate = 11 out of 323=3.4%

The reasons for conducting Cystoscopies in 312 cases are shows in Table 1.

Table 2: Shows the pain score level and frequency of Hematuria in 165 cases undergoing diagnostic cystoscopy.

Table 3 shows the pain score levels and frequency of Hematuria in 147 cases undergoing Therapeutic Cystoscopies

DISCUSSION

Rigid cystourethroscopic procedures under LA can be done safely in females with good patient satisfaction provided extra care is taken to maintain their modesty.

The feasibility and effectiveness of this procedure under LA in males is questioned. Several trials have been conducted in past with variable results.[15,6,7] Routine use of lignocain jelly in cystoscopy is quite

Table 1: Indication for Procedure

Group	Reason	Number of cases	Frequency counts
DIAGNOSTIC n = 165	Painless Hematuria	59	35.7%
	Recurrent UTI	23	13.9%
	Check Cystoscopy	45	27.2%
	Slow Urinary stream	38	23.1%
THERAPEUTIC n = 147	Bladder stone	21	14.2%
	Ureteric JJ Stenting Unilateral (42) Bilateral (16)	58	39.4%
	Ureteric Cathetrization	17	11.5%
	Removal of JJ Stent	38	25.8%
	Clot evacuation	13	8.8%

Table 2: Pain Score Levels and Frequency of Hematuria In Diagnostic Cystoscopic Procedures

No.	Indication	No. of patients	Overall Pain Score			Hematuria		Clot retention	Urinary retention
			1-3	4-6	7-10	Slight	Gross		
1	Painless Hematuria	59	41(69.4%)	17(28.8%)	1(1.7%)	17(28.8%)	0	0	0
2	Recurrent UTI	23	14(60.8%)	8(34.7%)	1(4.3%)	10(43.4%)	1(4.3%)	0	0
3	Check Cystoscopy	45	34(75.5%)	9(20%)	2(4.4%)	15(33.3%)	0	0	0
4	Slow Stream	38	25(65.7%)	10(26.6%)	3(7.8%)	10(26.3%)	0	0	0
	Total	165	114(69%)	44(26.6%)	7(4.2%)	52(31.5%)	1(0.6%)		

Table 3: Pain Score Levels and Frequency of Hematuria in Therapeutic Cystoscopic procedures

No.	Indication	No. of patients	Overall Pain Score			Hematuria		Clot retention	Urinary retention
			1-3	4-6	7-10	Slight	Gross		
1	Bladder Stone	21	12(57.1%)	7(33.3%)	2(9.5%)	16(76.1%)	1(4.7%)	0	0
2	Unilateral JJ Stenting	42	31(73.8%)	9(21.4%)	2(4.7%)	12(28.5%)	0	0	0
3	Bilateral JJ Stenting	16	8(50%)	5(31.2%)	3(18.7%)	10(62.5%)	2(12.5%)	0	0
4	Ureteric Ca-thetrization	17	14(82.3%)	3(17.6%)	0	6(35.2%)	0	0	0
5	Removal of evacuation	38	24(63.1%)	11(28.9%)	3(7.7%)	5(13.1%)	1(2.6%)	0	0
6	Clot eva-cuation	13	7(53.8%)	2(15.3%)	4(30.7%)	6(46.1%)	2(15.3%)	0	0
	Total	147	96(65.3%)	37(25.1%)	14(9.5%)	55(37.4%)	6(4%)		

safe.[8] Some studies have shown no advantage on pain perception comparing lignocaine jelly over plain water based lubrication[5,9,10] while another study has shown significant reduction in pain if 30ml of lignocaine jelly is used over 20 minutes before procedure.[7] Using cold anesthetic jelly also reduces the pain during instillation.[11] Patient tolerance is much better on second or subsequent cystoscopic session confirming that patient anxiety about the procedure also plays part in pain perception. Majority of the patients complain more pain at the time of instillation of local anesthetic jelly.[5,12] mainly due to chlorhexidine gluconate in it.[13] During the procedure it was the membranous urethra where most patients felt pain.[14]

Our study has shown that in majority of cases rigid cystoscopy can safely be done in men. The pain felt during instillation of jelly and during cystourethroscopy is well tolerated, especially if patients are informed and educated in advance and asked to relax their pelvis when scope passes through the membranous urethra. Once the scope is in the bladder, pain is minimal if movement of scope is restricted and care is taken to prevent overdistension of the bladder.

CONCLUSION

Rigid cystourethroscopic procedures under LA are very safe and patient tolerance to the procedure is also very good. Subjecting patients to GA and hospital admission is not needed in every case.

REFERENCES

1) Denholm SW, Connl G, Newsam JE, Chisholm GD. Morbidity following cystoscopy; comparison of flexible & rigid techniques. Br J Urol. 1990 Aug; 66(2); 152-4.

2) Kumar V, Patel HR, Nathan SM, Millar RA, Lawson AH. Do we need to perform cystoscopy in all adults attending urology centres as out patients? Urologia Internationalis 2004; 73: 198-200.

3) Almallah YZ, Rennie CD, Stone J, Lancashire MJR. Urinary tract infection and patient satisfaction after flexible cystoscopy and urodynamic evaluation. Urology. 56, Issue = I, Jul 2000; 37-39.

4) Kobayashi T, Nishizawa K, Ogura K. Is instillation of anesthetic gel necessary in flexible cystoscopic examination? A prospective randomized study. Urology. 2003; Jan; 61(1); 65-8.

5) Matsuda D, Irie A, Shimura S, Hirayama T, Kurosaka ST, Sumura H, Maru N, Baba S. Uncertain analgetic efficacy of intra urethral instillation anesthetic jelly in rigid cystoscopy for men. Nippon Hinyo Kika Gakkai Zasshi, 2005; Sep; 96(6): 617-22.

6) Shang B, Park HK, Cheol K, Oh SJ. How painful are shock wave lithotripsy & endoscopic procedure performed at out patients urology clinics?

7) Gold Fischer ER, Cromie WJ, Karison TG, Naszkiewiez L, Gerber GS. Randomized, prospective, double blind study of the effects on pain perception of lidocaine jelly Vs plain lubricant during out patient rigid cystoscopy. J Urol. 1997; Jan; 157 (1): 90-4.

8) Ouellete RD, Blute RS, Jaffe S, Bahde C. Plasma concentrations of lidocaine resulting from instillation of lidocaine jelly into genitourinary tract prior to cystoscopy. Urology. 1985; May: 25 (5); 490-1.

9) Steim MS, Lubetkin D, Taub HC, Skinner WK, Haberman J. The effects of intraurethral lidocaine anesthetic & patient anxiety on pain perception during cystoscopy. J Urol. 1994; June; 151 (6): 1518-21.

10) Palit V, Ashurst HN, Biyani CS, Elmasray Y, Puri R. Is using lignocaine gel prior to flexible cystoscopy justified? A randomized prospective study. Urologia Internationalis 2003; 71: 389-392.

11) Goel R, Aron M. Cooled lignicaine gel: does it reduce urethral discomfort during instillation? Int Urol Nephrol. 2003; 35 (3); 375-7.

12) Kobayashi T, Nishizawa K, Mitsumori K, Ogura K. Instillation of anesthetic gel is no longer necessary in the era of flexible cystoscopy. A crossover study. J Endourol 2004; Jun; 18 (5); 483-6.

13) Jayathilake, A, Davis FC. Chlorhexidine in urethral gel; Does it cause pain at flexible cystoscopy? Urology vol = 67. Issue 4. April 2006; 670-73.

14) Taghizadah AK, Madari AE, Gard PR, Li CY, Thomas RJ. When does it hurt? Pain during flexible cystoscopy in Men. Urologia Internationalis 2006; 76: 301-303.

ORIGINAL ARTICLE

COMPARATIVE STUDY OF VISUAL ACUITY IN PHACOEMULSIFICATION VS CONVENTIONAL EXTRACAPSULAR CATARACT EXTRACTION WITH POSTERIOR CHAMBER INTRAOCULAR LENS IMPLANTATION IN AGE- RELATED CATARACT

***Mohammad Alam, Zafar Iqbal, Mian Ihsan Ullah, Amir Mohammad, Mian Ihsanullah**

*Registrar, Department of Ophthalmology, Khyber Teaching Hospital, Peshawar

ABSTRACT

Background: Phacoemulsification and Extracapsular Cataract Extraction are the two standard surgical procedures in cataract management. In Extracapsular Cataract Extraction the incision is large which is closed with stitches. This results in more astigmatism and late rehabilitation. As there is large incision this results in more complications. Phacoemulsification is recent advanced procedure in cataract management. The incision is small and self-sealing. Complications are less and rehabilitation is early and also there is less astigmatism. However the learning curve is difficult. Once mastered then this is the best method of cataract management. The objective of this study was to compare visual acuity in Phacoemulsification VS Extracapsular Cataract Extraction with Posterior Chamber Intraocular Lens implantation in age- related cataract.

Research Methodology: The comparative study was conducted in the department of Ophthalmology Khyber Teaching Hospital Peshawar in collaboration with department of Pathology KMC/KTH for investigation/Screening from January 2001 to June 2002. 100 patients were selected with age related cataract. They were divided in two groups A and B each comprising of 50 patients. Group A underwent Phacoemulsification with Posterior Chamber Intra Ocular Lens (PMMA) Implantation while group B underwent Extra Capsular Cataract Extraction with Posterior Chamber Intra Ocular Lens Implantation in which 3-4 stitches of 10/0 Nylon suture were applied to close the wound which were removed after two months. Visual acuity was recorded on first post operative day, end of first week, first month, second month and third month.

Results: At the end of third month in group A 94% patients had best corrected visual acuity of 6/6, 4% had 6/9 and 2% had 6/18, while in group B 90% patients had best corrected visual acuity of 6/6, 4% had 6/9, 2% had 6/12 and 4% had 6/18. The results were statistically insignificant.

Conclusion: In Phacoemulsification the visual rehabilitation is early with rapid convalescence as compared to conventional Extra Capsular Cataract Extraction. However at the end of third month the visual acuity results in both the groups were nearly the same.

Keywords: Phacoemulsification, Extracapsular Cataract Extraction, Visual Acuity.

Abbreviations: Phacoemulsification (Phaco), Extra Capsular Cataract Extraction (ECCE), Posterior Chamber Intra Ocular Lens (PC-IOL) Visual Acuity (VA).

INTRODUCTION

Cataract is the most important cause of defective vision in aged people. Globally about 16 million people suffer from this reversible blindness[1]. About 1.3 million patients have defective vision due to cataract in Pakistan which according to an estimate accounts 70% of all causes of blindness[2].

Cataract has been managed by various methods since long ago comprising of couching, intracapsular cataract extraction (ICCE) and ECCE. In 1967 Charles Kelman introduced ultrasonic fragmentation of nucleus called Phacoemulsification[3]. Presently cataract surgery can be performed by conventional ECCE and small incision sutureless surgery called Phacoemulsification. In ECCE an incision of about 8-10 mm is given with manual expression of cataractous lens and then PC-IOL is implanted. 3-4 stitches with 10/0 Nylon suture are applied to close the wound. These stitches are removed after two months. In ECCE there is change in the curvature of cornea being the main refractory surface in the

eye. These changes may result in astigmatism and postoperative unaided visual acuity is badly affected. In ECCE rehabilitation is late and postoperative care is prolonged.

In Phacoemulsification nucleus is fragmented ultrasonically with small self-sealing incision of 3.2 mm which is then enlarged according to size of IOL. No stitch is applied. Corneal topographic changes are less, rehabilitation is early with good convalescence. Postoperative unaided visual acuity is good.

RESEARCH METHODOLOGY

We selected non-randomized 100 Patients of age-related cataract with no other ocular and systemic disorder. They were divided in to two groups A & B each comprising of 50% patients. Investigations like fasting blood sugar level, HBs Ag, and HCV were done in the pathology department KMC / KTH.

Inclusion Criteria:

1. Age 50-70 years
2. Blood Pressure less than 140/90mmHg
3. Fasting blood sugar level less than 126mg%
4. IOP less than 20 mmHg

Exclusion Criteria:

1. Diabetic patients
2. Hypertensive patients
3. Glaucomatous patients
4. Previously operated eyes
5. HBSAg and HCV Positive Patients

Preoperative visual acuity was in range of hand movement (HM) to 6/36. All surgeries were done with peribulbar local anesthesia. To avoid bias, all the observations were recorded by one observer. Group A patients underwent Phacoemulsification with PC-IOL by a single skilled surgeon and group B patients underwent ECCE with PC-IOL by another skilled surgeon to avoid bias. In group A patients 3.2 mm incision was given which was extended to 5.5 mm for implantation of IOL. In all patients PC-IOL (PMMA) lenses were implanted. No stitch was applied in any patient.

In ECCE 8 - 10mm incision was given for manual expression of cataractous lens. PC-IOL (PMMA) lenses were implanted. 3-4 stitches of 10/0 Nylon suture for closing the wound were applied which were removed after two months. Visual acuity was recorded on first postoperative day, at the end of first week, first month, second month and third month.

RESULTS

The visual acuity on 1st post-operative day in both groups is shown in Table 1. The visual acuity at end of 1st week, 1st month, 2nd month and 3rd month are shown in Table 2, 3, 4 and 5 respectively.

The best corrected visual acuity with refraction at end of 3rd month in shown in Table 6.

Table 1: 1ST Postoperative Day V.A

V.A	Group A		Group B		Significance
	No. of Patients	%age	No. of Patients	%age	
6/6	9	18	—	—	$P < 0.000$
6/9	3	6	—	—	$P < 0.000$
6/12	7	14	1	2	$P < 0.000$
6/18	12	24	6	12	$P < 0.001$
6/24	10	20	13	26	$P < 0.05$
6/36	5	10	8	16	$P < 0.05$
6/60	1	2	9	18	$P < 0.001$
CF	3	6	13	26	$P < 0.001$

Table 2: At The End of 1st Week

V.A	Group A		Group B		Significance
	No. of Patients	%age	No. of Patients	%age	
6/6	12	24	—	—	$P < 0.000$
6/9	16	32	—	—	$P < 0.000$
6/12	10	20	3	6	$P < 0.001$
6/18	8	16	16	32	$P < 0.001$
6/24	3	6	11	22	$P < 0.005$
6/36	1	2	19	38	$P < 0.000$
6/60	—	—	1	2	$P < 0.000$

Table 3: At the end of 1st Month

V.A	Group A		Group B		Significance
	No. of Patients	%age	No. of Patients	%age	
6/6	27	54	—	—	$P < 0.000$
6/9	12	24	1	2	$P < 0.000$
6/12	6	12	8	16	$P > 0.05$
6/18	4	8	15	30	$P < 0.001$
6/24	1	2	23	46	$P < 0.001$
6/36	—	—	3	6	$P < 0.000$

Table 4: At the end of 2nd Month

V.A	Group A		Group B		Significance
	No. of Patients	%age	No. of Patients	%age	
6/6	33	66	13	26	$P < 0.000$
6/9	9	18	22	44	$P < 0.001$
6/12	4	8	7	14	$P < 0.05$
6/18	3	6	7	14	$P < 0.05$
6/24	1	2	1	2	$P = 0.5$

Table 5: At the end of 3rd Month

V.A	Group A		Group B		Significance
	No. of Patients	%age	No. of Patients	%age	
6/6	37	74	31	62	$P < 0.05$
6/9	5	10	7	14	$P < 0.05$
6/12	4	8	8	16	$P < 0.001$
6/18	3	6	4	8	$P > 0.05$
6/24	1	2	—	—	$P < 0.000$

Table 6: Best Corrected V.A with Refraction at the end of 3rd Month

V.A	Group A		Group B		Significance
	No. of Patients	%age	No. of Patients	%age	
6/6	47	94	45	90	$P > 0.05$
6/9	2	4	2	4	$P = 0.5$
6/12	—	—	1	2	$P < 0.000$
6/18	1	2	2	4	$P < 0.01$

DISCUSSION

Phacoemulsification is the standard procedure of cataract management if patient can afford and surgeon is skilled. However ECCE has its own importance. It is easy, affordable and can be done even in camps.

Preoperative assessment is mandatory for better results. Patients with no ocular and systemic disorder show the confidence of surgeon that better visual acuity can be achieved postoperatively with Phacoemulsification and ECCE with PC-IOL except rehabilitation time. As far as visual acuity is concerned, early fruitful results are expected from phaco with PC-IOL and comparatively the same results will be achieved from ECCE with PC-IOL after 2-3 months as has been observed in our study.

In our study in group A 76% patients had VA 6/12 or better and 6% patients in group B had VA 6/12 or better after one week. Our results are comparatively better than that of SA Haider in which 43% of patients with phaco with PC-IOL had VA 6/12 or better and in ECCE with PC-IOL had VA 6/12 or better[4].

Surgery conducted on eyes without ocular morbidity had good results. According to study of Parul Desai, DC Minassian, Angela Reidy[5] 80% of patients in phaco with PC -IOL had best corrected VA of 6/9 while in ECCE with PC-IOL 72% had best corrected visual acuity of 6/9 or better. Our study has edge over it.

According to the study of Asad Aslam Khan, Shakil Ahmed, Sohail Sarwar et al,[6] in phaco with PC-IOL 58% patients achieved uncorrected VA of 6/12 or better, 18% had 6/18 and 24% less than 6/18.1n their subsequent study 51.7% patients had VA of 6/12 or better, 30.6% had visual acuity 6/18 and 17.7% had VA less than 6/18 which are comparable to our study.

The comparative study by Naseer Raja, Mohammad Khizer Niazi 8l% of patients in phaco with PC-IOL had final VA of 6/12 or better while 77% had the same results in ECCE with PC-IOL[7] So the final results are nearly comparable in phaco and ECCE with PC-IOL.

The study of Mustansir Siddique, Khalid Masood Ashraf, Mohammad Sohail Shehzad et al[8] 80% show unaided final VA of 6/12 or better in phaco with PC-IOL and 24% patients had the same results in ECCE with PC-IOL. Our study shows better results.

The changes in Corneal topography correlates with visual outcome after surgery. The changes are more in ECCE than phaco which results in poor outcome. Study of DC Mianssian et al showed that 11% patients had VA of 6/9 or better after three months in ECCE with PC-IOL[9]. Our results are better than this study.

Phaco has a difficult learning curve. Complications like endothelial damage. Posterior capsule rupture, Vitreous loss and nucleus drop in vitreous are more common. The visual outcome also correlates with the skill of surgeon. In study by Z. Kamal 81% patients had final VA of 6/12 or better[10].

IOL implantation in ECCE has progressive improvement in rehabilitation. According to study by Madurai et al[11] VA at two months follow up 30.7% patients had 6/12 and at six months follow up 95.8% had best corrected VA of 6/12 or better.

Phaco has good results in age-related cataract than manual phacofracture. The study of Vajpyee R.B[12] reveals that 68% of patients of phaco with PC-IOL had VA of 6/9 or better as compared to 37% patients in phacofracture on first post operative day.

ECCE with PC-IOL can be performed even in Eye camps. Harpreet Kapoor[13] study shows best corrected VA of 6/18 or better in 87.9% patients. This study is not comparable to our study. So it is recommended that surgery should be conducted in proper hospitals having full-fledged facilities.

In our study there was no effect of age, sex and preoperative VA on postoperative visual outcome[14].

CONCLUSION

Phaco with PC-IOL has better early results of VA and rehabilitation as compared to ECCE with PC-IOL which encourages the surgeon and makes the patients satisfied. Phaco is very safe procedure in skilled hands. Phaco is very expensive and every patient can not afford it. ECCE is relatively easy procedure and can be afforded by every patient. The study reveals that there

is no significant difference in clinical assessment of VA after three months except the time and duration factors.

The results are comparable with both national as well as international studies.

REFRENCES

1. Durrani. J. Blindness statistics for Pakistan. (Editorial). Pak. J. Ophthalmol, 1999; 15-1.

2. Khan MD, Qureshi M.B, Khan MA. Facts about the status of blindness in Pakistan. Pak J. Ophthalmol. Vol; 15 No: 1-1999.

3. Kelman CD. Phacoemulsification and Aspiration. A new technique of cataract Removal. Am J Ophthalmol 1967; 64: 2.

4. Haider S.A. Phacoemulsification vs Conventional Extra Capsular Cataract Extraction. A study of early Astigmatism and complication. Pak J. Ophthalmol 1999; Vol; 15. No: 1.

5. Desai P, Minassian DC, Reidy A. National Cataract Surgery Survey 1997-8: a report of results of clinical outcome. Br J Opthalmol 1999; 83: 1336-1340.

6. Khan AA, Ahmad S, Sarwar S, Chohan A. Phacoemulsification. A comparative analysis of first hundred and subsequent 150 cases. Pak Journal of Ophthalmology Vol. 14 No. 2, 1998.

7. Raja N, Niazi MK, Phacoemulsification vs Extracapsular Cataract Extraction, Visual outcome. Pakistan J Surg. Dec 2003; 19(2): 77-81.

8. Siddique M, Ashraf KM, Shehzad MS et al. Topographic Evaluation of changes in Corneal curvature after ECCE VS Phaco with PC-IOL. Pak J. Ophthalmol 2005, Vol. 21 No. 3.

9. Minassian DC, Dark JK. ECCE Compared with small incision surgery by Phaco. A randomized trial. Br J Ophthalmol 2001; 85: 822-9.

10. Kamal Z. An audit of 100 cases of Phaco Cataract Surgery. Ann. King Edward Med Coll Dec 2000; 6-4: 349-50.

11. Pranja NV, Chandrakanth KS, Kirn MD et al. The Madurai IOL study II. Clinical outcome. American Journal of Ophthalmology 1998; 125: 14-25.

12. Vajpayee RB, Sabarwal S, Sharma N, Angra SK. Phacofracture vs Phacoemulsification in eyes with age related cataract. J Cataract Refract Surg 1998. Sep; 24(9); 1252-5.

13. Harpreet K, Arin CJ, Richard D. Evaluation of visual outcome of cataract surgery in Indian eye camps. Br J Ophthalmol 1999; 83: 343-346.

14. Westcott MC, Tuft SJ, Minassian DC. Effect of age on visual outcome following cataract extraction. Br J Opthalmol 2000; 84: 1380-1382.

ORIGINAL ARTICLE

INCIDENCE OF DEEP VEIN THROMBOSIS IN CANCER PATIENTS IN NORTHERN PAKISTAN

***Abid Jameel, Shahid Jamil**

*Assistant Professor & Head, Department of Medical Oncology,
Hayatabad Medical Complex, Peshawar. E-mail: ajameel99@yahoo.com

ABSTRACT

Background: High incidence of deep vein thrombosis (DVT) or venous thromboembolism (VTE) has been reported in literature in the West, especially in patients suffering from various types of malignancies. In post-operative period in cancer patients, the incidence may be as high as 20%. In contrast, the incidence has been reported to be as low as 2% in many Asian countries.

Research Methodology: We conducted a study of our patients with various forms of malignancies presenting to Medical Oncology Ward at Khyber Teaching Hospital, Peshawar to look for the incidence of DVT/VTE in our population from Northern Pakistan. A total of 552 patients with various types of malignancies were admitted to Medical Oncology Ward from January 2000 to December 2000. Clinical probability score and color Doppler ultrasound and B-mode compression ultrasound (Duplex scanning) were used for the diagnosis of DVT. Lung perfusion scan or CT scan was used for pulmonary embolism (PE).

Results: Out of 552 patients, 10 (1.8%) were found to have DVT. Out these 10 patients, four had non-Hodgkin's lymphoma, two patients had gynecological cancers, two had metastases of unknown origin, one patient had hepatocellular carcinoma and one patient had colon cancer. These patients were treated with Inj. Enoxaparin 1 mg/kg, subcutaneously twice a day for 3 days followed by 1 mg/kg/day once a day for another 3-5 days along with oral warfarin 5 mg/day for 4-6 months (for an INR of 2.5-3.0). No serious bleeding disorders or other adverse events were encountered with this dose and an INR of 2.5-3.0.

Conclusion: DVT in cancer patients is not an uncommon phenomenon in the West but the incidence seems to be on the lower side (2%) in Asian population (including Pakistanis). The treating physician should be aware of the sign/symptoms and risk factors for DVT (clinical probability) and should screen patients suspected with DVT with duplex scanning ultrasonography or lung perfusion scan. Inj. Enoxaparin (or any other LMWH) in combination with warfarin is a safe alternative to Heparin and does not require frequent monitoring.

Keywords: Deep Vein Thrombosis (DVT), Incidence, Asia, Venous Thromboembolism (VTE).

INTRODUCTION

Deep vein thrombosis (DVT) or venous thromboembolism (VTE) is a common occurrence in pregnancy, trauma, surgery, prolonged immobilization and malignancy. Almost 20% of all new cases of DVT/VTE are related to some form of malignancy[1]. Most surveys carried out in the West have shown a 6-10 fold increase in the incidence of DVT in cancer patients[2,3].

Some of the newer therapeutic agents used in malignancies (such as thalidomide, bevacizumab, L-asparaginase, tamoxifen etc.) are also reported to be associated with an increased risk of DVT[4,5,6]. It is also known that cancer patients who present with DVT carry a poorer prognosis and have a shorter survival time compared to cancer patients without DVT[7,8].

Due to the high incidence of DVT and its related morbidity, the American College of Chest Physicians (ACCP) has recognized this as a serious issue and in its 7th ACCP conference has come out with guidelines for prevention and treatment of DVT[9,10]. But despite such a high incidence in the West, many studies have shown a low incidence of DVT in Asian population[11,12,13,14].

In order to look for the incidence of DVT in our population from Northern Pakistan with various forms of malignancies, we conducted a study of our patients presenting to Medical Oncology ward with various types of cancer and our results are presented and discussed here.

RESEARCH METHODOLOGY

All patients presenting to Medical Oncology ward, Khyber Teaching Hospital (KTH), Peshawar from January to December 2000 (12 month period) were included in the study. KTH is one of the largest tertiary care Teaching Hospitals in North West Fron-

tier Province (NWFP) with catchment area including the whole of NWFP as well as adjoining parts of Afghanistan. Inclusion criteria included all cancer patients who presented to Medical Oncology ward within the study period and had a biopsy proven malignancy. Those patients with no malignancy were to be excluded. A total of 552 cancer patients were admitted in the 12 month study period. Routine baseline investigations including complete blood picture (CBC), routine biochemistry, INR, ultrasound, x-ray etc were done on all patients. Diagnosis of DVT was based on history, physical examination, clinical probability score and diagnostic duplex ultrasonography. Taking into consideration the cost as well as availability of various diagnostic procedures, color Doppler ultrasound complimented with real time B-mode (brightness modulation) ultrasound (Duplex Scanning) was carried out for the diagnosis on patients with suspected DVT (Fig. 3 and 4). Non-compressibility of vein with ultrasound probe and altered venous blood flow was diagnostic of DVT. Clinical probability score[18] (Table 1) along with Duplex scanning being cheap, non-invasive, readily available and sensitive as well as specific (in 98% patients) was the only diagnostic procedure used for confirmation of diagnosis of DVT (see discussion section for details). Lung perfusion scan (and CT chest, if required) was carried out in case pulmonary embolism was suspected. Follow-up of patients included history, physical examination and serial Duplex ultrasounds (along with INR).

Treatment protocol of patients diagnosed with DVT included Inj. Enoxaparin 1 mg/kg subcutaneously twice a day for 3 days followed by 1 mg/kg/day for another 3-5 days along with oral warfarin 5-10 mg/day (for a target INR of 2.5-3.0) for 4-6 months. This protocol was according to the ACCP guidelines for the treatment of DVT[9,10] and was in addition to any chemotherapy required for the primary cancer.

RESULTS

Out of 552 patients diagnosed with cancer and admitted in Medical Oncology Ward in the 12 month period, 10 patients were found to have a DVT giving an incidence of DVT of 1.8%. Age of these patients ranged from 18 years to 58 years (median 47 years). Six patients were female while four were male. Of these, one patient had axillary vein involvement (Fig. 1), one had pulmonary embolism while eight patients had extensive popliteal or femoral vein involvement (Fig. 2, 3 and 4). Types of malignancies in these patients included non-Hodgkin's lymphoma (four), gynecological cancers (two), metastases of unknown origin (two), hepatocellular carcinoma (one) and colon cancer (one). Main complaints of these patients included swelling of the affected limb (100%), pain in the affected area (100%) and redness of the affected area (70%). Breathlessness and chest pain was the main complaint in patient with pulmonary embolism (PE). After commencement of treatment for DVT with Inj. Enoxaparin, edema and pain subsided within 5-10 days but patients were advised to continue oral warfarin 5 mg/day for at least 06 months as per ACCP recommendations (with check-up of INR). All our patients responded very well to this treatment protocol with disappearance of swelling and redness in 5-10 days and other symptoms including pain in 10-15 days. No serious side-effects including any bleeding episodes were noted in these patients treated with anti-coagulants (with the maintenance of INR between 2.5-3.0). This treatment with anti-coagulation therapy was in addition to any chemotherapy required for the treatment of primary cancer which was started as soon as the patient was stabilized. As for long term results, since majority of patients with advance cancer do not turn up for long term follow-up, therefore it was not possible to note the rate of recurrence of DVT or the overall survival of these cancer patients.

Table 1: Clinical Probability Score for predicting DVT (modified from Hirsh and Lee[18]).

Clinical characteristic	Score
Active cancer	1
Paralysis, paresis or recent plaster immobilization of lower limbs	1
Recently bed-ridden > days or major surgery within 4 weeks	1
Localized tenderness long the distribution of deep venous system	1
Entire leg swollen	1
Calf leg swelling > 3 cms compared to asymptomatic side	1
Pitting edema confined to symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Medications (Tamoxifen, Bevacizumab, Thalidomide, L-asparaginase, Erythropoeitin)	1
Alternate diagnosis greater than DVT	-2

High probability of DVT with a total score >3; moderate probability with a total score 1-2; low probability with total score 0. Patients scoring 2 or more points should be evaluated further for DVT.

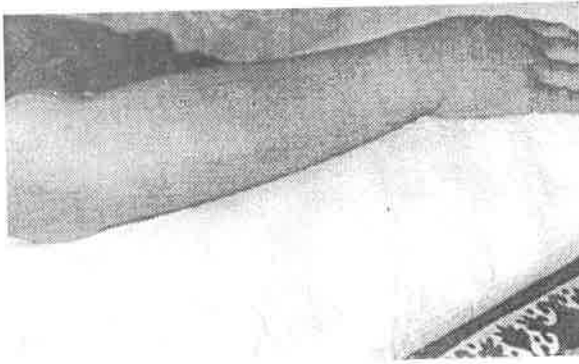

Fig. 1: Redness and swelling of the fore-arm in a patient with axillary vein DVT.

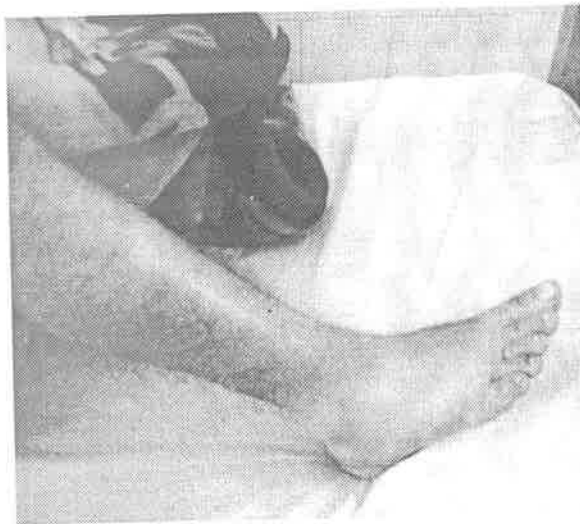

Fig. 2: Redness and swelling of the lower limb (unilateral) in a patient with DVT in the femoral and popliteal veins.

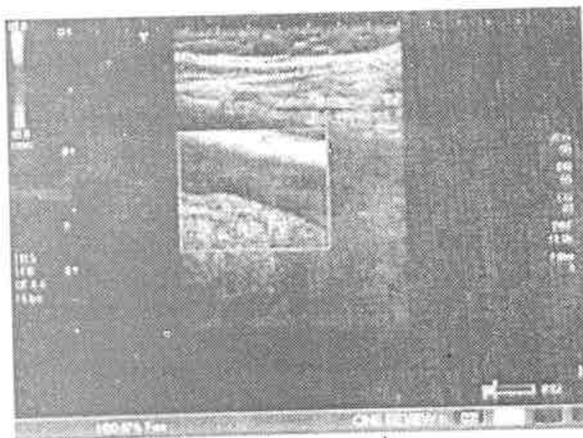

Fig. 3: Doppler ultrasound showing a big thrombus throughout the length of the right femoral vein (RT-FV).

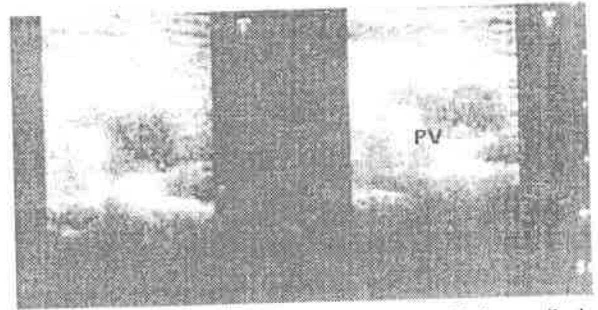

Fig. 4: Doppler ultrasound of a patient with lower limb DVT showing lack of compressibility of popliteal vein and thrombus in the popliteal vein (PV).

DISCUSSION

Diagnosis of DVT can be confirmed, in addition to clinical probability score, by a battery of tests including venography, impedance plethysmography, D-dimer assay, I^{125} radiolabelled fibrinogen scanning, CT scan, MRI and ultrasonography. Venography, although very sensitive and specific, is invasive, expensive and not readily available everywhere in developing countries. MRI and nuclear imaging tend to be quite expensive as well. High resolution ultrasonography using vein compression has been shown to have specificity and sensitivity of 95% and is extremely accurate in detecting first time proximal symptomatic DVT and has completely revolutionized the diagnosis of DVT, although sensitivity decreases below knee[15,16,17]. Duplex scanning (color Doppler ultrasound and B-mode high resolution ultrasound using vein compression) gives extremely good results. It is non-invasive, readily available and inexpensive and therefore is the diagnostic method of choice in the diagnosis as well as follow-up of patients with proximal DVT[16,17,18]. The triad of intermediate or high clinical probability score (Table 1), a positive Duplex ultrasound scan and a positive D-dimer assay confirms the diagnosis of DVT in 100% of cases thereby eliminating the need for venography in a vast majority of cases. A positive D-dimer assay lacks specificity but a negative D-dimer assay is extremely sensitive and specific for eliminating the diagnosis of DVT and therefore a negative D-dimer assay along with a negative duplex ultrasound result virtually excludes the diagnosis of DVT. Considering this, we chose the clinical probability score and Duplex ultrasound scanning as our diagnostic tools for the diagnosis of DVT in our patients. This also resulted in patient compliance since no battery of invasive or expensive tests were advised that may take many days to confirm the diagnosis. Considering its high specificity and sensitivity as well as high positive and negative predictive value (97-98%), Duplex-scanning, along with clinical probability score and D-dimer assay, is currently the method of choice for the diagnosis of DVT[15,17,18]. Other diagnostic tests referred to above and reviewed extensively by Hirsh and Lee[18] may be added if required for confirmation of diagnosis in case of any

discrepancy with Duplex-scanning or in case of recurrent DVT.

DVT has a high incidence in the Western countries, especially in cancer patients. Considering its frequency in various types of patient population and morbidity associated with DVT, the American College of Chest Physicians (ACCP) has recommended guidelines for the prevention and treatment of DVT/VTE in its 7th ACCP conference[9,10]. ACCP has recommended prevention and treatment with low molecular weight heparin (LMWH) for 5-7 days followed by 3-6 months of oral warfarin as first line treatment of DVT. We used the same protocol which was in use even before its final recommendation in 2004 by ACCP. We also found very good results with edema and pain subsiding within 5-15 days. We did not encounter any severe bleeding problems and no severe side-effects were observed with an INR of 2.5-3.0. We recommend at least 06 months of oral warfarin after 5-10 days of Inj. Enoxaparin (or any other LMWH) with INR kept between 2.5-3.0 and even longer oral warfarin in case there is a recurrence or if cancer or predisposing event persists. Further details regarding the length of treatment in various situations have been published by Hirsh and Lee[18]. LMWH being relatively safer than Heparin, no close monitoring is required and once daily administration via subcutaneous route is also comparatively easier. Majority of patients treated with LMWH can be treated on out-patient basis which is an added advantage for a busy unit with limited number of beds. Although the prognosis of cancer patients with DVT is extremely poor as already pointed out, we can not comment on the prognosis and long term outcome in our patients since the drop out rate in the long term in our patients is high and as a custom, terminal patients are not usually brought to the Hospital.

Despite its high incidence in the west, DVT is found uncommonly in Asian population[11,12,13,14]. Although the number of patients in our study was low and this was only an institutional study, we also found a relatively low incidence of DVT (2%). This is in line with the studies described above where low incidence of DVT (as low as 1/5th to 1/10th compared to Western population) was found in Asian population. Also, even after this study period, we have continuously noted a low incidence of DVT in our patients thus further confirming this study. The reason for this low incidence is not clear. It can partially be explained by the fact that our patient population is younger in age compared to the Western population and it is known that the incidence of DVT increases with increase in age[19]. The study by Anderson (also called the Worcester study) showed that the incidence of DVT increased with age exponentially by a factor of 200 when the age of the patient increased from 20 to 80 years. Since the average age of our patients was only 47 years therefore vast majority of our patients were young and therefore at a low risk of DVT as far as age is considered. Also in an Iranian study, the average age of patients was 43 years again pointing towards a younger age group compared to the older age group in the West. Racial factors can be another reason for low incidence of DVT in Asian population[20,21]. Other risk factors such as absence of hazardous mutations, immobility, hormone use in the form of contraceptive pills etc are also low in our population which may reflect in the low incidence of DVT[21]. It can also partially be explained by the fact that symptoms of DVT are usually non-specific and therefore in many cases, especially in the terminal patients, it goes undetected.

CONCLUSION

The incidence of DVT in cancer patients seems to be on the lower side in the Asian population compared to the West. Racial factors, absence of hazardous mutations predisposing to DVT/PE and factors such as low use of hormone therapy, mobility of patients and younger age at diagnosis may be the reason for the lower incidence of DVT in Pakistan. Color duplex scanning along with clinical probability score (and D-dimer assay, if available) can be used as the diagnostic tool for DVT in countries that lack resources and funds. Enoxaparin given subcutaneously once a day for 5-10 days followed by oral warfarin is the recommended treatment for patients with DVT.

REFERENCES

1. Heit JA, O'Fallon WM, Petterson TM, et al. Relative impact of risk factors for deep vein thrombosis and pulmonary embolism: a population based study. Arch Intern Med 2002; 162: 1245-48.
2. Blom JW, Doggen CJ Osanto S, et al. Malignancies, prothrombotic mutations and the risk of venous thrombosis. JAMA 2005; 293: 715-22.
3. Heit JA, Silverstein MD, Mohr DN, et al. Risk factors for deep vein thrombosis and pulmonary embolism: a population based case control study. Arch Intern Med 2000;160: 809-15.
4. Heit JA. Cancer and venous thromboembolism: scope of the problem. Cancer Control 2005; 12 (S1): 5-10.
5. Zangari M, Barlogie B, Anaissie E, et al. Deep vein thrombosis in patients with multiple myeloma treated with thalidomide and chemotherapy: effect of prophylactic and therapeutic anti-coagulation. Br J Haematol 2004; 126: 715-21.
6. Hurwitz H, Fehrenbacker L, Novotny W, et al. Bevacizumab plus irinotecan, fluorouracil and leucovorin for metastatic colorectal cancer. N Engl J Med 2004; 350: 2335-42.
7. Sorensen HT, Mellemkjaer L, Olsen JH, et al. Prognosis of cancers associated with venous thromboembolism. N Engl J Med 2000; 343: 1846-50.
8. Levitan N, Dowlati A, Remick SC, et al. Rates of initial and recurrent thromboembolic disease

among patients with malignancy versus those without malignancy: risk analysis using Medicare claims data. Medicine 1999; 78: 285-91.

9. Buller HR, Agnelli G, Hull RD, et al. Anti-thrombotic therapy for venous thromboembolic disease. The Seventh ACCP Consensus Conference on Antithrombotic and thrombolytic therapy. Chest 2004; 126 (S3): 401s-428s.

10. Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism. The Seventh ACCP Consensus Conference on antithrombotic and thrombolytic therapy. Chest 2004; 126 (S3): 338s-400s.

11. Woo KS, Tse LKK, Tse CY, et al. The prevalence and pattern of pulmonary thromboembolism in the Chinese in Hong Kong. Int J Cardiol 1988; 20: 373-80.

12. Lee HM, Suk KS, Moon SH, et al. Deep vein thrombosis after major spinal surgery: incidence in an east Asian population. Spine 2000; 25: 1827-30.

13. Hwang WS. The rarity of pulmonary thromboembolism in Asians. Singapore Med J 1968; 9: 276-79.

14. Cheuk BL, Cheung GC, Cheng SW. Epidemiology of venous thromboembolism in a Chinese population. Br J Surg 2004; 91: 424-28.

15. Goldhaber SZ. Diagnosis of deep vein thrombosis. Clin Cornerstone 2000; 2: 29-37.

16. Kearon C, Ginsberg JS, Hirsh J. The role of venous ultrasonography in the diagnosis of suspected deep vein thrombosis and pulmonary embolism. Ann Intern Med 1998; 129: 1044-49.

17. Gaitini D. Current approaches and controversial issues in the diagnosis of deep vein thrombosis via duplex Doppler ultrasound. J Clin Ultrasound 2006; 34: 289-97.

18. Hirsh J, Lee AYY. How we diagnose and treat deep vein thrombosis. Blood 2002; 99: 3102-10.

19. Anderson FA Jr, Wheeler HB, Goldberg RJ, et al. A population based perspective of the hospital incidence and case fatality rates of deep vein thrombosis and pulmonary embolism, the Worcester DVT study. Arch Intern Med 1991; 151: 933-38.

20. Nossent JC, Egelie NC. Incidence and course of symptomatic deep venous thrombosis of the lower extremities in a black Caribbean population. Thromb Haemost 1993; 70: 576-78.

21. Klatsky AL, Armstrong MA, Poggi J. Risk of pulmonary embolism and/or deep vein thrombosis in Asian-Americans. Am J Cardiol 2000; 85: 1334-37.

ORIGINAL ARTICLE

PROGNOSTIC FACTORS IN UNILATERAL IDIOPATHIC SUDDEN SENSORINEURAL HEARING LOSS

***Amjad Khan, Waqaruddin, Altaf Hussain, Saeedullah**

*Assistant Professor of ENT,
Naseer Teaching Hospital, Peshawar

ABSTRACT

Background: The objective of this study was to determine the effect of severity of hearing loss, time to treatment and presence of additional symptoms on hearing recovery in idiopathic sudden sensorineural hearing loss (ISSNHL).

Research Methodology: A retrospective observational study was conducted from January 2001 to June 2006 at Naseer Teaching Hospital, Peshawar and Pakistan Institute of Medical Sciences, Islamabad. Sixty five patients of idiopathic sudden sensorineural hearing loss, treated with 60mg prednisolone tapered over 14 days, were included. Pre and post-treatment pure tone audiogram was performed and hearing recovery was assessed in relation to different prognostic factors. Chi-square test was used for statistical analysis. Significance levels for all analysis were set at $p<0.05$.

Results: Of the 65 patients, 23 were females and 42 were males. Hearing recovery was obtained in 52.1% of females and in 47.6% of males. Recovery was obtained in 75% of patients with mild hearing loss, in 48.1% of patients with moderate hearing loss and in 31.8% of patients with severe hearing loss. Recovery was observed in 61.5% of patients who received treatment within 2 weeks, in 33.3% of patients who received treatment between 2 -4 weeks and in 27.2% of patients who received treatment after 4 weeks. Recovery was observed in 33.3% of patients with additional symptoms and in 58.5% of patients without additional symptoms.

Conclusion: Better hearing outcome should be expected in ISSNHL if patient has mild to moderate hearing loss, no additional symptoms and less time elapsed between the onset of disease and the beginning of treatment.

Keywords: Steroids, Prognostic factors, Idiopathic sudden sensorineural hearing loss (ISSNHL).

INTRODUCTION

There are two types of rapidly progressive sensorineural hearing loss: sudden hearing loss and rapidly progressive sensorineural hearing loss, which develops over days or months. Idiopathic sudden sensorineural hearing loss (ISSHL) is a clinical diagnosis characterized by a sudden deafness of cochlear or retrocochlear origin in the absence of a clear precipitating cause. It is generally unilateral and develops in less than 72 hours. ISSNHL affects 5 to 20 persons per 100,000 annually[1]. The origin of sudden deafness is difficult to establish. Several etiopathogenic factors have been postulated, such as viral infection, autoimmune origin, vascular and metabolic disease, rupture of the labyrinthine membrane and recently, immune-mediated inner ear disease.

Systemic steroids in sudden sensorineural hearing loss (SSHL) appear to be the most effective and the most widely accepted treatment today[2,3,4,5]. More recent studies applying treatment protocols including vasodilators, plasma expanders, anti-coagulants, and carbogen inhalations have shown no improvement over the rate of spontaneous recovery without therapy[6]. Different factors may influence the prognosis like age, gender, severity of hearing loss, duration of symptoms before treatment, presence of vertigo or tinnitus and type of audiogram.

The aim of this study was to determine and identify those factors that play an important role in the prognosis of the condition. This is a retrospective chart review study in which 65 patients suffering from idiopathic SSHL were assessed. All patients received the same treatment protocol i.e. 60mg tapered over 14 days. A homogenous sample was obtained by applying strict inclusion criteria. Four prognostic factors i.e. gender, severity of hearing loss, time to treatment and additional symptoms were evaluated in relation to hearing recovery. Chi-square test was applied to determine the statistically significant association between prognostic factors and hearing outcome. Significance levels for all analysis were set at $p < 0.05$.

RESEARCH METHODOLOGY

This study was conducted at the ENT departments of Naseer Teaching Hospital, Peshawar and Pakistan Institute of Medical Sciences, Islamabad from January 2001 to June 2006. It was a retrospective chart review study.

Eligible patients were patients between the ages of 18 to 60 years who had unilateral hearing loss of at least 30 dB across three contiguous frequencies within 72 hours; who had an audiogram before and after treatment; who had received a course of 60mg prednisolone orally tapered over 14 days. Patients were excluded if they had any chronic ear disease (e.g. chronic suppurative otitis media, otosclerosis etc), had history of ototoxic drugs within three months of developing sudden hearing loss, both ears were affected, non-affected ear had poor hearing (PTA > 50dB) and if they had received any other treatment for ISSNHL.

A record was made of age, sex, severity of hearing loss (i.e. mild, moderate and severe), presence or absence of additional symptoms (i.e. tinnitus, vertigo) and the time between the onset of hearing loss and starting of treatment. The severity of hearing loss was assessed on the basis of pre-treatment pure tone audiogram (PTA). Mild hearing loss was a hearing threshold between 26 to 40dB, moderate hearing loss was a hearing threshold between 41 to 70dB and severe hearing loss was a hearing threshold between 71 to 90dB. On the basis of time to treatment, patients were divided into 3 groups i.e. group A including patients who had received treatment within 2 weeks of onset of hearing loss, group B including patients who had received treatment between 2-4 weeks of onset of hearing loss and group C including patients who had received treatment after 4 weeks of onset of hearing loss.

The hearing recovery was assessed on the basis of post-treatment PTA. A clinical success was considered to be recovery of hearing to within 50% of the difference between affected and unaffected ear. Group success rates were compared by chi-square (χ^2) test. Correlations were used to examine for relationships among patient demographics and hearing improvement (i.e. recovery). Significance levels for all analysis were set at $p < 0.05$.

RESULTS

A total of 65 patients fulfilling the inclusion criteria were included in the study. There were 23 females and 42 males, ranging in age from 18 years to 60 years. Hearing recovery was observed in 32 (49.2%) out of 65 patients. Recovery was obtained in 12 (52.1%) out of 23 females and in 20 (47.6%) out of 42 males. After application of chi square test, p value was calculated to be 0.2 i.e. less than 0.05 (Table 1).

Regarding the severity of hearing loss, 16 patients had mild hearing loss, 27 had moderate hearing loss and 22 had severe hearing loss. The post-treatment PTA revealed hearing recovery in 12 (75%) out of 16 patients with mild hearing loss, in 13 (48.1%) out of 27 patients with moderate hearing loss and in 7 (31.8%) out of 22 patients with severe hearing loss. After application of chi square test, the p value came to be 0.03 i.e. less than 0.05 (Table 2).

Regarding the time to treatment, 39 (60%) patients received treatment within 2 weeks of onset of hearing loss, 15 (23%) patients received treatment between 2-4 weeks and 11 (17%) patients received treatment after 4 weeks. Hearing recovery was observed in 24 (61.5%) out of 39 patients who received treatment within 2 weeks, in 5 (33.3%) out of 15 patients who received treatment between 2-4 weeks and in 3 (27.2%) out 11 patients who received treatment after 4 weeks. After application of chi square test, the p value came to be 0.05 (Table 3).

Regarding the presence of additional symptoms with ISSNHL, 24 (36.9%) suffered from additional symptoms (i.e. tinnitus, vertigo etc), while 41 (63%) patients were without additional symptoms. Recovery was observed in 8 (33.3%) out of 24 patients with additional symptoms and in 24 (58.5%) out of 41 patients without additional symptoms. After application of chi square test, p value was calculated to be 0.05 (Table 4).

Table No. 1: Gender and Hearing Recovery

Hearing Recovery	Gender		Total
	Female	Male	
No	11	22	33
Yes	12	20	32

Chi square value = 0.12 P value = 0.72

Table No. 2: Severity Of Hearing Loss And Hearing Recovery

Hearing Recovery	Grades of hearing loss			Total
	Mild	Moderate	Severe	
No	4	14	15	33
Yes	12	13	7	32
Total	16	27	22	65

Chi square value = 6.93 P value = 0.03

Table No. 3: Time To Treatment And Hearing Recovery

Hearing Recovery	Time to treatment			Total
	Within 2 weeks	2-4 weeks	After 4 weeks	
No	15	10	8	33
Yes	24	5	3	32
Total	39	15	11	65

Chi square value = 6.002 P value = 0.05

Table No. 4: Additional Symptoms And Hearing Recovery

Hearing Recovery	Additional symptons		Total
	Absent	Present	
No	17	16	33
Yes	25	7	32
Total	41	24	65

Chi square value = 5.03   P value = 0.02

DISCUSSION

The outcome (hearing recovery rate) of patients with unilateral ISSNHL is related to different variables i.e. the dose of steroid, the length of time of medication, the severity of hearing loss, the time to start treatment and the presence or absence of additional symptoms etc. Several studies even report that the rate of spontaneous recovery is almost equal to the recovery in the treated group[7,8,9]. Several reasons for the lack of consistent findings are inconsistent patient inclusion criteria, small and variable sample sizes and the need for a better disease marker than simply audiologic profile.

Different factors may influence a prognosis like age and gender of patients, severity of hearing loss, duration of symptoms before treatment, presence of vertigo or tinnitus and type of audiogram. The aim of our study was an evaluation of the hearing improvement in sudden deafness in relation to some of these factors. In this study 65 patients with unilateral ISSNHL were included and their recovery (post-treatment PTA) was studied with reference to sex, severity of hearing loss, time to treatment and the presence or absence of additional symptoms.

Regarding the sex of the patients, we found no significant difference in recovery rate between males (47.6%) and females (52.1%). According to Zadeh MH et al, outcome was not significantly related to gender[10]. They used the same treatment protocol for all patients i.e. steroids and antiviral therapy. Another study conducted in Israel studied 133 patients with ISSHL. Sixty patients were treated with carbogen inhalation and seventy three patients were treated with carbogen inhalation and intravenous MgSO4, but regardless of the treatment regimen, sex had no significant impact on hearing recovery[11]. Xenellis J et al concluded that intratympanic (IT) steroid administration after failed intravenous steroids is a safe and effective treatment in sudden sensorineural hearing loss, but sex had no significance influence on the outcome[2]. However there are few studies that showed that sex had a significant effect on the outcome. For example, Samim E et al showed that females had better prognosis than males but treatment regimen had no superiority to the reported spontaneous hearing recovery.

Another important prognostic factor is the severity of hearing loss. Our study revealed that patients with mild hearing loss had better prognosis than patients with severe hearing loss. The same was stated by Slattery WH et al, who concluded that post treatment outcome differed significantly by the amount of hearing present at the time of receiving the first treatment and mild to moderate hearing loss was associated with better hearing outcome, regardless of the amount of oral steroid given as treatment[12]. Another study concluded that level of hearing loss may significantly influence an outcome[13]. In this study hearing improvement was more frequent in patients with initially mild (51.6%) than severe (38.7%) and profound hearing loss (25%) (51.5% vs 25%, $p < 0.05$). The severity of hearing loss is the only prognostic factor reported significant in relation to hearing outcome by many studies in the previous literature[1,14].

Regarding the time between the onset of hearing loss and treatment started, significant association was found between hearing recovery and time to treatment. Recovery occurred in 61.5% of patients in whom treatment was started within 2 weeks, in 33.3% of patients in whom treatment was started between 2-4 weeks and in 27.2% of patients in whom treatment was started after 4 weeks. In a national survey done in 2004 in Limerick, consultants considered an optimistic outcome if treated within two weeks[15]. In another study patients were divided into two groups on the basis of treatment. Group A was given blood -flow promoting drugs, glucocorticoids in high doses, betahistine and hyperbaric oxygen therapy, while group B was given blood flow-promoting drugs and glucocorticoids in low doses. They concluded that improvement was better in group A as compared to group B and in addition, the best results are achieved if treatment is started as early as possible[4]. In another study, carbogen inhalation and intravenous MgSO4 were used and they concluded that patients who commenced the treatment 8 days or more after onset had poorer recovery as compared to those who started treatment earlier ($p < 0.03$), regardless of the treatment regimen '. So although the above two studies used different treatment regimen, but still the time to treatment had a significant effect on the final outcome. There are studies showing no significance of time to treatment and hearing recovery, for example, a study conducted in France 2005, concluded that delay in treatment has no influence on audiometric outcome but in this study the time frame was different. Patients were divided whether treatment was started within 24 hours or within 1 week[16]. In majority of studies, a better outcome was found in patients in whom treatment was started within one or two weeks of time and the poor recovery group of patients was that in which treatment was started after 2 weeks. Another study using a double blind approach, revealed

no association between time to treatment and recovery[9]. In this study, patients were divided into four treatment groups; prednisolone tablets, placebo tablets, carbogen inhalation or room air inhalation and they concluded that steroid or carbogen inhalation have no therapeutic advantage over placebo. Whenever the treatment options used were not superior to placebo, how can one conclude that time to treatment did not significantly affect the outcome? So many studies have revealed that a better hearing outcome is related to the less time elapsed between onset of hearing loss and the beginning of treatment[13,17].

Additional symptoms associated with sudden hearing loss may be vertigo, tinnitus and heaviness in the head. In our study 33.3% of patients with additional symptoms recovered while 58.5% of patients without additional symptoms recovered and the presence of additional symptoms significantly affected the outcome. These results are consistent with the previous literature on prognostic factors of ISSNHL[13,18]. However there are studies showing no effect of prognostic factors on the hearing outcome[9,10] but these studies had small sample sizes. An interesting study including 133 patients revealed that Vertigo was a poor prognostic factor but tinnitus had no significant impact on hearing recovery[11]. Another study showed that patients with 2 additional symptoms may have the poorest prognosis, regardless of the amount of steroid treatment[12]. So it may be possible that the presence of more than one additional symptom with sudden hearing loss will worsen the prognosis but the presence of only one additional symptom with sudden hearing loss may or may not worsen the prognosis of recovery. Further studies should be directed toward a better understanding of the role of additional symptoms in idiopathic sudden hearing loss.

CONCLUSION

Better hearing outcome should be expected if a patient with ISSNHL has mild to moderate hearing loss, absence of additional symptoms and less time elapsed between the onset of disease and the beginning of treatment, while gender has no effect on the outcome.

REFERENCES

1- Cadoni G, Agostino S, Manna R. Clinical associations of serum antiendothelial cell antibodies in patients with sudden sensorineural hearing loss. *Laryngoscope* 2003: **113(5):** 797-81.

2- Xenellis J, Papadimitriou N, Nikolopoulos T, Maragoudakis P, Segas J, Tzagaroulakis A, *et al.* Intratympanic steroid treatment in idiopathic sudden sensorineural hearing loss: a control study. *Otolaryngol Head Neck Surg* 2006; **134(6):** 940-5.

3- Chen CY, Halpin C, Rauch SD. Oral steroid treatment of sudden sensorineural hearing loss: a ten year retrospective analysis. *Otol Neurotol* 2003; **24(5):** 728-33.

4- Narozny W, Sicko Z, Przewozny T, Stankiewicz C, Kot J, Kuczkowski J. Usefulness of high doses of glucocorticoids and hyperbaric oxygen therapy in sudden sensorineural hearing loss treatment. *Otol Neurotol* 2004; **25(6):** 916-23.

5- Salahaldin AH, Bener A, ElHakeem AA, Abdulhadi K. Management of idiopathic sudden sensorineural hearing loss: experience in newly developing Qatar. *Int Tinnitus J* 2004; **10(2):** 165-9.

6- Schweinfurth JM, Parnes SM, Very M. Current concepts in the diagnosis and treatment of sudden sensorineural hearing loss. *Eur Arch Otorhinolaryngol* 1996; **253(3):** 117-21.

7- Wei BP, Mubiru S, O'Leary S. Steroids for idiopathic sudden sensorineural hearing loss. Cochrane Database *Syst Rev* 2006; 1: CD003998.

8- Samim E, Kilic R, Ozdek A, Gocmen H, Eryilmaz A, Unlu I. Combined treatment of sudden sensorineural hearing loss with steroid, dextran and piracetam: experience with 68 cases. *Eur Arch Otorhinolaryngol* 2004; **261(4):** 187-90.

9- Cinamon U, Bendet E, Kronenberg J. Steroids, carbogen or placebo for sudden hearing loss: a prospective double-blind study. *Eur Arch Otorhinolaryngol* 2001; **258(9):** 477-80.

10- Zadeh MH, Storper IS, Spitzer JB. Diagnosis and treatment of sudden-onset sensorineural hearing loss: a study of 51 patients. *Otolaryngol Head Neck Surg* 2003; **128(1):** 92-8.

11- Gordin A, Goldenberg D, Golz A, Netzer A, Joachims HZ. Magnesium: a new therapy for idiopathic sudden sensorineural hearing loss. *Otol Neurotol* 2002; **23(4):** 447-51.

12- Slattery WH, Fisher LM, Iqbal Z, Liu N. Oral steroid regimens for idiopathic sudden sensorineural hearing loss. *Otolaryngol Head Neck Surg* 2005; **132:** 5-10.

13- Pajor A, Durko T, Gryczynski M. Prognostic factors in sudden deafness. *Otolaryngol Pol* 2003; 57(2): 271-5.

14- Byl FM Jr. Sudden hearing loss eight years' experience and suggested prognostic table. *Laryngoscope* 1984; **94(5):** 647-61.

15- Ahmed I, Fenton JE, Manning K, Keogh P. Management of sudden sensorineural hearing loss - a national survey. *Ir Med J 2004;* **97(5):** 146-7.

16- Huy PT, Sauvaget E. Idiopathic sudden sensorineural hearing loss is not an otologic emergency. *Otol Neurotol* 2005; **26(5):** 896-902.

17- Xenellis J, Karapatsas I, Papadimitriou N, Nikolopoulos T, Maragoudakis P. Tzagkaroulakis M, *et al.* Idiopathic sudden sensorineural hearing loss: prognostic factors. *J Laryngol Otol* 2006; **120:** 1-7.

18- Psifidis AD, Psillas GK, Daniilidis JCh. Sudden sensorineural hearing loss: long-term follow-up results. *Otolaryngol Head Neck Surg* 2006; **134(5):** 809-15.

ORIGINAL ARTICLE

FREQUENCY OF ASYMPTOMATIC HYPOCALCEMIA IN MULTIPAROUS WOMEN

***Parveen Azim, M. Amjad Taqweem, Saima Gilani, Zafar Ali, Amjad Mahboob**

*Assistant Professor, Gynae 'B' Unit, Khyber Teaching Hospital, Peshawar

ABSTRACT

Background: Hypocalecemia is defined as abnormally low levels of Ca (<8.4mg/dl) in circulating blood. In over-populated country, like ours, multiparity is seen with increased frequency in females. Repeated pregnancies followed by lactation, low socio-economic status, can lead to disturbances in normal body trace elements and especially calcium. Therefore the objective of my study was to determine the frequency of asymptomatic hypocalecemia in multiparous women in tertiary care hospital.

Research Methodology: This was a hospital based non-interventional, descriptive study. It included 100 multiparous women of more than 20 years of age, presenting to Teaching Hospitals, Peshawar NWFP, in May and June 2006. Subjects were selected by non-probability convenient sampling method after obtaining an informed consent. Blood samples were collected under standard conditions for measurement of serum calcium level.

Results: Out of 100 subjects, serum calcium levels were low in 48 (48%). Serum calcium levels ranged from 6.29 mg/dl to 8.40 mg/dl, with mean values of 7.51 mg/dl ± 0.5128. Age of the subjects ranged from 20 to 60 years. Mean age was 35.01 ± 8.39 years. Majority of subjects, i.e., 95 (95%) were of < 50 years of age. Parity ranged from 3 to 14, mean parity was 5.67 ± 2.27.

Conclusions: Asymptomatic hypocalcemia is a common condition in females with multiparity. Screening and calcium supplementation is suggested.

Keywords: Hypocalcemia, Asymptomatic hypocalcemia, Mineral metabolism, Multiparous women, Parity.

INTRODUCTION

Calcium is the most obvious and persistent of the micronutrients; the 5th most abundant element and the most abundant cation in the body. A total of about 1-2 kg of calcium is present in the average adult (about 2% of body weight). About 98-99 % of this is present in the skeleton.[1] The total calcium concentration in the plasma is 4.5-5.1 mEq/L (9-10.2 mg/dL). Fifty percent of plasma calcium is ionized, 40% is bound to proteins (90% of which binds to albumin), and 10% circulates bound to anions (phosphate, carbonate, citrate, lactate, sulfate).[2] Hypocalcemia is defined as abnormally low levels of calcium (<8.4 mg/dl) in the circulating blood.

The calcium level in the blood can be moderately low without producing any symptoms.[3] Clinical signs and symptoms are observed only with decreases in ionized calcium concentration <4.4 mg/dl (1.1 mmol/l). Overtime, hypocalcemia can affect the brain and cause neurologic or psychologic symptoms, such as confusion, memory loss, delirium, depression, and hallucinations.[4] An extremely low calcium level may cause tingling (often in the lips, tongue, fingers, and feet), muscle aches, spasms of the muscles in the throat (leading to difficulty breathing), stiffening and spasms of muscles (tetany),[5] and abnormal heart rhythms.[6]

In an over-populated country, like ours, multiparity is seen with increased frequency in females. Repeated pregnancies[7] followed by lactation, besides other problems/ morbidities, also lead to disturbances in trace elements. The purpose of this study was to determine the frequency of asymptomatic hypocalcemia in multiparous women in a tertiary care setting because if not detected early with further pregnancies it can lead to frank osteomalacia, pelvic deformities, cephalopelvic disproportion, obstructed labour and increased rate of perinatal morbidity, perinatel mortality, maternal morbidity, maternal mortality and backache in late stage, so we wanted to diagnose and treat at asymptomatic stage to prevent all above complications.

RESEARCH METHODOLOGY

This was a hospital based non-interventional, descriptive study. It included 100 multiparous women, presenting to Teaching Hospitals, Peshawar NWFP, in May and June 2006 without any symptoms of hypocalcemia. (By asymptomatic we mean that not having classical proximal myopathy/osteomalacia).

The study included all adult female subjects of more than 20 years of age. For the purpose of study multiparity was defined as 'females who have given birth at least three times to an infant, live born or not,

or having an estimated length of gestation of at least 20 weeks'. Subjects' selection was done by non-probability convenient sampling method. An informed consent of the subjects was taken for their inclusion in the study.

Subjects younger than 20 years, with parity of less than 3, and those with symptomatic hypocalcemia (tetany, facial twitching, oro-facial numbness/ paresthesia, laryngospasm, seizures) were excluded from the study. None of the subjects were on calcium supplements or anti-convulsant therapy.

Information was collected regarding demographic and presenting features, and laboratory parameters such as serum calcium and serum albumin. Normal serum urea and creatinine levels ruled out renal failure. Past history of neck surgery was asked for possible parathyroidectomy. Any history of diarrhea was obtained.

In order to provide a more valid index of ionized calcium value, corrected serum calcium (adjusted with albumin) was calculated according to the formula:

Corrected serum calcium = serum calcium (mg/dl) + (0.8 x [4.0-serum albumin (g/dl)].

Serum calcium level was measured by Selectra XL analyzer. Whole blood samples were collected in the fasting state, in a lithium heparin tube from each patient,[8] keeping in mind the necessary precautions to avoid pre-analytical errors (e.g. blood sample withdrawn with a single prick, and avoiding use of an occluding cuff or tourniquet on the arm, and fist clenching. Analysis of whole blood was done within 4 hours of collection to avoid changes in pH and anion chelation. Hypocalcemia was defined as serum calcium level of 8.4 mg/dl or a value less than that at presentation. Serum albumin level was measured by photometry endpoint methodology on Synchron Cx system.

Data Analysis:

Statistical Package for Social Sciences (SPSS) version 8.0 was utilized for data storage, processing and analysis. Descriptive statistical analysis was employed to describe data for frequencies, percentages, ratios, range, and mean value with one standard deviation.

RESULTS

These subjects were having diverse ethnicity from different geographical locations. Demographically 18% cases were from Peshawar Urban, 08% from Peshawar (Rural), 6% from Bara, 13% from Parachinar, 10% from Miranshah (Waziristan), 7% from Bannu, 5% from Dera Ismail Khan, 4% from Afghanistan 9% from Tribal areas 3% from Swat and 17% from Other areas. Age of the subjects ranged from 20 to 60 years. Mean age of these subjects was about 35.01 ± 8.39 years. Sixty subjects (60%) were in the age range of 20-35 years, 35 (35%) subjects were in the age range of 36-50 years and 05 subjects (05%) were above 50 years of age. Majority of subjects, i.e., 95 (95%) were of less than 50 years of age.

Parity of the subjects ranged from 3 to 14, with mean parity of 5.67 ± 2.27. Most frequently occurring (mode) parity was 6(21%), and median parity was 7(12%). Serum calcium levels were low in 48 (48%) subjects. Serum calcium levels of the whole sample ranged from 6.29mg/dl to 9.80mg/dl with mean values of 8.19mg/dl ± 0.7827. Most frequently occurring (mode) calcium values was 8.60mg/dl (12%), and median calcium value was 7.60mg/dl (3%). Serum calcium levels of the 48 hypocalcemic subjects ranged from 6.29mg/dl to 8.40mg/dl, with mean values of 7.51 mg/dl ± 0.5128.

DISCUSSION

Calcium regulation is critical for normal cell function, neural transmission, membrane stability, bone structure, blood coagulation, and intracellular signaling.[9] Abnormally low levels of calcium can occur in a variety of acute and chronic illnesses.[10] Hypocalcemia may vary from a very mild and asymptomatic biochemical abnormality to a severe life-threatening disorder depending on the duration, severity, and rapidity of development.[11,12]

The 100 subjects included in the study were having diverse ethnicity with vast variation in parent areas from where they belonged. Although it was not a community based study, demographically 18% cases were from Peshawar Urban, 08% from Peshawar (Rural), 6% from Bara, 13% from Parachinar, 10% from Miranshah (Waziristan), 7% from Bannu, 5% from Dera Ismail Khan, 4% from Afghanistan 9% from Tribal areas 3% from Swat and 17% from other areas.

Age of the subjects ranged from 20 to 60 years. Mean age of these subjects was about 35.01 ± 8.39 years. Sixty subjects (60%) were in the age range of 20-35 years, 35 (35%) subjects were in the age range of 36-50 years and 05 subjects (05%) were above 50 years of age. Majority of subjects, i.e., 95 (95%) were of less than 50 years of age. It may be due to marriages at relatively younger ages and lack of contraceptive practices leading to high parity, repeated pregnancies, lactation and calcium and other mineral losses.[7,13,14]

Karrison and colleagues compared average bone mineral density measurement of 73 lactating postpartum women with the bone measurement of 55 age-matched women who served as controls.

Mothers who were breastfeeding for duration of 1 to 5 months had decreased femoral neck bone mineral density by 2.0% +/- 1% during the first 5 months postpartum.[15]

In a population based study of residents near a cadmium smelter in china, forearm bone density was shown to density was decreased linearly with age.[16]

Parity of the subjects ranged from 3 to 14, with mean parity of 5.67 ± 2.27. Most frequently occurring (mode) parity was 6 (21%), and median parity was 7(12%). Pakistan, with an estimated population of 145-159 millions, is the seventh most populous country in the world.[17] It has a total fertility rate in excess of five births per woman which has shown a stubborn resistance to change.[13]

In another study a group of 39 multiparous with greater than 4 births was compared with a control group that consisted of 58 premenopausal women who had a maximum of two births. The results were controlled for differences in total fat mass and total lean mass. Lumbar bone mineral density was 7.6%+/- 0.1% and total bone mineral density was 3.9+/- 0.1% lower in women postpartum than in the controlled group.[15]

Serum calcium levels were low in 48 (48%) subjects. Hypocalcemia is encountered frequently in subjects. The incidence of ionized hypocalcemia is difficult to quantify, but it has been reported to be 15-50% for intensive care unit subjects.[18]

Serum calcium levels ranged from 6.29 to 9.80 with mean values of 8.19 ± 0.7827. Most frequently occurring (mode) calcium values was 8.60 (12%), and median calcium values was 7.60 (3%). Serum calcium levels of the 48 hypocalcemic subjects ranged from 6.29 to 8.40, with mean values of 7.51 ± 0.5128. The frequency as reported by Guise TA, and Prendiville S, was relatively low as compared to the present study.[19,20]

CONCLUSION

Asymptomatic hypocalcemia is a common condition in females with multiparity.

RECOMMENDATION

Screening and calcium supplementation is suggested to prevent osteomalacia.

REFERENCES

1. Holick MF, Krane SM. Disorders of bone and mineral metabolism. In: Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD eds. Harrison's Principles of Internal Medicine. 16th ed. New York: *McGraw Hill;* 2005; 2263-4.
2. Bushinsky DA. Electrolyte quintet: calcium. Lancet 1998; 352: 306-7.
3. Singer GG. Fluid and electrolyte management. In: Ahya SN, Flood K, Paranjothi S eds. The Washington Manual of Medical Therapeutics. 30th ed. Philadelphia: *Lippincott-Williams and Wilkins;* 2001; 64-5.
4. Drury PL, Howlett TA. Endocrine disease: disorders of calcium metabolism. In: Kumar P, Clark M eds. Clinical Medicine. 5th ed. London: *W.B. Saunders;* 2002; 1059-63.
5. Beckerman P, Silver J. Vitamin D and the parathyroid. *Am J Med Sci* 1999: 317: 363-9.
6. Hurley K, Baggs D. Hypocalcemic cardiac failure in the emergency department. *J Emerg Med* 2005; 28: 155-9.
7. Serenius F, Elidrissy AT, Dandona P. Vitamin D nutrition in pregnant women at term and in newly born babies in Saudi Arabia. J *Clin Pathol* 1984: 37: 444-7.
8. Toffaletti JG, Wildermann RF. The effects of heparin anticoagulants and fill volume in blood gas syringes on ionized calcium and magnesium measurements. *Clin Chem Acta* 2001; 304: 147-51.
9. Mundy GR, Guise TA. Hormonal control of calcium homeostasis. *Clin Chem* 1999; 45: 1347-52.
10. Rickels MR, Mandel SJ. Celiac disease manifesting as isolated hypocalcemia. *Endocr Pract* 2004; 10: 203-7.
11. Itani O, Tsang R. Bone disease. In: Kaplan LA, Pesce AJ, Kazimieczak SC, eds. Clinical chemistry: theory, analysis and correlation. 4th ed. Philadelphia: *Mosby* 2003; 527-8.
12. Fukagawa M, Kurokawa K, Papadakis MA. Fluid and electrolyte disorders. In: Tierney LM, McPhee SJ, Papadakis MA, eds. Current medical diagnosis and treatment. 44th ed. New York: *Appleton and Lange;* 2006; 876-8.
13. Siddiqi S, Haq IU, Ghaffar A, Akhtar T, Mahaini R. Pakistan's maternal and child health policy: analysis, lessons and the way forward. *Health Policy* 2004; 69: 117-30.
14. Durst R, Meirovitz A, Gross D, Kolker O, Muszkat M. Post-partum hypocalcemia: idiopatic hypoparathyroidism manifested early in lactation. *J Endocrinol Invest* 2002; 25:561-3.
15. Risk Factors for Osteoporosis J Midwifery Womens Health 2003; 48 (1): 39-54.
16. George KC. Osteoporosis and calcium metabolism. Bio Metals, 2004; 17 (5): 493-8.
17. World Bank. World development report 2004. Washington: *World Bank* 2004.
18. Zivin JR. Hypocalcemia: a pervasive metabolic abnormality in the critically ill. *Am J Kidney Dis* 2001; 37: 689-90.
19. Guise TA, Mundy GR. Clinical review 69: evaluation of hypocalcemia in children and adults. *J Clin Endocrinol Metab* 1995; 80: 1473-8.
20. Prendiville S, Burman KD, Wartofsky L. Evaluation and treatment of post-thyroidectomy hypocalcemia. *Endocrinologist* 1998; 8: 34-5.

ORIGINAL ARTICLE

COMPLICATIONS OF THE NASAL SEPTAL CORRECTIVE SURGERY

***Inayat Ullah, Sharafat Ali, Naseer Ahmad, Muhammad Yousaf, Arif Raza Khan**

*Senior Registrar, Department of Ear, Nose & Throat,
Khyber Teaching Hospital, Peshawar

ABSTRACT

Background: Septoplasty and Sub Mucosal Resection are the two techniques indicated for correction of symptomatic deviated Nasal septum (DNS). Both techniques carry its merit and demerits. An attempt is made to know the outcome of septal surgery including submucosal resection and septoplasty.

Research Methodology: This study was carried out in the department of ENT Govt. Lady Reading Hospital, Peshawar for a period of two years from July 1997 to July 1999. It included 180 patients. They were divided into two groups. Group A included 100 patients in whome SMR was performed and in Group B 80 patients were included who underwent septoplasty.

Results: Both the surgical procedures ended up with complications. In 8 patients (8%) of Submucosal Resection the septal perforation occurred compared to 2 patients (2.5%) in case of septoplasty. Nasal adhesion, excessive crust formation and recurrence of symptoms occurred in 5 patients (5%) each in SMR group, whereas it occurred in 2 patients each and recurrence in 4 (5%) patients in septoplasty group. The overall complications rate was 30% in SMR group and 17.5% in septoplasty group.

Conclusion: Complication are related to the type of procedure performed and are more common in SMR. Septal perforation is the commonest complication.

Keywords: Deviated nasal septum, submucosal resection, septoplasty, complication.

INTRODUCTION

Nasal septal surgery is one of the most commonly performed procedures in ENT practice throughout the world. The operation is indicated for correction of symptomatic deviated nasal septum (DNS), as part of septorhinoplasty, source of grafting material, epistaxis, and to obtain surgical access. The techniques used on the nasal septum are septoplasty and the classical submucous resection (SMR). Anterior septal deviation is commonly corrected by septoplasty while posterior deviation is treated with (SMR). If the DNS needs correction in children, septoplasty is performed because removal of septal cartilage interferes with subsequent development of the nose and maxilla.[1] In septoplasty minimal resection of the deviated parts of the septal cartilage is done after unilateral mucoperichondrial flap elevation. Spurs of the maxillary crest are removed. The bony septum is isolated and straightened when indicated. The procedure allows access to and manipulation of the entire nasal septum involving the caudal septum, dorsal margins of the septal cartilage, upper lateral cartilage, nasal spine and maxillary crest area. The septum is fired in the midline. The classical SMR involves removal of obstructing portion of the cartilaginous and bony septum while preserving adequate caudal and dorsal struts of the septal cartilage. In theory these struts preserve the supporting framework of the nose. Most of the authorities think that the operation for DNS should not be a single standardized procedure but should be tailored to the needs of the patients. The pathology of the septum varies from patient to patient and so should be the surgeon's technique. There are however some general principles cardinal to all types of nasal or septal surgery.[2,3] The complication may be due to an anaesthesia local and/or general related surgical procedure. The surgical complications are hemorrhage, septal haematoma/abscess, septal perforation, nasal adhesions, excessive crust formation, recurrence of symptoms, palatal perforation and intracranial complications. Certain complications are related with nasal packing.[4] The purpose of this study was to highlight the complications that can arise after nasal septal corrective surgery.

RESEARCH METHODOLOGY

This study was conducted at the department of ENT and head and neck surgery, Govt. Lady Reading Hospital, Peshawar over a period of two years from July 1997 to July 1999. One hundred and eighty patients with symptomatic DNS were selected randomly from both the sexes. They were all admitted to ENT department to undergo nasal septal surgery. The criteria for diagnosis were based on history, clinical examination and relevant investigations.

The inclusion criteria was

- Both sexes were included
- The obstruction was purely because of deviated nasal septum.

The exclusion criteria was

Patients with allergic rhinitis

- Patients with gross enlargement of inferior turbinate
- Any granulamatous disease in nose
- Patients with previous history of nasal surgery
- Having deformity at nasal bridge or columelar retraction.

On admission in the ward, each case was evaluated and the findings were recorded. Relevant investigations were done and the patient prepared for surgery. Local anesthesia alone was used in co-operative adult patients and both local and general anesthesia was used in children and un co-operative patients. All of them underwent nasal septal surgery according to the extent of pathology, septoplasty was performed in 80 patients below 16 years of age with caudal septal dislocation and adults with minimal deviation confined to cartilaginous septum. Classical SMR was performed in 100 cases. Intranasal splints cut from empty plastic infusions were put in all cases for 10 days. Anterior nasal packing was done in all patients for 24 hours. In all cases routine post-operative antibiotics, analgesics and antihistamines were given. Patients were discharged from the ward on second post-operative day. A follow up register was maintained in the OPD having entries of the patients included in the study. Follow-up register of these patients was maintained for 8 months.

Data was analyzed and described in terms of frequency.

RESULTS

Septoplasty was performed in 80 (44.4 %) cases and SMR in 100 {55.5%} cases. The age range was between 13 and 45 years. There were 110 {61.1%} males and 70 {38.8%} females. Local anaesthesia alone was given in 105 (58.3%) cases and both local and general anaesthesia was given in 75 (416%) cases. The overall surgical complications were observed in 44 (24.4%) patients. The complications were more frequently observed in SMR (30%) as compared to septoplasty (17.5 %). Details are shown in Table 1

DISCUSSION

In this study the frequency of overall complications after corrective nasal surgery was 24.4% (44). The primary hemorrhage occurred in 1.1% of cases. An about 150ml to 200ml of blood loss occurred in a single patient. Von-Shoenberg et al noticed that about 100ml of blood loss occurred in his series of 200 patients.[4] Reactionary hemorrhage usually occurs in about 7.1% of cases both after SMR and septoplasty.[5] It was noticed that SMR being more radical surgery, was associated with more bleeding.

Septal haematoma occurred in 2.5% of cases in this study. The blood is collected in between the two flaps in case of SMR and between the cartilage and mucosal flaps in case of septoplasty.

This collected blood between the flaps if prolongs will lead to atrophy and necrosis of septal cartilage.[6] Septal haematoma may organize and will lead to thickening of nasal septum or it may get infected leading to septal abscess. The septal abscess if left as such will cause necrosis of cartilage and nasal bridge

Table 1: Frequency of Complications after Nasal Septal Surgery

Complications	**SMR n =100**	**Septoplasty n =80**	**Total n =180**
Reactionary hemorrhage	1 (1 %)	1 (1.25%)	2 (1.1%)
Septal haematoma	3 (3 %)	2 (2.5 %)	5 (2.7 %)
Nasal adhesions	5 (5 %)	2 (2.5 %)	7 (3.8 %)
Septal perforation	8 (8 %)	2 (2.5 %)	10 (5.5%)
Excessive crust formation	5 (5 %)	2 (2.5 %)	7 (3.5 %)
Saddle nose deformity	2 (2 %)	0 (0 %)	2 (1.1 %)
Columellar retraction	1 (1 %)	1 (1.25%)	2 (1.1 %)
Recurrence of symptoms	5 (5 %)	4 (5.0 %)	9 (5.0 %)
Total	**30 (30 %)**	**14(17.5%)**	**44 (24.4%)**

depression, supratip depression and columelar retraction. Septal abscess is also a threat of extension of infection to orbit or cranial cavity.[7] Septal haematoma can be prevented by non apposing tears in the flaps and appropriate nasal picking.[8]

In our study 3.8% cases had postoperative nasal adhesions. The use of intranasal flaps has reduced the chances of adhesions, but still, they can develop if postoperative douching with nasal saline is not done properly.[8] Adhesions occur between the opposing raw surfaces of nasal septum and inferior turbinates especially if the mucosa has been injured during nasal packing.[10] Adhesion may interfere with respiration and cause disagreeable crustings. Septal perforation occurred in 5.5% cases. The main cause of septal perforation is intraoperative tears of mucoperichondriam. Small opposing bilateral tears or larger bilateral tears may not heal if they are not stitched property and end up in septal perforation.[11] Septal perforation usually causes no problem. Sometimes it produces whistling noises during inspiration, which are annoying to the patient. Larger perforation may be associated with crust perforation and bleeding from the edges of the perforation.

It may also lead to hypertrophy of the inferior turbinate resulting nasal obstruction.[12] Excessive crusting occurred in 3.8% of cases. Crust formation is a common problem after nasal septal surgery and some studies have shown a high frequency.[13] Saddling of nose a cosmetic deformation and columelar retraction occurred in 1.1% of cases. These complications occurred more in SMR group. It has been suggested that these complications may develop as a result of contraction which may take place over a period of may months even if adequate cartilaginous framework have been preserved. Lowering of the nasal dorsum occurs following septoplasty as well but is usually not significant.

Recurrence of deflection or deformation may be due to angulation or deforming of the neochondrogenesis in the septal area after submucos resection.[14] Persistant or recurrent nasal obstruction had been found to be a problem in 30% of the cases on a long term follow up of two years.

Nasal obstruction is done to unfavorable airflow pattern as a result of complication of residual septal deviation.[15] Some rare complications were also noted in the past like palatal perforation and intracranial spread of sepsis.[16] Fortunately in our study no rare complications occurred.

CONCLUSION

In the light of the results of our study as well as other studies, it can be concluded that the high incidence of complications still exists after the surgical correction of the deviated nasal septum. Classical SMR is associated with higher incidence of complications. Septal perforation is the commonest complication. It is recommended that the technique in each case of corrective nasal septal surgery should be tailored according to the pathology of nasal septum and care should be taken to avoid complications.

REFERENCES

1. Brain D. The Nasal Septum. In: Scott-brown's otolaryngology, Edited by Ken- AG, 5th Ed; London; butterworth and Co. 1987; 4: 159-179.
2. Beeson WH. The Nasal Septum. Otolaryngol, din North AM. 1987; 20 (4): 743-767.
3. Tardy Jr ME. Chronic rhinitis and Nasal obstruction. In Ballenger JJ ed. Diseases of the Nose, threat, ear, head and neck. 14th Ed. Philadelphia lea and firbiger, 1991; 24-78.
4. Vor-Schoenberg M, Robinson P, Ryan R. Nasal packing after routine nasal surgery. Is it justified?; J laryngol. Otol. 1993; 107 (10): 902-905.
5. Hinton AE, Buckley YJ, Blood loss and hematological consequences related to nasal surgery, Cline. Otolaryngology. 1990; 15 (3): 253-256.
6. Renner GJ, Management of nasal fractures. Otolaryngol. Clin. North. AM. 1991; 24(1): 192-212.
7. Price JC, Septoplasty: In Johns ME; price CP; mattox DE, eds: atlas of head and neck surgery. Philadelphia: BC. Decker, 1990; vol-1 109-120.
8. Zia MR; Butt MIH. Overview of septoplasty vis-a-vis SMR. Specialist, Pakistan's med. Sci 1996; 12 (3): 235-238.
9. Cook JA, Murrant NJ, Even KL, Lavelle RJ. Intranasal splints and their effects on intranasal adhesion and septal stability. Oto laryrgol. 1992; 17(1): 24-27.
10. Fairbanks DNF. Complications of nasal packing. Otolaryrgal. Head. Neck. Surg.1986; 94: 412-415.
11. Guyuron B, Michelow BJ. Management of entara - aqeratine nasal septal tears find perforations. As thetic. Plast. Surg. 1994; 18 (1): 61-63.
12. Korriloff DB; Nasal septal preparations and nasal obstructions clin. North. Am. 1989; 22 (2): 333-349.
13. Iqbal M, Mohibullah, Saeedullah, Septoplasty versus submucous resection in young adults. JPMI-1999. vol. 13 No.1: 109-112.
14. Agouodo DL, Monserrat JR, Pirero BP, Babales MEC, Gutierres R. Neochondrogenesis in the septal area after submucous cartilage resection. Auta otolaryngol 1992; 112: 539-44.
15. Low WK. Willet DJ. Submucous resection for deviated nasal septum a cortical appraisal. Singapore Med J 1992; 33:617-9.
16. Iqbal A, Mohammad and Nabil-ur-Rahman, Complications of the surgery for deviated nasal septum, JCPS 2003; Vol.13 (10): 565-568.

ORIGINAL ARTICLE

CASE BASED SERIES, OF PERCUTANEOUS ANTEGRADE STENTING FOR LOWER URETERIC OBSTRUCTION SECONDARY TO PELVIC MALIGNANCY

***Asif Malik, Sabina Aziz Asif, Hamid Hussain, JS Gellister**

*Associate Professor of Surgery, Khyber Teaching Hospital, Peshawar

ABSTRACT

Background: Uraemia caused by ureteric obstruction secondary to pelvic malignancy is a terminal event if left untreated. Palliative decompression of the obstructed urinary system by Percutaneous Nephrostomy or Ureteric stenting or combination of both is a recognized method of improving renal function with low morbidity. Antegrade stenting is preferred method because of its high success rate with minimum morbidity. Uthappa and Cowan suggest that antegrade stenting should be a preferred method of treatment if imaging shows tumour occlusion at ureteric orifices or if there is a tight stricture close to ureterovesical junction. This case series study was conducted to document the effect of antegrade stenting on improvement in the renal function without significant morbidity in cases of lower ureteric obstruction secondary to pelvic malignancy.

Research Methodology: Patients who presented with lower ureteric obstruction secondary to pelvic malignancy from Jan 1993 to Oct 1995 at Department of Urology, Edgware General Hospital, U.K. were included in this study. Patients who presented with ureteric obstruction secondary to any other cause were excluded. Percutaneous Nephrostomy was performed under local anesthesia with ultrasound guidance, followed by antegrade stent placement. Cook Urological stents were used in all 8 patients. Five patients had stents placed in a single setting (simple procedure). Stent placement was delayed in 3 cases due to failure to negotiate lower ureteric obstruction. These 3 cases were subsequently stented with cystoscopic assistance (combined procedure). Renal function was assessed before and after the procedure and the improvement was analyzed for statistical significance.

Results: Seven of the cases were male and 1 female. Mean age was 77.4±5.8 years. All cases of obstruction were secondary to urological malignancy. Approximately 63% (5 out of 8) were due to transitional cell cariconoma (TCC) Bladder; 25% (2 out of 8) were due to cancer (Ca) of prostate and a single case was due to both TCC Bladder and Ca Prostate. Pattern of ureteric obstruction did not appear to reflect underlying pathology. Renal function in 87.5% (7 out of 8) cases were abnormal prior to stent placement; Creatinine 508±305 mmol/L Urea 21.8±10.9 mmol/L. (Normal Range Creatinine 42-130 mmol/L; Urea 2.5-6.5 mmol/L). After stenting serum Creatinine significantly improved ($p < 0.05$). There was little or no change in serum urea. A single case had normal urea and Creatinine levels before and after stent placement, this was due to the presence of a normal unobstructed kidney. Patient were discharged within 2 weeks (Median 7.5 days; mean 9.75±5.8 days) after the procedure was performed. Antegrade stent were left in situ for median time of 13 weeks (mean was 26.4±29 weeks), only a single stent was changed and replaced at 14 weeks. The median time patients survived after stenting was 28 weeks. At the time of death 63% (5 out of 8) died with stent in situ, the remaining 37% (3 out of 8) had no stent at time of death because their primary disease had been treated.

Conclusion: Antegrade stenting can be a permanent or temporary solution to lower ureteric obstruction secondary to pelvic malignancy. It is safe and effective. It improves renal function and has minimal post procedural complications. In our case-series only a single patient was readmitted for change and replacement of ureteric stent at 14 weeks. It may be suggested that a functional stent may be left in situ longer than current practice of replacing it in 16-24 weeks as recommended by manufacturers.

Keywords: Ureteric stents, antegrade stents, urinary diversion appliances, malignant ureteric obstruction, pelvic malignancy and elderly.

INTRODUCTION

Gustav Simon first reported ureteric stenting in the 19th century when he placed a tube into the ureter while performing an open cystostomy[1]. The first purpose designed ureteric catheter was devised by Joaquin Albarrano.[1,2] In the late 1960, ureteric stenting became more commonplace, long-term stents were being made out of silicon, the main drawback of these stents was that they migrated easily[2]. Gibbon in 1967 described a silicon stent, which had multiple barbs along its shaft and a flange at its distal end.[3] The disadvantage of this stent was that the outer diameter was relatively large making placement difficult, the inner diameter was small making urine flow relatively poor. Also the flange and barbs failed to prevent the migra-

tion of stent. The development of double J Stent in 1978 was a technological breakthrough.[4,5]

Antegrade ureteric stenting is a safe procedure. However recognized complications include infections and hemorrhage and occasionally urinoma formation[7,8]. Despite these complications, the procedure is normally very safe. Percutaneous, antegrade stenting is a well documented method of reliving lower utreteric obstruction especially with regard to pelvic malignancy.[9,10] This case series study was conducted to document the effect of antegrade stenting on improvement in the renal function without significant morbidity in cases of lower ureteric obstruction secondary to pelvic malignancy.

RESEARCH METHODOLOGY

This quasi-experimental study was carried out at Edgeware General Hospital, (Edgeware) UK from January 1993 to October 1995. Eight consecutive cases in this time period who presented with lower ureteric obstruction secondary to pelvic malignancy were included in this study. Patients who presented with ureteric obstruction secondary to any other cause were excluded. The following parameters were recorded.

i) Serum Creatinine
ii) Serum Urea
iii) Length of Hospital Stay
iv) Duration of Stent Placement (time stent was left in situ)
v) Survival After Stent Placement

Percutaneous nephrostomies were carried under local aneasthesia with ultrasound guidance. The middle pole of the calyx of the kindly was punctured using an 18 gauge cyst puncture needle and 0.035 guide wire was passed into renal pelvis. Nephrostomies were followed by antegrade stenting. All patient received antibiotic cover and were sedated with pethidine and intravenous diazepam for stent placement. Cook Urological antegrade ureteric stent were placed, diameters varied from 8.4-10.4 French and length from 23-26cm. A GE SFX fluoroscopy Unit with a C-arm facility was used for image guidance in all the cases. Five patients had stents placed in the first setting (simple procedure). Stent placement was delayed in three patients because the lower ureteric obstruction could not be negotiated with the stent after the guide wire was passed into the bladder, subsequently a combined procedure was undertaken. The patients were given general anaesthesia or deep sedation, then the guide wire was grasped through a cystoscope inside the bladder and delivered per urethrum. The stent was then passed retrogradely back up the wire, which was tensioned by traction at both ends. The sex of patient, the type of primary pathology, type of obstruction and renal functions were assessed before the procedure and approx 6 weeks after the procedure.

The parameters checked prior to start of intervention were again recorded. T-test was used to calculate statistical significance for interval scale parameters. Mean and median values were calculated for parameters recorded post intervention.

RESULT

Out of all our cases; 7 were male and 1 female. The mean age was 77.4±5.8 years. All cases of obstruction were secondary to urological malignancy. Approximately 63% (5 out of 8) were due to transitional cell carcinoma (TCC) bladder; 25% (2 out of 8) were due to cancer (Ca) of prostate and single case was due to TCC bladder and Ca prostate. Pattern of uteretric obstruction did not appear to reflect underlying pathology.

Table 1: Renal functions before and after stent placement

	Pre intervention	Post intervention	P value
Creatinine (mmol/L)	Mean 508±305 Median 426	Mean 206±96 Median 200	.049
Urea (mmol/L)	Mean21.6±12 Median 19.2	Mean 14.±10.4 Median 10.8	> 0.05

Table 2: Post procedural hospital stay and status of stent at time of death

Number of patients	Length of Hospital stay after procedure (days)	Duration of stent placement (weeks)	Survival after stent placement (weeks)
8	Mean 9.75±5.8 (< 2 weeks) median**** 7.5	Mean 26.4±29 Median 13	Mean 37.5±34 Median 29

Five patients had antegrade stents placed in a single setting (simple procedure) and 3 patients had stents placed with cystoscopic assistance (combined).

The Renal functions expressed in term of serum creatinine and urea determine before and after the intervention is shown in Table 1.

Post procedural parameters expressed as length of hospital stay duration of stent placement and survival time are shown in Table 2.

DISCUSSION

Palliative decompression of urinary system, either by percutaneous nephrostomy (PCN), ureteric stent or a combination of both is a recognized method of improving renal function, with low morbidity.[19] In a study conducted by Sharma et al.[21], antegrade stenting is recommended as a temporary or permanent solution to ureteric obstruction. The technique is safe, acceptable to patients and avoids the need for general anesthesia. Similarly in our study approximately 63% (5 out of 8) of our patients had stents placed in a single setting under local aneasthesia. Only 3 required general anesthesia. In our case series the success rate for stent placement was 100%. Stents were placed in all 8 cases, only one stent required change after 14 weeks and was replaced. The overall success rate in other studies[19,21] for antegrade stent insertion was 83%. Failure was greatest (4 out of 6) in cases of ureteric injury following gynaecological procedure. In another study conducted in 2002, endoscopic retrograde stenting had success rate of 21%, whereas two-stage procedure (i.e. Percutaneous Nephrostomy followed by antegrade ureteric stenting) was successful in 98% of patients[20] Uthappa MC and Cowan NC had a success rate of 96% when antegrade placement was attempted in 25 ureters. In our case series none of the patients experienced any major complications, similar to other studies.[20,21,22] Renal functions improved in (7 out of 8) cases who had stent placements, there was significant fall in serum creatinine levels, with little or no change in serum urea. Tanagho and McAninch state that endogeous creatinine clearance test has become the most accurate and reliable measure of renal function.[23] An elevated blood urea nitrogen level is less specific, because approximately two-thirds of renal function must be lost before a significant rise in blood urea nitrogen level becomes evident. A single case had normal renal functions before and after stent placement. This case had a normal functioning (right) kidney.

In our case series the median length of hospital stay was under 2 weeks (7.5 days). Only one stent was changed at 14 weeks and replaced. Approximately 63% of patients (5 out of 8) died with stents in situ, whereas 37.5% (3 out of 8) had no stents in place at time of death. Stent were removed in these three cases because the primary malignancy which was transitional cell carcinoma (TCC) of the bladder was treated with transuretheral resection of the bladder tumour and radiotherapy. All three cases had muscle invasive disease.

The mean survival time after stents were placed was 29 weeks. Similar studies[19,20,21,22] document that antegrade stent placement has short hospital stay, low post procedural complications and improves renal function. However long-term survival is limited, and it is a palliative measure[19].

Most manufacturers recommend that stent should be replaced in 16-24 weeks. However studies[16,17] do show stent placement time of 40-72 weeks, for biocompatible co-polymer ureteric stents which are safe without significant complications. In our case-series the mean time stent remained in situ was 13 weeks, which complied with manufacturers recommendations; However approximately 25% (2 of 8) of the cases in our series had stents placed for more than 24 weeks and they did not experience, any complication related to the stent.

CONCLUSION

Percutaneous antegrade stenting can be beneficial to most patients with malignant ureteric obstruction resulting in safe urinary diversion with improvement of renal function. It may also be suggested that stents may be left in situ for periods longer than 16-24 weeks as recommended by manufacturers. The patients should be reassessed clinically rather than using stent placement time (stent dwell time) as a single indicator for replacement.

REFERENCES

1. Herman JR A Urinary diversion appliances: J Urol 70; 551: 1973.
2. Zimskind PD. Clinical use of long term indwelling silicone rubber ureteral stents injected cystoscopically. J Urol 97: 840: 1967.
3. Gibbon RP. experience with indwelling silicon rubber ureteral catheters. J Uroll III; 594: 1976.
4. Finney RP. Experience with new JJ ureteral stents. J Urol, 120: 678; 1978.
5. Hepperlen TW. Self retained internal ureteral stents. A new approach. J. Urol; 119: 731: 1978.
6. Camacho MF. Double ended pigtail ureteral stent. Useful modification to single end ureteral stents. Urology; 13: 516: 1979.
7. Cowan NC, Cafferty IMC. Malignant ureteric obstruction; ante grade or retrograde stent placements. British society of interventional urologists. Annual general meeting Glasgow UK 1998.
8. Patel U. Primary ante grade ureteric stenting, success rate, cost advantage, and technical factors. British society of interventional urologists. Annual general meeting. Glasgow UK 1998.

9. Law MW, Temperely De. Urinary tract obstruction and nephrostomy drainage in pelvic malignant disease. British journal of urology November 1995 76 (5): 565-9.

10. Desportes L, Blanchet P. Neoplastic ureteral obstrucion drainage by percutaneous nephrostomy or double J catheterization. Press Med October 1995.

11. Chye RW, Lickis JN. Palliative care in bilateral malignant ureteric obstruction. Annals of the academy of medicine, Singapore, March 1994; 23 (2): 197-203.

12. Abramson AF, Mitty HA. Update on Interventional treatment of urinary obstruction. Uro Radiol 1992; 14; 234-6.

13. Andriole GL, Bettman MA. Indwelling double J ureteric stents for temporary and permanent urinary drainage: experience with 87 patients. J Urol 1994; 131: 239-41.

14. Zadra A, Jewett MAS. Non operative urinary diversion for malignant ureteral obstruction. Cancer 1984: 142: 831-2.

15. Mitty HA. Ureteral stenting facilitated by ante grade transurethral passage of a guide wire. Am J Radiol 1984: 142: 831-2.

16. Cardella JF, Castaneda-Zuniga WR. Urine compatible polymer for long term ureteral stenting. Radiology 1986: 161: 313-18.

17. Rackson ME, Mitty HA. Biocompatible copolymer ureteric stent; maintenance of patency beyond 6 months. Am J Radiol 1989: 153: 783-4.

18. Lee WJ, Patel U. Complications of the universal ureteral stent. Cardiovasc Interyen Radiol 1990: 12: 329-33.

19. Wilson JR, Urmn GH, Slower MJ. The role of percutaneous nephrostomy in malignant ureteric obstruction, Ann R Coll Surg Eng 2006 May; 88 (3): 336.

20. Chita SV, Scott BLS, Ho ET, Burgess NA. The management of ureteric obstruction secondary to malignant pelvic disease. Clin Radiol. 2002 Dec, 57 (12): 1118-21.

21. Sharma SD, Persad RA, Haq A. Appleton DS. A review of antegrade stenting in the management of the obstructed kidney. Br J Urol. 1996 Oct; 78(4): 511-5.

22. Uthappa MC, Cowan NC. Retrograde or antegrade double-pigtail stent placement for malignant ureteric obstruction. Clin Radiol. 2005 May, 60 (5) 608-12.

23. Tanagho A, Ened MC, Aninch W. Smithy General urology, 15, Edition McGraw-Hill, Page 61.

ORIGINAL ARTICLE

FREQUENCY OF PLACENTAL ATTACHMENT ON SCARRED UTERUS

***Nighat Shaheen, Abida Nasreen**

*Consultant Gynaecologist, District Hospital, Charsadda, NWFP

ABSTRACT

Background: Placenta Praevia is that placenta which is attached in the lower uterine segment and being cause of significant maternal and fetal morbidity and mortality, it is important to know its causating factors. The objective of this study was to know the prevalence of Placenta Praevia in scarred uterus.

Research Methodology: This study was conducted at department of Obstetrics and Gynaecology, Govt. Lady Reading Hospital, Peshawar from January 1997 to December 1997. 85 patients with previous scarred uteri (due to lower segment Caesarean Section) were analyzed for site of placental attachment.

Results: In total of 6200 obstetrical admission, 3230 deliveries occurred. (Including both abdominal and vaginal). Total Caesarean Section were 601 and of these 86 (14.3%) were done for placenta Praevia and 87 Caesarean Section (14.4%) were done for previous scar in uterus. Placenta Praevia on previously scarred uteri were 7 (8%) and of these 3 were morbidity adherent (accreta). The incidence of placenta Praevia in previous Caesarean Section scar increases as the No. of cesareans increases i.e. 14.28% in previous one Caesarean Section, 28.5% in previous two Caesarean Sections and 57.1% in previous three and more Caesarean Sections.

Conclusion: The relationship of scarred uteri and placent Praevia is established. And the greater the no of scars in uterus more are the chances of placenta Praevia.

Keywords: Placenta Praevia, scarred uterus, accreta.

INTRODUCTION

Placenta Praevia is defined as placenta that is attached to the lower part of uterus instead of upper uterine segment.[1] It is the cause of significant blood lost and life endangering emergency in obstetrics. Causes of Placenta praevia are frequently unclear. It may merely be accidental in nature, commonly, encountered in multiple pregnancies,[3] and defective decidual formation. Other associated conditions includes implantation of placenta over a previous uterine scar. The previous uterine scar may be either due to previous Caesarean Section, due to myomectomy, metroplasty, hysterotomy or uterine curettage.

Endometrial myometrial damage is the main factor for aetiology.

The goal of this study was to find out relation between a scarred uterus & placenta praevia. And also to find influence of increasing no's of scars over this relation.

RESEARCH METHODOLOGY

This was a prospective descriptive study carried out in obstetrics and gynaecology unit "A" of PGMI LRH Peshawar from January 1997 to December 1997 and 87 patients with previous scarred uterus were analyzed for placental attachment. The following was the inclusion criteria.

1. Clinical and ultrasound evidence of placenta praveia.
2. Previous history of lower segment caesareans section.

Following was the exclusion criteria:

1. Any of the above who were delivered vaginally.
2. Any of the above who had twin or triplets pregnancy.

A proforma was made in which all the details of history, examination, investigations, deliveries, operative findings, post operative complications and post partum period were carefully recorded. Total number of hospital deliveries, total lower segment caesarean section and total episodes of antipartum hemorrhage due to placenta Praevia were recorded. Both booked and unbooked patients were included. The patients were particularly enquired about age, parity, previous caesarean section, the number of previous caesarean sections, interval between last caesarean section and subsequent pregnancies, for placental attachment on scared uterus, only pregnancies with singleton fetus were included in the study.

The method of diagnosis of placental attachment and localization was made by clinical findings and ultrasonography and from operative findings at caesarean section.

The diagnosis of abnormal placental adherence was made at the time of Caesarean Section when there was difficult manual piecemeal removal of Placenta.

All the patients delivered by lower segment cesarean section received liberal blood transfusion, preoperative and postoperative antibiotics.

RESULTS

During the study time period of one year, a total of 87 women underwent caesarean section for previous scar on uterus and among these, placenta praevia was found in 7 women giving a frequency count of 8% and an annual incidence rate of 80 per 1000 women with scarred uterus. The rest of demographic and clinical details of these 7 cases are shown in Table 1.

DISCUSSION

When placenta is situated wholly or partially within the lower uterine segment at or after 24 weeks of gestation then it is called placenta Praevia.[2]

Scarred uterus is one of the leading cause of placenta Praevia. It is also reported by different workers at different times and places that incidence of placenta Praevia increases if the incidence rate of caesarean section increases, as caesarean section is the most important cause of scarred uterus. The uterine scar provides a focus for lower placental implantation.

Our study showed a very high incidence (one in 12 women with scarred uterus) of placental attachment on scarred uterus, which is not comparable with any study performed in the world, even with those studies performed in Asian countries.[4,5,6,7,8]

Because of rising rate of caesarean section in modern obstetrics, the proportion of the scarred obstetric population is increasing, so overall incidence of placenta Praevia also increases. This conclusion is

Table No.1: Demographic Characteristics (N=5)

Total No. of patient = 87

No. of patients with placental attachment on scar = 7 (8.004%)

S. No.	Admission	Number	Percentage %
1.	Admission status		
	Booked	3	42.8%
	Unbooked	4	57.2%
2.	Parity status		
	P1 &2	1	14.2%
	P3&4	3	42.8%
	P5 & above	3	42.8%
3.	Age		
	< 30 years	2	28.5%
	>30 years	5	71.4%
4.	Mode of delivery		
	Elective cesarean section	2	28.5%
	Emergency cesarean section	5	71.4%
5.	Diagnostic method for placenta Praevia		
	Clinical findings + EUA	2	28.5%
	Ultra sound	5	71.4%
	Surgically	7	100%
6.	Incidence of morbidity adherent placenta		
	Normal placental attachment on scar	4	57.14%
	Morbidity adherent placenta (accreta)	3	42.85%
7.	No of previous lower segment caesarean section scar		
	Previous 1 caesarean section	1	14.28%
	Previous 2 caesarean sections	2	28.5%
	Previous 3 & more caesarean sections	4	57.1%

Table No.2: Comparison of Incidence of Placenta Praevia in Scarred Uterus in different Studies

S. No.	Study conducted	Year	Place	Placenta Praevia incidence on scarred uterus
1.	Our study	1997	Peshawar	8:00%
2.	Rakushan Shaheen	1996	Lahore	5.75%
3.	Obed & Yand adeqok[4]	1996	Nigeria	3.8%
4.	Zaidh SM et al[5]	1995	Jordan	1.87%

evident from our results (Table 1) and also noticed by Zaideh S.M, Abu Heija A[5] and Shaheen[7].

So it could be assumed that the presence of scars in uterus is the triggering event for pathogensis of placenta Praevia in these patients as long as scar remains there, the risk will therefore, always exist.

Another important aspect highlighted in one study was the danger of pathological placental adherence in cases having combination of placenta Praevia and scarred uterus (42.8%) and was also noted by other's mentioned in (Table 2). Advance maternal age and parity was also founded to be a risk factor (Table 1). These findings were also observed by other authors.[4,6]

Placenta implanted in lower part of uterus tends to migrate to upper uterine segment during 2nd and 3rd trimester, owing to the development of lower uterine segment. This process of the placental migration is less likely if placenta is posterior,[9] or if there has been a previous caesarean section scar.[10] Repeated uterine instrumentation was associated with an increase risk of placenta praevia.[11] The relationship between endomyometrial injury and placenta accreta remains unclear, however the number of women requiring manual removal of placenta were higher with the previous history of instrumentation.[12]

CONCLUSION

Our conclusion is that the incidence of placental attachment on scarred uterus is quite higher, due to increasing incidence of caesarean section in modern obstetrical era which is the commonest cause of scarred uterus. There is linear relation ship between placenta Praevia and the number of prior incisions in the uterus and abnormal placentation including, accreta, increta, percreta has strong association with placenta Praevia and scarred uterus. Patients with an antipartum diagnosis of placenta Praevia who have had a previous caesarean section should be considered at high risk of developing placenta Praevia and accreta and all patients especially those with previous history of surgery on uterus must be regularly followed up in antenatal clinics.

ACKNOWLEDGMENT

Special appreciation is expressed to Mr. Gohar Said Uninet Computer Services for his help in typing and giving a final shape to this paper.

REFERENCES

1. Lewis TLT, Chamber lain GVP. Abnormal pregnancy. Obstetrics by Ten Teachers, 15th ed, 1990; Edward Arnold, Kent; 80-81.
2. Penna LK, Pearce JM; Placenta Praevia progress in obstet. Gynaecol, vol II, 1994; 161-181.
3. James P. Antepartum hemorrhage. Deuherst textbook of obstetrics and gynaecology 5th ed, 1995; Black Well London, 164-74.
4. Obed JY. Placenta Praevia. A late sequela of previous lower uterine segment caesarean section scars, as manifest in subsequent pregnancies; J Obstet. Gynaecol, Eastern and central Africa, 1996; 12(1): 15-17.
5. Zaideh SM, Heij A. et al; Placenta Praevia and accreta; Gynaecol. Obstet. Innes, 1998 Aug; 46 (2): 96-8.
6. Najmi RS. Association between previous caesarean section and occurance of placenta Praevia and pathological placental adherence. J Coll P. Surg Pak, 1996; vol 6 (5): 262-264.
7. Bender S. Placenta Praevia and previous lower segment caesarean section surgery; Obstetrics and Gynaecolgoy. 1998; 625-628.
8. Singh PM, Rodrigues C, Gupta AN. Placenta Praevia and previous caesarean section; Acta Obstet Gynaecol scand, 1981; 60: 367-8.
9. Royal College of Obstetricians and Gynaecolgists Green top guideline. Placenta Praevia and placenta accreta. Diagnosis and management. Guideline No. 27. London RCOG 2005.
10. Uszynski W, Uszynski M, Placenta accreta; epidemiology, molecular mechanisms, (hypothesis) and some clinical remarks. Ginek Pol 2004; 75: 971-8.
11. Rose GL, Chapman MG. Aetiological factors in placenta Praevia a case controlled study. BrJ Obstet Gynaecol, 1986; 93: 596-8.
12. Beuker JM, Erwich JJ, Khong TY. Is endomyometrial injury during termination of pregnancy or curettage following miscarriage the precursor to placenta accreta? J Clin pattol. 2005; 58: 273-5.

Original Article

A CRITICAL APPRAISAL OF THE OBSTETRICAL CORRELATES OF CESAREAN SECTION RATE AT A TEACHING HOSPITAL

***Gulrukh Qazi, Shahnaz Akhtar**

*Assistant Professor, Department of Obstetrics & Gynaecology,
Lady Reading Hospital, Peshawar

ABSTRACT

Background: The aim of this study was to examine the trend in cesarean section deliveries and to obtain an estimate of the indications and consequences of cesarean sections recruited from unit "A" of the Department of Ob/Gynae, PGMI, Lady Reading Hospital, Peshawar.

Research Methodology: Information was obtained on cesarean deliveries during one year period, from 1st Jan- 31st Dec 2005. In this study, data were recorded on 817 consecutive cesarean sections with regard to the obstetrical variables, indications, associated complications and materno-foetal morbidity and mortality. A hospital-based maternal health data was used from history records and direct interviewing of the patients and information were recorded for all the cases on structured proformae. The data analysis included simple proportions and rates.

Results: The overall frequency of cesarean section was 13.62%. Among the 817 cesarean section cases, 25.3% were primigravidas, 30.7% had come from rural areas, 20.8% were referred including 11.6% with history of interference. 10.5% were booked cases, period of gestation was less than 37 weeks in 22% and in 16.4% the surgery was elective. Major indications for cesarean section included dystocia 48%, fetal distress with or without meconium aspiration 14.9%, repeat section 19.6%. malpresentations 25.2% and PIH 6.5%. Maternal and perinatal mortality was 979/100 000 and 128.5/1000 deliveries, respectively, and is high despite high cesarean section rate. There was incomplete information for some of the variables in some cases.

Conclusions: There is a need for effective implementation of strategies for standardized collection and compilation of relevant data on all aspects of childbirth. This is to ascertain the incidence and indications of cesarean section so that comparison and improvements of care can take place at a national level and to reduce the cesarean section rate.

Keywords: Cesarean section; Indications; Complications.

INTRODUCTION

Cesarean delivery has been practiced for ages, although originally as a universally postmortem procedure. Since the Renaissance, the objective of the procedure has gradually shifted towards saving the lives of both the mother and the child, and this has become even more possible, as maternal and perinatal mortality and morbidity decreased significantly during the twentieth century[1]. Caesarean section is a major obstetric operation that remained a matter of controversy for several years and gained popularity in recent decades with a dramatic rise in its rate all over the world especially over the past three decades both in the developed[2] and in the developing world[3,4,5]. The reasons for this marked increased has not been completely evaluated but the possible explanations are, electronic fetal monitoring which helps in early detection of fetal distress resulting in increased number of caesarean deliveries, most of the breech deliveries by caesarean section, falling trends of forceps deliveries and social reasons. This has been a cause of concern to both the profession and the public as it increases the health risks for mothers as well as the cost of health care compared with normal deliveries[6]. Globally efforts are ongoing to evaluate interventions to curtail this as the WHO[7] recommends that a cesarean section rate of more than 15% is not justified. Ensuring safe pregnancy and motherhood occupies a pivotal role and is considered as one of the key issues in the framework of reproductive and child health programs. Unjustified cesarean deliveries are an undesirable burden on scarce resources in this country where more than half of the deliveries take place at home due to lack of adequate and accessible obstetric care. It is crucial to analyze the factors responsible for apparently high caesarean section rate and to assess maternal morbidity and mortality as well fetal outcome after caesarean section.

It was, therefore, deemed necessary to obtain an estimate of cesarean delivery rate and examine the indications and consequences in a unit at a teaching hospital.

RESEARCH METHODOLOGY

This study was conducted during the year 2005 from January 1st to December 31st in unit "A" of the Ob/Gynae Department of Lady Reading Hospital. Post Graduate Medical Institute, Peshawar, NWFP, Pakistan. A hospital-based maternal health data was used from history records and direct interviewing of the patients and information was obtained on a total number of cesarean deliveries during the study period. Data were recorded on structured proformae. Thus, a total of 817 cesarean sections, carried out during this period, formed the study sample. The data analysis included simple proportions and rates.

RESULTS

A general and clinical profile of the cesarean delivery cases for the study sample is shown in Table 2, although there was incomplete information for some of the variables in some cases. The average age of women delivered by cesarean was 28.93±5.22 years. The annual rate of caesarian section for the study period is shown in Table 1. Booking status and referrals has been depicted in Fig. 1. The referred cases from government and private sectors are further shown in Fig. 2.

Approximately 51.9% of the women were already in labor at the time of admission to the hospital. This included 11.6% of cases with a history of interference. The maximum number of interference was noted by the private doctors and traditional birth attendant as shown in the Table 2. Cephalic presentation was found in almost 90% of these women.

Indications for cesarean section are shown in Table 3, which have been analyzed in ten broad categories. Others indications, in Table 3 included cesar-

Table 1: Rate % of cesarean sections including current study sample in Gynae 'A' Unit in the last decade

Year	Total Deliveries	% C.S
1997	2327	28.1
1998	3143	15
1999	4802	12.18
2000	3625	17.43
2001	3974	18.17
2002	4657	14.75
2003	4463	16.13
2004	5072	13.80
2005	6000	13.62

Table 2: Profile of cesarean section cases

Parameters	No.	%
Age (in years)		
<20	4	0.5
20-24	129	16
25-29	289	35.3
30-34	216	26.4
>35	179	21.9
Gravida		
1	207	25.3
1+	610	74.7
Place of residence		
Rural	261	38.9
Urban	424	61.1
Type of cases		
Booked	86	10.5
Unbooked	727	89
Not known	0.4	0.5
Place of referral		
Not referred	647	79.2
Referred from		
PHC*	49	6.0
Government Hospital	62	7.6
Maternity Hospital	12	1.5
Private Hospital	47	5.7
Delivery attempted by:		
Family/relative	11	1.4
Traditional birth attendant	32	3.8
Female paramedical worker	11	1.4
Doctor	41	5.0
Not referred/not attempted	722	88.4
Time of admission		
Antenatal	377	46.2
In labor	424	51.9
Not recorded	16	1.9
Period of gestation		
<37 weeks	177	22.
37+ weeks	620	76.
Not recorded	20	2
Presentation		
Cephalic	729	89.2
Non-cephalic	88	0.6

*Primary Health Center

Table 3: Indications for cesarean delivery

Indication Category	% women para 1 with indications	% women para 2+ with indications	% women with indications
	n=321	n=496	n=817
Previous > 2 sections/Uterine surgery	0.3	17.9	19.6
Dystocia/CPD	47.1	48.5	48
Obstructed labour	21.3	21.9	21.7
Fetal distress	18.2	12.8	14.9
Mal presentation	24.5	25.5	25.2
PIH/Eclampsia	9.3	4.7	6.5
Failed induction	9.8	3.8	6.2
APH	11.4	22.2	17.9
Medical causes	0.1	0.2	0.2
Others	1.1	0.9	1

Percentages total more than 100 because of more than one indication.

Table 4: Procedures, complications and outcome of cesarean delivery cases

	No.	%
Type of CS Elective	138	16.4
Emergency	683	83.6
Type of anesthesia G.A.	675	82.6
Spinal	23	2.8
Epidural	13	1.6
Not recorded	106	13
Outcome of pregnancy Live birth	726	88.9
Still birth	91	11.1
Complications Anesthetic	5	0.6
Surgical	63	7.7
Post-operative	42	5.1
Blood transfusion	54	6.6
Mortality Maternal	8	Rate/1000 9.79
Perinatal	105	128.5

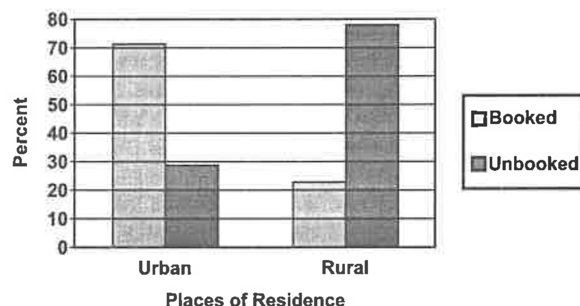

Fig. 1. Percentage of booked cases among cesarean sections with respect to urban and rural population.

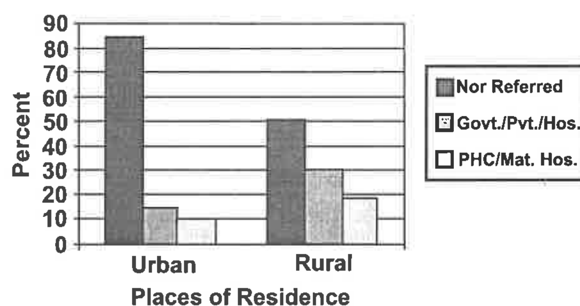

Fig. 2. Percentage distribution by place of referral with respect to urban and rural population.

ean section for high-risk situations like PROM, post dated pregnancy, precious pregnancy, elderly primigravidas and previous bad obstetric history and low biophysical profile of the baby. The majority of the women had cesarean section for more than one indication. On the whole, repeat section/previous uterine

surgery was one of the indications for cesarean delivery in 19.6% but alone it accounted for only 11% of the cases. The average duration of hospital stay for cesarean section was 5.9±2.9 days where most of the patients were discharged on third day. Duration of hospital stay was more than a week for about 20% of the cases as these women came from far off places and were only discharged after the skin stitches were removed on day 8-9.

Procedures, complications and outcome of cesarean section are shown in Table 4. Anesthetic complications included severe hypotension, reintubation, misplacement of endotracheal tube, delayed recovery from anesthesia, uterine atony, one in each case. Surgical complications included tear of uterine angle 3.4%, excessive bleeding 2.4%, and broad ligament hematoma 1.7%, bladder injury 0.2%. Postoperative complications were observed in the form of UTI, PPH, puerperal pyrexia, wound sepsis, respiratory infection, paralytic ileus, septicemia, multiple organ failure and deep venous thrombosis. The causes of 8 maternal deaths included hemorrhage in 4 cases, amniotic fluid embolism, septicemia, eclampsia, and adult respiratory distress syndrome one in each case. There was no death due to anesthetic complication. The perinatal mortality was 128.5/1000 cesarean births.

DISCUSSION

Increasing specialization, anesthesia, availability of blood transfusion and skilled neonatal intensive care has lowered the overall threshold of performing cesarean section leading to an alarming increase in abdominal delivery[2]. A variable and high rate of cesarean section was observed during the last decade in Gynae "A" unit, which ranged from 12.18 % to 28.1 % (Table 1) including 13.62% for the present study 2005. This is not associated with women's positive attitudes toward cesarean section but the main cause of this trend of cesarean section rates may have its origins in health care practitioners and the health care system in which they work as shown by other studies as well[8]. Some of the above figures are almost the same, 13.7% as observed from10 similar hospitals in the early 1980s in India[9]. Moreover this estimate of cesarean section rate from a tertiary level public hospital, however, may not reflect the true picture, as even in the developed world the proportion of cesarean sections in private hospitals is higher than that seen in public sector hospitals[10,11,12]. This trend may be a reflection of the present malpractice crisis. This is definitely a matter of concern for both policy makers and medical professionals.

In the suburbs of Peshawar, more than 50% are home deliveries and only high risk cases are referred to the tertiary hospitals contributing to the increase in cesarean delivery rates. It was observed that on the whole there were significantly more booked cases among women coming from urban areas (71.2%) as compared with those from rural areas (22.4%) Fig. 1. Hence, as expected the referrals were higher among women coming from rural areas (48.9%) as compared with those from urban areas (15.7%).These referred cases from government and private sectors are shown in Fig. 2.

Increase in cesarean delivery also raises questions about the considerable financial implications involved. The cost of cesarean section was either borne by the hospital or by the patient herself if the hospital stores could not meet the requirements for operation.

This country has enormous medical needs, but if scarce resources are being used inappropriately, it raises not only economic but ethical issues.

Worldwide efforts are ongoing mainly by USA. Italy and WHO to evaluate interventions that could bring about a reduction in cesarean delivery rate[13,14,15]. In this study, we found that on the whole repeat section contributed to 19.6% of the cases. The efficient way to lower the repeat cesarean rate is trial of labor in women having a previous caesarean section. Several studies including one in Zimbabwe indicated that 33-75% of all women with previous cesarean delivery can be delivered vaginally particularly if the cesarean has been for a non-recurring indication with a smooth postoperative recovery[16,17]. A Meta analysis, showed a small increase in the perinatal mortality and uterine rupture among women undergoing a trial of labor than among those undergoing elective repeat cesarean delivery but no difference was found in maternal mortality risk between the two groups while some authors suggested increased risk of maternal death in elective caesarean sections[17,18]. Maternal morbidity, including febrile morbidity and the need for transfusion or hysterectomy may be reduced with a trial of labor[16,18]. But at the same time an optimal decision for a trial of labor or a repeated cesarean section is substantially determined by the wish for future pregnancies[19].

Overall morbidity rises continually with each successive CS[20]. Utero-cervical lacerations and massive hemorrhage were the most frequent Intraoperative complications in the present study. Expertise of the operator is of utmost importance in such cases, as also agreed by other authors[21,22].

Moreover self-evaluation of obstetricians by delivery data of each obstetrician could significantly reduce the cesarean section rate. The implementation of this strategy may result in saving a lot of national expense and also improving the standard of care in obstetrics.[23]

Another matter of concern is that more than one quarter of the women in this study were primigravidas. Most of them were referred cases and as shown in Table 3 they were mainly due to cephalopelvic disproportion, malpresentation and obstructd labour.

Obviously their chances of having a repeat section in the subsequent pregnancy increases. The prudent way to reduce the number of primary cesareans is in practicing of the guidelines for various indications even at district and rural health center level. The cesarean surveillance system can solidify these guidelines, leading to a lower rate and avoidance of inappropriate indications[24,25].

Dystocia was one of the main indications for caesarean section both in primigravidas and multigravida. Modification of epidural analgesia, limiting unnecessary induction of labor and the use of prostaglandin preparations for cervical ripening if induction is necessary in patients with an unfavorable cervix, more accurate estimation of the fetal body weight, proper use of oxytocin dosage which can correct malrotation of vertex, may lead to subsequent reduction in CS rate for dystocia. Moreover policies, such as: active management of labor, trial of scar, maintenance of the skills required to supervise vaginal delivery when there is a breech presentation and better definition of the deliveries in which fetal monitoring will be useful in the diagnosis of fetal distress; all will achieve acceptable cesarean rate, performed for dystocia[26].

As cesarean section can be life saving for both mother and child, a predictive model consisting of maternal age, parity and height can be used to identify those women who are likely to require cesarean section[27]. This study also showed that there were almost 22% women aged >35 years. The risk of cesarean section at this advanced age is 6.54-fold. The determinants are included in the pregnancy, delivery and neonatal outcome[28]. A study in Taiwan also confirmed this relationship between advancing maternal age and an increased likelihood of a cesarean section[29].

A maternal mortality rate of 979/100,000 deliveries in this study, although lower than 1540/ 100 000 from Nigeria[30] is much higher than the maternal mortality rate of 22.3/100,000, reported from Massachusetts, USA[31]. Increased involvement of specialists in the care and improved intra and post-operative management of the cases are advocated to reduce this high rate.[32,33] Perinatal deaths also continue to be a major concern especially as cesarean section is being increasingly performed for fetal indications. This study reveals that this is still high, 105 perinatal deaths including 91 still births even though cesarean section for fetal indications have increased. The effective implementation of the above mentioned strategies to reduce cesarean rates may depend on the social and cultural milieu and on associated beliefs and practices.

CONCLUSION

The trend of increasing Cesarean section rates is a problem in itself, but more importantly it may indicate that we are heading toward a more costly medical delivery system. For all of these reasons, the reduction of Cesarean section rates should be a priority for any reproductive health program in order to improve the quality of prenatal care and to reduce the number of maternal deaths and morbidity. Reduction of cesarean delivery rates will need concerted action from Public Health authorities, medical associations, medical schools, health professionals, the general population and the media. It is important that those who need a cesarean get one under optimum conditions and the others get appropriate care and support through labor so as to minimize damage and maximize satisfaction. There is also a need for standardized collection of information on all aspects of childbirth to ascertain the incidence and causes of cesarean section nationally so that comparison and improvements of care can take place. If the government does not consider this as a public health issue of significance, the obstetrical societies could use its members to do so. Today at the beginning of twenty-first century, we are not only concerned with the safety and health of the mother and the child, but also with mother's desires and preferences and the child's rights.

REFERENCES

1. Lurie S. The changing motives of cesarean section: from the ancient world to the twenty-first century. Arch Gynecol Obstet. 2005; 271: 281-5.
2. Leitch CR, Walker JJ. The rise in cesarean section rate: the same indications but a lower threshold. Br J Obstet Gynaecol 1998; 105: 621-626.
3. Pai M, SundaramP , Radhakrishnan KK, Thomas K, Muliyil JP. A high rate of Cesarean sections in an affluent section of Chennai. Is it a cause of concern? Natl Med J India 1999; 12:56-58.
4. Chanrachakal B, Herabutya Y, Udomsubpayakul U. Epidemic of cesarean section at the general, private and university hospitals in Thailand. J Obstet Gynecol Res 2000; 26: 357-361.
5. Tampakoudis P, Assimakopoulos E, Grimbizis G, Zafrakas M, Tampakoudis G, Mantalenakis S, et al. Cesarean section rates and indications in Greece: data from a 24-year period in a teaching hospital. Clin Exp Obstet Gynecol. 2004; 31: 289-92.
6. Shearer E. Cesarean section: medical benefits and costs. Soc Sci Med 1993; 37: 1223-1231.
7. World Health Organisation. Appropriate technology for birth. Lancet 1985; ii: 436-437.
8. Lee SI, Khang YH, Lee MS. Women's attitudes toward mode of delivery in South Korea – a society with high cesarean section rates. Birth. 2004; 31: 108-16.
9. Collaborative study on high risk pregnancies and maternal mortality. ICMR task force study. New Delhi: ICMR, 1990.
10. Belizan J, Althabe F, Barros F, Alexander S. Rates and implications in Latin A. J. Obs Gynae. 1999; 7: 128-129.

Obviously their chances of having a repeat section in the subsequent pregnancy increases. The prudent way to reduce the number of primary cesareans is in practicing of the guidelines for various indications even at district and rural health center level. The cesarean surveillance system can solidify these guidelines, leading to a lower rate and avoidance of inappropriate indications[24,25].

Dystocia was one of the main indications for caesarean section both in primigravidas and multigravida. Modification of epidural analgesia, limiting unnecessary induction of labor and the use of prostaglandin preparations for cervical ripening if induction is necessary in patients with an unfavorable cervix, more accurate estimation of the fetal body weight, proper use of oxytocin dosage which can correct malrotation of vertex, may lead to subsequent reduction in CS rate for dystocia. Moreover policies, such as: active management of labor, trial of scar, maintenance of the skills required to supervise vaginal delivery when there is a breech presentation and better definition of the deliveries in which fetal monitoring will be useful in the diagnosis of fetal distress; all will achieve acceptable cesarean rate, performed for dystocia[26].

As cesarean section can be life saving for both mother and child, a predictive model consisting of maternal age, parity and height can be used to identify those women who are likely to require cesarean section[27]. This study also showed that there were almost 22% women aged >35 years. The risk of cesarean section at this advanced age is 6.54-fold. The determinants are included in the pregnancy, delivery and neonatal outcome[28]. A study in Taiwan also confirmed this relationship between advancing maternal age and an increased likelihood of a cesarean section[29].

A maternal mortality rate of 979/100,000 deliveries in this study, although lower than 1540/ 100 000 from Nigeria[30] is much higher than the maternal mortality rate of 22.3/100,000, reported from Massachusetts, USA[31]. Increased involvement of specialists in the care and improved intra and post-operative management of the cases are advocated to reduce this high rate.[32,33] Perinatal deaths also continue to be a major concern especially as cesarean section is being increasingly performed for fetal indications. This study reveals that this is still high, 105 perinatal deaths including 91 still births even though cesarean section for fetal indications have increased. The effective implementation of the above mentioned strategies to reduce cesarean rates may depend on the social and cultural milieu and on associated beliefs and practices.

CONCLUSION

The trend of increasing Cesarean section rates is a problem in itself, but more importantly it may indicate that we are heading toward a more costly medical delivery system. For all of these reasons, the reduction of Cesarean section rates should be a priority for any reproductive health program in order to improve the quality of prenatal care and to reduce the number of maternal deaths and morbidity. Reduction of cesarean delivery rates will need concerted action from Public Health authorities, medical associations, medical schools, health professionals, the general population and the media. It is important that those who need a cesarean get one under optimum conditions and the others get appropriate care and support through labor so as to minimize damage and maximize satisfaction. There is also a need for standardized collection of information on all aspects of childbirth to ascertain the incidence and causes of cesarean section nationally so that comparison and improvements of care can take place. If the government does not consider this as a public health issue of significance, the obstetrical societies could use its members to do so. Today at the beginning of twenty-first century, we are not only concerned with the safety and health of the mother and the child, but also with mother's desires and preferences and the child's rights.

REFERENCES

1. Lurie S. The changing motives of cesarean section: from the ancient world to the twenty-first century. Arch Gynecol Obstet. 2005; 271: 281-5.
2. Leitch CR, Walker JJ. The rise in cesarean section rate: the same indications but a lower threshold. Br J Obstet Gynaecol 1998; 105: 621-626.
3. Pai M, SundaramP , Radhakrishnan KK, Thomas K, Muliyil JP. A high rate of Cesarean sections in an affluent section of Chennai. Is it a cause of concern? Natl Med J India 1999; 12:56-58.
4. Chanrachakal B, Herabutya Y, Udomsubpayakul U. Epidemic of cesarean section at the general, private and university hospitals in Thailand. J Obstet Gynecol Res 2000; 26: 357-361.
5. Tampakoudis P, Assimakopoulos E, Grimbizis G, Zafrakas M, Tampakoudis G, Mantalenakis S, et al. Cesarean section rates and indications in Greece: data from a 24-year period in a teaching hospital. Clin Exp Obstet Gynecol. 2004; 31: 289-92.
6. Shearer E. Cesarean section: medical benefits and costs. Soc Sci Med 1993; 37: 1223-1231.
7. World Health Organisation. Appropriate technology for birth. Lancet 1985; ii: 436-437.
8. Lee SI, Khang YH, Lee MS. Women's attitudes toward mode of delivery in South Korea – a society with high cesarean section rates. Birth. 2004; 31: 108-16.
9. Collaborative study on high risk pregnancies and maternal mortality. ICMR task force study. New Delhi: ICMR, 1990.
10. Belizan J, Althabe F, Barros F, Alexander S. Rates and implications in Latin A. J. Obs Gynae. 1999; 7: 128-129.

11. Muraleedharan VR. Cesarean sections on the rise. Natl Med J India 2000; 13: 46.
12. Ryan K, Schnatz P, Greene J, Curry S. Change in cesarean section rate as a reflection of the present malpractice crisis. Conn Med. 2005; 69: 139-41.
13. US Department of Health and Human Services, Public Health Service. Healthy people 2000: national health promotion and disease prevention objectives. Washington, DC: DHHS, 1991.
14. Zanetta G, Tampieri A, Currado I, Nespoli A, Midwife T, Fei F, et al. Changes in cesarean delivery in an Italian university hospital, 1982-1996: a comparison with the national trend. Birth 1999; 26: 144-148.
15. Annual technical report. Dept. of RHR including UNDP/UNFPA/WHO/World Bank special programme of Research, development and research training in human reproduction. Geneva: World Health Organization, 2000.
16. Thistle PJ, Chamberlain JA. Vaginal birth after cesarean section in a rural African setting. Int J Gynecol Obstet 2002; 77: 3-32.
17. Mozurkewich EL, Hutton EK. Elective repeat cesarean delivery versus trial of labor: a meta-analysis of the literature from 1989 to 1999. Am J Obstet Gynecol 2000; 183: 1187-1197.
18. Wen SW, Rusen ID, Walker M. Liston R, Kramer MS, Baskett T, Heaman M, Liu S; Comparison of maternal mortality and morbidity between trial of labor and elective cesarean section among women with previous cesarean delivery. Am J Obstet Gynecol. 2004; 191: 1263-9.
19. Mankuta DD, Leshno MM, Menasche MM, Brezis MM. Vaginal birth after cesarean section: trial of labor or repeat cesarean section? A decision analysis. Am J Obstet Gynecol. 2003; 189: 714-9.
20. Makoha FW, Felimban HM, Fathuddien MA. Roomi F, Ghabra T. Multiple cesarean section morbidity, nt J Gynaecol Obstet. 2004; 87: 227-32.
21. Loverro G, Greco P, Vimercati A, Nicolardi V, Varcaccio-Garofalo G, Selvaggi L. Maternal complications associated with cesarean section. J Perinat Med. 2001; 29: 322-6.
22. Bergholt T, Stenderup JK, Vedsted-Jakobsen A, Helm P, Lenstrup C. Intraoperative surgical complication during cesarean section: an observational study of the incidence and risk factors. Acta Obstet Gynecol Scand. 2003; 82: 251-6.
23. Kunthonkitidej K, Ngernset O. Self-evaluation of obstetrician by delivery data to reduce caesarean section rate In Chai Nat Hospital. J Med Assoc Thai 2001; 84: 1587-93
24. Liang WH, Yuan CC, Hung JH. Yang ML. Yang MJ. Chen YJ, Yang TS. Effect of peer review and trial of labor on lowering cesarean section rates. J Chin Med Assoc. 2004; 67: 281-6.
25. Saunders DL, Makutu SL. Cesarean section deliveries in Fiji, 1986 to 1996. Pac Health Dialog. 2001: 8: 71-7.
26. Hindawi IM, Meri ZB. The Jordanian cesarean section rate.: Saudi Med J. 2004 Nov; 25: 1631-5.
27. Seshadri L, Mukherjee B. A predictive model for cesarean section in low risk pregnancies. Int J Gynaecol Obstet. 2005 May; 89: 94-8.
28. Kozinszky Z, Orvos H, Zoboki T, Katona M, Wayda K, Pal A, Kovacs L. Risk factors for cesarean section of primiparous women aged over 35 years. Acta Obstet Gynecol Scand. 2002 Apr; 81: 313-6.
29. Lin HC, Sheen TC, Tang CH, Kao S. Association between maternal age and the likelihood of a cesarean section: a population-based multivariate logistic regression analysis. Acta Obstet Gynecol Scand. 2004 Dec; 83: 1178-83.
30. Ozumba BC, Anya SE. Maternal deaths associated with cesarean section in Enugu, Nigeria. Int J Gynecol Obstet 2002; 763: 307 -309.
31. Sachs BP, Yeh J, Acker D, Driscoll S, Brown DAJ, Jewitt JF. Cesarean section-related maternal mortality in Massachusetts, 1954-1985. Obstet Gynecol 1998: 713: 385-388.
32. Ozumba BC, Anya SE. Maternal deaths associated with cesarean section in Enugu. Nigeria. Int J Gynaecol Obstet. 2002 Mar; 76: 307-9.
33. Walker R, Turnbull D, Wilkinson C. Strategies to address global cesarean section rates: a review of the evidence. Birth. 2002 Mar; 29: 28-39.

ORIGINAL ARTICLE

CLINICAL, BIOLOGICAL AND RADIOLOGICAL PROFILE OF TB IN CHILDREN UNDER 5 YEARS OF AGE

***Amin Jan Gandapur, Nayyar Raza Kazmi, Fazlur Rahim, Nadeem Khawar**

* Associate Professor of Pediatrics, Department of Child Health, Khyber Teaching Hospital, Peshawar

INTRODUCTION

Tuberculosis (TB) has reached epidemic proportions in many developing countries, but the burden of tuberculous disease in children often is underappreciated. In 1990, the World Health Organization estimated that there were approximately 1.3 million new cases of TB and 450 000 deaths worldwide from TB in children under age 15.[1]

Tuberculosis remains one of the major public health problems in our country inspite of the spectacular developments in the field of science and medicine. Childhood tuberculosis is one of the seven vaccine preventable diseases under Expanded Program of Immunization (EPI) for which continuous surveillance activities are going on. Nearly 1.8 per cent population above 5 years in age is suffering from radiologically active tuberculosis of lungs of which 25% are sputum positive and infectious to others[2]. Further, 2.8% of the children below 5 years in age are infected with tubercle bacilli. The annual incidence rate of infection in the 0 to 4 years age group is 0.8%. Though the acute forms of tuberculosis have been largely controlled due to improved coverage by BCG vaccination, there is no dent yet on chronic pulmonary disease.

Diagnosing PTB in the pediatric population presents challenges. Symptoms of MTB infection are often nonspecific or absent in affected children.[3] Adequate clinical diagnostic specimens often are difficult to obtain in children under age 8 because of a lack of sputum production.[5] Furthermore, currently available diagnostic tests are costly, slow, and lacking in sensitivity, and even under the best circumstances MTB is isolated in fewer than 50% of pediatric cases.[4]

Certain scoring systems have been devised with different sensitivities and specificities for diagnosis of Pediatric TB. Keith Edwards and Kenneth Jones criteria are commonly used for this purpose.

In this backdrop, we decided to evaluate the relative frequency of those features of Kenneth Jones Score, which relatively are more common in various forms of Pediatric Tuberculosis.

RESEARCH METHODOLOGY

This descriptive observational cross-sectional study was carried out at the Paediatrics "A" Unit of Khyber Teaching Hospital, Peshawar over a period of one year from January 2005 to December 2005. Children under 5 years of age with Kenneth Jones Score of 5 or more were included in the study. All subjects underwent a detailed assessment which included investigation for biological, biochemical and radiological parameters. All subjects with a different Final diagnosis were excluded from the final data analysis. Final Sample after exclusion constituted 63 subjects. Relative frequencies of parameters described above were calculated.

RESULTS

Table 1:

Age Range	Total Number of Cases	Male	Female
Less than 6 months	7	5(71%)	2(29%)
6-24 months	35	21(60%)	14(40%)
24-60 months	21	17(81%)	4(19%)
Total	63	43(68%)	20(32%)

Table 2: Major Clinical Features in children under 5 years with Tuberculosis

Age Groups	FTT	Fever	Cough	Loose motions	Vomiting
Less than 6 months (n=7)	3 (43%)	7 (100%)	7 (100%)	2 (28%)	2 (28%)
6-24 months (n=35)	25 (71%)	34 (97%)	31 (89%)	13 (37%)	7 (20%)
24-60 months (n=21)	18 (86%)	18 (86%)	20 (95%)	7 (33%)	3 (14%)
Total (n=63)	46 (73%)	59 (94%)	58 (92%)	22 (34%)	12 (19%)

Table 3: Prior History of Measles and Pertussis in children under 5 years with Tuberculosis

Age Group	History of Measles	History of Pertussis
< than 6 months (n=7)	- None	- None
6-24 months (n=35)	9(26%)	1(3%)
24-60 months (n=21)	2(9.5%)	- None
Total (n=63)	11(17%)	1(1.6%)

Table 4: Duration of Illness in children under 5 years with Tuberculosis

Age Group	Duration of Illness			
	2 Weeks and less	2-8 Weeks	2-6 Months	6 months and more
< than 6 months (n=7)	3(43%)	4(57%)	–	–
6-24 months (n=35)	3(9%)	13(37%)	10(28%)	9(26%)
24-60 months (n=21)	1(5%)	5(24%)	3(14%)	12(57%)
Total (n=63)	7(11%)	22(35%)	13(21%)	21(33.33%)

Table 5: History of Contact in children under 5 years with Tuberculosis

Age Groups	History of Contact	History of Close Contact	History of Contact with Other relation
< than 6 months (n=7)	6(86%)	4(67%)	2(33%)
6-24 months (n=35)	15(43%)	5(33%)	10(67%)
24-60 months (n=21)	9(43%)	4(44%)	5(56%)
Total (n=63)	30(48%)	12(40%)	18(60%)

Table 6: Nutritional Status of children under 5 years with Tuberculosis

Age Groups	Normal	Malnourished	Mild	Severe
Less than 6 months (n=7)	4 (57%)	3 (43%)	1 (33%)	2 (67%)
6-24 months (n=35)	11 (31%)	24 (69%)	9 (38%)	15 (62%)
24-60 months (n=21)	6 (29%)	15 (71%)	5 (33%)	10 (67%)
Total (n=63)	21 (33%)	42 (67%)	15 (36%)	27 (64%)

Table 7 :Developmental Status of children with Tuberculosis

Age Groups	Normal	Delayed or regressed
Less than 6 months (n=7)	6 (86%)	1 (14%)
6-24 months (n=35)	11 (31%)	24 (69%)
24-60 months (n=21)	14 (67%)	7 (33%)
Total (n = 63)	31 (49%)	32 (51%)

Table 8: BCG vaccination status according to age

Age Groups	BCG Scar Present	Good Scar	Faint
Less than 6 months (n=7)	3(43%)		
6-24 months (n=35)	11(31%)	8(73%)	3(27%)
24-60 months (n=21)	8(38%)	6(75%)	2(25%)
Total (n=63)	22(35%)		

Table 9: BCG Positivity in children under 5 years with Tuberculosis

Based on Following Criteria With BCG Scar Absent: Positive, if indurations > 5 mm With BCG Scar Present: Positive, if indurations > 10 mm		
Age Groups	Positive	Negative
< than 6 months (n=4)	3(75%)	1(25%)
6-24 months (n=25)	17(68%)	8(32%)
24-60 months (n=15)	9(60%)	6(40%)
Total(n=44)	29(66%)	15(34%)

Table 10: Anemia is more Significant than ESR in children under 5 years with Tuberculosis

Age Groups	Anemia	Raised ESR
Less than 6 months (n=7)	4(57%)	3(43%)
6-24 months (n=35)	27(77%)	8(23%)
24-60 months (n=21)	14(67%)	7(33%)
Total (n=63)	45(71%)	18(29%)

Table 11: Radiological Findings in Children with Tuberculosis

Age Groups	Suggestive of TB	Non Specific changes	Normal
Less than 6 months (n=7)	4 (57%)	2 (29%)	1 (14%)
6-24 months (n=35)	17 (48%)	10 (29%)	8 (23%)
24-60 months (n=21)	11 (53%)	7 (33%)	3 (14%)
Total (n = 63)	32 (51%)	19 (30%)	12(19%)

Table 12: Kenneth Jones Score in Children with Tuberculosis

Age Groups	Kenneth Jones Criteria	
	Score 5-6	Score 7-8
<than 6 months (n=7)	3 (43%)	4 (57%)
6-24 months (n=35)	19 (54%)	16 (46%)
24-60 months (n=21)	11 (52%)	10 (48%)
Total (n = 63)	32 (51%)	31 (49%)

Table 13 :Types Of Tuberculosis

Age Groups	Pulmonary TB	Abdominal TB	Neuro tuberculosis
Less than 6 months (n=7)	7 (100%)	Nil	Nil
6-24 months (n=35)	32 (91%)	2 (6%)	1 (3%)
24-60 months (n=21)	17 (81%)	2 (9.5%)	2 (9.5%)
Total (n= 63)	56 (89%)	4 (6%)	3 (5%)

DISCUSSION

This study shows a male preponderance (almost 2:1 ratio) but the non randomization makes it of little clinical significance. However across both sexes, we found out that the disease frequency was more in the age group less than 2 years against those aged more than 2 years (66% vs 34%). A search through literature showed that even across Africa, the same findings have been reflected even in randomized studies with a large sample size [5,6,7].

Fever and cough occurred with 100% frequency in children less than 2 years of age, the frequency dropping slightly in children aged more than 2 years, where relatively Failure to thrive was as common as fever. One of the probable reason for decreasing fever frequency in this age group itself is explained by high frequency of the Failure to thrive (86%), which depresses immune functions to the level that fever response is reduced in such patients. Bloomroeder[8] have come with similar findings on a cohort of Afghani children suffering from Pulmonary TB.

History of close contact was more common in infants (67%) again understandably because of excessive handling of these children by close contacts as compared to those who were aged greater than 2 years where history of contact with other relations was relatively more common (56%)

Malnutrition was present in 67% of the sample, relatively being more common in those aged greater than 2 years. The same pattern of increasing malnutrition frequency has been found out by Deitels (1983)[9], Ayush and Vishnu (1988)[10] and Bloemroeder (1995)[8]. Most of these workers have found out a positive correlation between the degree of malnutrition, its frequency and length of the disease. However in this study it is difficult to comment on this aspect, because of the small sample size, and because the length of the disease couldn't be properly ascertained in our study and within a small sample, there is high probability of recall bias.

Developmental regression was common in the age group 6-24 months (69%), however again because of the cross sectional nature of the study, a cause effect relationship cannot be generated between the two. Some other studies: DS Akram (1998)[11] and TI Bhutta (1991)[12] have found out similar findings, but those studies were also non randomized and based on small sample size coupled with cross sectional nature of those studies.

BCG vaccination status as determined by BCG Scar was evidently low across all the age groups (43%, 31% and 38%) implying a problem with the BCG component of the National EPI Program. Neutinzeusche (1994)[13] interestingly found out a high TB rate in BCG immunized children in Kenya. However it is difficult to comment on how efficacious is BCG vaccination in preventing TB. Nevertheless there is a consensus among Paediatricians that BCG vaccination prevents against more severe form of TB[13].

We also found out that diagnostic BCG had a moderately good positive predictive value of 75%, 68% and 60% in children aged less than 6 months, those between 6-24 months and those aged above 24 months respectively. With BCG scar present or absent, this can be a good diagnostic tool in the very young.

REFERENCES

1. World Health Organization. Childhood tuberculosis and BCG vaccine: EPI update supplement. Geneva: WHO, 1989.
2. Curtis A B, Ridzon R, Vogel R et al. Extensive transmission of *Mycobacterium tuberculosis* from a child. N Engl J Med 1999; 341: 1491–1495.
3. Miller F J W, Seal R M E, Taylor M D. Tuberculosis in children. Boston, MD: Little, Brown, and Co, 1963.
4. Houwert K A F, Borggreven P A, Schaaf H S, Nel E, Donald P R, Stolk J. Prospective evaluation of World Health Organisation criteria to assist diagnosis of tuberculosis in children. Eur Respir J 1998; 11: 1116–1120.
5. Olesanjo AA, Abel T. Spectrum of Pediatric TB in Kenya, Bulletin of the WHO 15 (3): 1189-1197
6. Rhodowski FF, Smith PL, Johnson ER. Prevalence of Pediatric TB in rural Uganda. Arch of Dis of Child 22 (10): 3023-3029
7. Oswaye P, Bhardoaj TH. Is TB still a problem in Nigeria? Jour of Infect Dis 2002 (5): 77-85
8. Bloomroeder MV. War, poverty and TB in displaced children. Amer Jour of Pub Health. 18(2): 1945-1949
9. Dietels MS. Pediatric TB in affectees of Chrenobyl Accident. Oxford Jour of Pub Health. 1987. Vol. 21. No.1: 23-35
10. Ayush SA, Vishnu MM, Trivardum B. Whats the relation between Malnutrition and TB ? Indian J of Peds. 1988(6): 12-18
11. Akram DS et al. Frequency of Malnutrition in a Tertiary Care Hospital of Karachi. Jour of Coll Phy Surg. 1998(12): 45-51
12. Bhutta TI, Khan SR, Baig SS. Precursors of malnutrition in rural Punjab. Soc Sci Med 212(4): 1123-1129
13. Neutinzeusche JH, Beigel TR, Halmer YSR, Joshua AS. Does BCG really prevent TB?. Bull WHO. 1994(7): 56-63.

ORIGINAL ARTICLE

THE OUTCOME OF TOTAL ABDOMINAL HYSTERECTOMY BY GENERAL SURGEONS. A PROSPECTIVE STUDY OF 100 CASES

***Ata Ur Rehman Khalil, Muhammad Yunas, Amir Amanullah, Mukhtiar Ali, Wasim Yar Khan, Muhammad Janisar**

*Assistant Professor, Surgical 'A' Unit, Khyber Teaching Hospital, Peshawar

ABSTRACT

Background: The objective of the study was to determine the early outcome (2 to 6 months Post-operation) of total abdominal hysterectomy for various indications in terms of intra and post operative complications.

Research Methodology: This prospective study was carried out in Department of Surgery, Khyber Teaching Hospital Peshawar and Medicare Hospital Peshawar from April 2003 to March 2006. Women with the complaints / history of fibroid uterus, post menopausal dysfunctional uterine bleeding, polymenorrhagia, and Ca endometrium were evaluated and 100 of them were selected who underwent total abdominal hysterectomy. Patients below 30 yrs of age, patients own wish against TAH, unmarried women, those with incomplete family and those with uterine prolapse were excluded. All the patients were followed for 2-6 months and the clinical and symptomatic improvement was recorded in terms of wound heeling, urinary and bowel functions. All the specimens were sent for histopathological examination.

Results: Early complications like fever were noted in 7(7%) cases on the first post operative day, wound infection in 3(3%) cases and bladder dysfunction in 6(6%) cases. There was no ureteric, bladder / bowel injury in our study. No mortality occurred in 100 cases of total abdominal hysterectomy. Out of 100, only 3(3%) cases turned out to be having carcinoma endometrium. Fibroid uterus was found in 50(50%) of patients, dysfunctional uterine bleeding in 28(28%) cases while polymenorrhagia was found in 19(19%) cases. The mean age of cases was 50 yrs.

Conclusion: Total abdominal hysterectomies done by general surgeons produced comparable results with that of the world literature.

Keywords: Total abdominal hysterectomy, Dysfunctional uterine bleeding, Menorrhagia, Carcinoma Endometrium.

INTRODUCTION

Total abdominal hysterectomy is performed world wide for various indications. The obstetrical hysterectomy can be performed both in emergency as well as an elective procedure. It is also performed to combat severe life threatening infections, haemorrhage and when the mother's life is in danger[1]. The other indication is ruptured uterus.

Total abdominal hysterectomy in emergency is a life saving procedure but the elective one is always either curative or palliative. Elective abdominal hysterectomy is a planned procedure. Caesarean hysterectomy may be used as an alternative to Caesarean section in patients with history of menorrhagia, leiomyoma or cervical dysplasia[2].

First successful Caesarean hysterectomy was performed in 1876[3].

New trends are also practiced by surgeons and gynaecologists with a more conservative approach in abdominal hysterectomies which include sub-total abdominal hysterectomy and Laparoscopic abdominal hysterectomy.

Total abdominal hysterectomy is also performed for postpartum bleeding with adherent placenta[4].

The aim of the study was to see both the intra-operative and early postoperative complications in patients undergoing TAH by the general surgeons.

RESEARCH METHODOLOGY

This study was conducted from April 2003 to March 2006 over a period of 3 yrs in Khyber Teaching Hospital Peshawar and Medicare Hospital Peshawar. All the patients were thoroughly evaluated by history, clinical examination and relevant investigations. The patient's age, parity and presenting complaints were also considered.

All the patients with dysfunctional uterine bleeding, fibroids, pressure perineum, chronic pelvic pain and discomfort were included. Three patients were known cases of carcinoma endometrium on histopathology report after D & C.

The exclusion criteria was:

- Patients below 30 years of age.
- Patient's own wish against TAH.
- Unmarried women.
- Patients with incomplete families.
- Patients with Uterine Prolapse.

In all patients, general physical and systemic examination was done after thorough history. All patients were subjected to per-vaginal examination. Ultrasonography of abdomen and pelvis along with routine investigations for fitness for anesthesia and surgery were done. The patients were admitted 1-2 days before surgery and were counselled for surgery, anesthesia and post-operative complications.

All the patients were catheterized before surgery to keep the bladder empty. A prophylactic dose of second or third generation cephalosporin was administered with induction of anesthesia. All the patients were given triple regimen of i/v antibiotics for 3 days and then orally for 3-4 days.

Lower midline incision was used in all the patients for total abdominal hysterectomy. The uterus was removed along with the cervix and care was taken in separating the cervix from the bladder and during ligation of uterine arteries to avoid ligation / injury to the ureters.

Only in selected pre-menopausal women the healthy ovaries were left behind while salpingo-oophorectomy was performed in post-menopausal women.

Haemostasis was secured and ureters checked before closure of abdomen. Drains were put in selected cases to avoid post-operative collections.

The patients were observed for following outcome parameters:

- Fever
- Haemorrhage
- Wound infection
- Bladder dysfunction (Frequency/urge incontinence)
- Incisional hernia
- Iatrogenic injuries
- Mortality

All the patients were followed for 2-6 months. At each follow up visit, they were subjected to history, examination and investigations esp. ultrasound for pelvic abscess. The outcome of each parameter was recorded as a 'Percentage of Total Cases'.

RESULTS

Early complications are shown in Table 1. The indications are shown in Table 2 while the age distribution of our cases is shown in Table 3.

Table 1: Complications

Complications	%age
Bladder dysfunction	(08) 08%
Fever	(07) 07%
Wound infection	(03) 03%
Haemorrhage	(02) 02%
Incisional hernia	(01) 01%
Iatrogenic injuries	(00) 0%
Mortality	(00) 0%

Table 2: Indications for total abdominal hysterectomy

Indications	%age
Fibroids	(50) 50%
DUB	(28)28%
Polymenorrhagia	(19) 19%
Ca endometrium	(03) 03%

Table 3: Age Distribution

Age group	%age
39-44 yrs	30 (30%)
45-49 yrs	60 (60%)
50-54 yrs	07 (07%)
55-59 yrs	03 (03%)

DISCUSSION

Total abdominal hysterectomy is an old and time tested procedure being practiced by gynaecologists since long[5]. The new procedures like sub-total hysterectomy and laparoscopic hysterectomy are also practiced by general surgeons and gynaecologists. It reflects more conservative approach in gynaecological surgery[6,7]. It is clear from our study that proper selection and proper procedure was the key to success. In our study we evaluated the results of total abdominal hysterectomy done by general surgeons only which were found comparable to studies done by gynaecologists[1,2,9].

We evaluated 100 cases from April 2003 to March 2006 in Khyber Teaching Hospital Peshawar and Medicare Hospital Peshawar.

The major indications for total abdominal hysterectomy were fibroids in 50 (50% cases) followed by dysfunctional uterine bleeding 28(28%), polymenorrhagia in 19(19%) and carcinoma endometrium in 3(3%) of the cases as shown in Table 2. DUB and Uterine Fibroids are the most common indications for elective hysterectomy in other centers as well, as mentioned in Ewies Study[7].

The age range was 39-44 years in 30(30%) cases, 45-49 years in 60(60%) and over 50 years only in 10(10%). The mean age was 50 years (39 yrs to 59 yrs) with SD±4.46. The ureteric or bladder injuries encountered in total abdominal hysterectomy are at times because of the obscure anatomy due to previous surgery or inadequate dissection of the anatomy, pelvic adhesions or big tumours. The complications of total abdominal hysterectomy become obvious when the patient is found anuric or develops pain in the loins because of hydronephrosis or pyonephrosis. The incidence of ureteric and bladder injuries is much higher in case of emergency procedures than prepared elective procedures (as evident in Gonsoulin's Study[2] for the same reason.

The intra-operative complications like excessive haemorrhage, ureteric/ bladder and gut injuries were not encountered in our study although the reported ureteric injury in total abdominal hysterectomy is 0.5 - 3%[8] which is quite a significant figure. On the other hand ureteric or bladder injury is more common in cases which had either previous surgery or any abdominal pathology like intestinal tuberculosis, pelvic inflammatory diseases or traumatic injuries during previous surgery to the bladder, colon or intestine causing adhesion[7]. We didn't encounter any iatrogenic injuries because non of the patients had any problem causing obscure anatomy and all were elective cases.

The ureteric injury in laparoscopic hysterectomy is much higher than open total abdominal hysterectomy[9]. Bowel injuries are less common than ureteric injuries but can be encountered in situations mentioned above.

The operative time in our study was 45-90 minutes, which is much shorter than laparoscopic surgery[10]. In comparison to total abdominal hysterectomy, the operative time in sub total surgery is shorter[11]. The literature has reported sexual dysfunctions like decreased libido, fear and dyspareunia after total abdominal hysterectomy. These complications are much less common in sub-total abdominal hysterectomies as compared to total abdominal hysterectomies. In our study because of the social and educational barriers these were not properly explained by the patients on follow up visits. Vander et al and Van Beek et al have showed increased sexual activity after total abdominal hysterectomy because of no fear of pregnancy[6,12,13,14,15].

The post-operative complications both early and late were evaluated in all patients. On the first post-operative day, fever was noted in 7(7%) cases, post-operative pyrexia occurred in similar range in other studies (4%-10%)[4,15], wound infection in 3(3%) and post-operative bladder dysfunction in 8(8%) cases. Wound infection occurred in 1-4% patients in other studies[4,9,15,17] consistent to our study.

Haemorrhage was seen in 2(2%) cases. It is 3% in Ewies study[7]. In other studies it ranges from 2% to 18%[1,2,7,17,18], incidence being more in emergency hysterectomy[2] than elective hysterectomy as in our study. Other complication like incisional hernia was noticed in 1(1%) case. Incidence of incisional hernia in our study is less than shown in literature probably because of short duration of follow up. The urinary frequency was noticed in 8(8%) cases (6% in Thakar Study[9]). No postoperative pelvic abscess was noted on ultrasound after total abdominal hysterectomy in our study whereas the reported incidence of pelvic abscess after total abdominal hysterectomy is higher than laparoscopic hysterectomy[13].

The conclusion of the study is that the early outcome of total abdominal hysterectomies done by general surgeons is more or less similar to those done by gynaecologists.

REFERENCES

1. Noor S, Majeed S, Ruby N. An audit of obstetrical hysterectomy. JCPSP Oct 2001; 11(10): (642-45).
2. Gonsoulin W, Kennedy RT, Guidry KH. Elective versus emergency caesarean hysterectomy cases in the residency program setting. A review of 129 cases from 1984 to 1998. Am J Obstet Gynaecol 1991 to 1999. 165: 91-4.
3. Ketz VL, Cefelo RC. Hysterectomy and evaluation of caesarean delivery in: Phelan JP, Clork SL (Edi) caesarean delivery New York: Elsevier 1998: 9-10.
4. Zeiop CM, Harlow BL, Fredic D. Emergency peripartum hysterectomy. Am J Obstet Gynecol 1993; 168: 1443-8.
5. Garry R, Fountain J, Mason S, Have J, Napp V, Abbott J, et al. The evaluate study: two parallel randomized trials, one comparing with abdominal hysterectomy, the other comparing laparoscopic with vaginal hysterectomy. 129; Vol 1, 328. 2004.
6. Paul J, Roovers WR, Vander CHV. Hysterectomy and sexual well being, Prospective observational study of vaginal hysterectomy, sub total abdominal hysterectomy, and abdominal hysterectomy. BMJ 2003; 774-9.

7. Ewies AAA, Olah KSJ, Sub-total hysterectomy: a surgical advance or a backward step? Br J Urol 4; 2000; 107: 1376-9.

8. Whitelaw JM. Hysterectomy: a medical legal perspective, 1975-1985. Am J Obstet Gynecol 1990; 162: 1451-8.

9. Thakar R, Ayers S, Klarkson P. Outcome after total versus subtotal abdominal hysterectomy; 1329: N Engl J Med, 2002, 347.

10. Johnson N, Ballow D, Lethaby A, Tavender E, Curr L, Garry R. Methods of hysterectomy: Systemic review and meta-analysis of randomized controlled trials. BMJ 2005; 330; 1480-3.

11. Many-Yonada IT, Welch CR, Mcwinney NA, Ross LD. The inference of suture material on vaginal vault granulation following abdominal hysterectomy .Br J Obstet Gynaecol 1990: 97: 608-12.

12. Vander Stage JG, Van Beek JJ. Problems related to the cervix stump at follow up in laparoscopic supra-cervical hysterectomy, JSLS 1999; 3: 5-7.

13. Von Shoultz B. Consumer's attitude to hysterectomy, the experience of 6789 women. Acta obstet gynaecol scaned, 1992; 71: 230-4.

14. Nausheen F, Iqbal J, Bhatti FA, Khan AT, Sheikh S. Hysterectomy: The patients perspective; Ann King Edward Med Coll 2004; 10 (4): 339-41.

15. Bashir R, Parveen Z, Sultana R, Khan B. A two years audit of complications of hysterectomy at Ayub Teaching Hospital, Abbottabad. JAMC 2005; 17(2): 47-9.

16. Khanum Z, Lodhi SK. Emergency Obstetric Hysterectomy: A Life-saving procedure Ann King Edward Med Coll 2004; 10(3): 292-4.

17. Akhtar S. Short and long term complications of abdominal and vaginal hysterectomy for benign Diseases. Pak Armed Forces Med J 2004; 54 (l): 71-5.

18. Abbasi RM, Mumtaz F, Mughal R. An audit of indications and complications of obstetrical hysterectomy at a tertiary care hospital of Hyderabad. J Liaqat Uni Med Health Sci 2002; 1(1): 15-8.

ORIGINAL ARTICLE

CONSULTATION LIAISON PSYCHIATRY IN A MULTI-DISCIPLINARY TEACHING HOSPITAL

***Sayed Mohammad Sultan, Mohammad Riaz**

*Associate Professor of Psychiatry, Khyber Teaching Hospital, Peshawar
E-mail: smsultan2006@yahoo.com

ABSTRACT

Background: Psychiatric services are well established in tertiary multidisciplinary hospital in our country and provide liaison consultation liaison service but liaison psychiatry is not yet established as a sub specialty.

Research Methodology: This study was conducted to evaluate the pattern of referral and to study various psychiatric diagnostic categories associated with physical disorders and to study the attitudes of clinicians towards psychiatric illness. This study was carried in Psychiatry Department Khyber Teaching Hospital over a period of six months. There were 200 referrals during this period. Patients were assessed on especially designed structured pro forma and psychiatric disorders were diagnosed according to ICD criteria.

Results: Females out numbered males, the most common reason for referrals were psychosomatic, un-explained physical symptoms, agitated behaviour and pseudo seizures. Patients were predominately referred from the medical and allied departments (84%). Depression was the most common psychiatric diagnosis (38%) followed by conversion disorder (12%) and delirium (11%). Management mainly consisted of advice and recommendation of medicines followed by referral to Outpatient for follow up management.

Conclusion: There is lack of awareness and appreciation of the emotional problems of patients and poor interaction between clinicians of and psychiatrists. Psychiatrists and other clinician need to have more interaction and understanding to improve the care of their patients.

Keywords: Psychiatric referral. Liaison psychiatry, Consultation, conversion disorder.

INTRODUCTION

Psychiatric services for general hospital are widely referred to as consultation liaison services. In consultation work the psychiatrist is available to give opinion on patients referred by physicians and surgeons[12]. Liaison psychiatry is concerned with the psychiatric care of patients in general hospital setting. It involves the psychiatric management of patients who present with physical symptoms.

Establishment of psychiatry departments in general hospital have provided opportunities for interactions between psychiatrists and other medical specialists during the past three decades in Pakistan. A number of studies have reported high psychiatric morbidity in medical inpatients in developing countries[3,4,5,6]. Similarly there is high prevalence of psychiatric morbidity among general hospital outpatients[6,7].

20th century has brought revolutionary changes in the concept of mental health care as a result of new information and has seen a shift from mental illness to mental health.

Lipowsky advocate that biological as well as psychological factors should be considered in the diagnosis, treatment and prevention of disease. The association between physical illnesses and psychiatric morbidity may be in the form of emotional reaction to physical illness or as a wide range symptomatology of physical illness.

Psychiatric services are well established in the teaching hospital in our country and these units also provide consultation liaison service to various medical, surgical and allied specialties. Liaison psychiatry is not yet established as a sub specialty in our country. In view of the increasing emphasis on consultation work in the hospital, a study was conducted in Psychiatry Department Khyber Teaching Hospital to know the socio-demographic variables, reasons for referral, to study the attitude of the clinician to psychiatric disorder and to know the possible relationship between psychiatric and physical illness and the nature of ensuing management of such referral.

RESEARCH METHODOLOGY

This study was carried out in Psychiatry Department Khyber Teaching Hospital, Peshawar which is a multi-disciplinary teaching hospital, with a huge catchment area of NWFP and a significant number of patients are referred for specialist treatment from Afghanistan.

The study included all consecutive inpatient referral from various medical and surgical units. Patients were assessed mostly on the same day or within 24 hours of referral.

The data was collected on a specially designed, structured proforma consisting of demographic details,

information on reason for referral, present, past, family psychiatric history, detailed mental state examination and recent medical management. All inpatients referral were included in the study.

The information was obtained from the patients, their relatives, the concerned physicians and other professional involved in the care of these patients. The diagnoses of various psychiatric disorders were based on the 10th edition of "international classification of diseases ICD-10.

RESULTS

There were 200 inpatient psychiatric referrals during the six months study period. These patients were hospitalized for medical or surgical reasons. Among them 59% were female and 41% were male. The source of referral is shown in Table 1, while the marital status is shown in Table 2. The age distribution of these patients is shown in Table 3. Majority of the patients were uneducated (64%), 21% were matriculate and 15% had achieved primary level.

As for as socio economic status is concerned most of them 71%, came from poor background, 22% from middle social class, 47% from upper social class.

Reasons for referral are shown in Table-4. The most frequent probable diagnosis made by referring clinicians were psychosomatic, depression, "Anxiety neurosis, hysteria and psychic".

Psychiatric diagnosis of these cases is shown in Table 5.

The type of management offered to these cases is shown in Table 6.

Table. 1: Source of referral

S. No.	Referral Departments	%age	No. of cases
1.	Medical & allied departments	84%	168
2.	Surgical & allied departments	16%	32

Table 2: Marital status

	%age	No. of cases
Married	74%	148
Unmarried	17%	34
Widows or separated	9%	18

Table 3: Age range

S. No.	Age Range 9-82 years	%age	No. of cases
1.	9-15	4%	8
2.	15-30	43%	86
3.	30-50	26%	52
4.	50-65	20%	40
5.	65-82	7%	14

Table 4: Reason for referral

S. No.		%age	No. of cases
1.	Psychosomatic symptoms	42%	84
2.	Disruptive/agitated behaviour	16%	32
3.	Pseudo seizures	11%	22
4.	Low mood	10%	20
5.	Past psychiatric history	8%	16
6.	Attempted suicide	5%	10
7.	Drug dependence	4%	8
8.	Emotional problems	4%	8

Table 5: Psychiatric Diagnosis

S. No.	Psychiatric Diagnosis	%age	No. of cases
1.	Depressive disorder	38%	76
2.	Conversion disorder	12%	24
3.	Delirium	11%	22
4.	Anxiety disorder & panic disorder	6%	12
5.	Postpartum psychoses	6%	12
6.	Deliberate self harm	5%	10
7.	Drug dependence	4%	8
8.	Schizophrenia	4%	8
9.	Substance abuse	4%	8
10.	Manic illness	3%	6
11.	Others	5%	10

Table 6: Management of patients

S. No.	Management of patients	%age	No. of cases
1.	Medication & advise offered	64%	128
2.	Referral to outpatient deptt for follow up	25%	50
3.	Admitted for inpatient psychiatric care	9%	18
4.	Discharged from Home	2%	4

DISCUSSION

Keeping in view considerable psychiatric morbidity in general hospital, 200 consecutive psychiatric referrals over a six months period showed under recognition and under utilization of liaison psychiatric ser-

vice in our study. Similar morbidity and the limited extent of use of Liaison psychiatric service within a general hospital was found by Mayon & Lloyd[10], Anderson,[11] Larkin et al[12] and Gous et al[13] in their individual studies of Liaison psychiatry.

In our study females over numbered the males. Chen & Yeh[14] had reported more males than females in Taiwan but Creed et al had found higher number of females in psychiatric referrals. Our study perhaps reflects the higher prevalence of depression, conversion disorder and anxiety in female population[15].

Majority of patient (64%) in our study were formally uneducated and only 21% were matriculate, which generally represent the literacy rate in our country. Bhugale et al in India had reported majority of their patients were educated but they had commented that their figure does not represent the Indian population in general[5].

74% of the patients were married which generally represents the marital status in the country. 59% of patients were in the age range of 15-50 years. Similar figures have been reported by Aghwana et al from West African General Hospital and Bhugale et al from a multidisciplinary hospital in India. 7% of cases were above 65 years of age which is similar to that reported by Bhugale in India[5]. Wallen et al had reported 30% of their cases were elderly above 65 years of age.[16]

In our study 4% patients reported substance abuse. This figure is similar to the one reported by Canadian and other Western studies carried out by Michalen et al and Nihall and Beharry. They reported 5% substance dependence in their cases.[17-18]

When examined with regard to the source of referrals, 84% of referral were made by the medical and allied specialties as compared with only 16% referral from surgical and allied departments. This is line with Chen & Yeh, Bhugale et al, Fryn A, Buchkyet al[7], Mayour R et al[19]. This may be due to greater sensitivity and appreciation of psychological problems of patient by the referring physicians. Secondly a number of chronic medical conditions like hepatitis, cardiovascular accidents, myocardial infarction are associated with higher psychiatric morbidity.

With regard to reasons for low referral rate and discrepancy between medical and surgical referrals, there are many reasons. These include the demographic characteristics of the patients, presenting symptoms and the characteristics of the physicians such as diagnostic accuracy, biases towards making psychiatric diagnosis and differences in attitudes towards psychiatric symptoms.

Other relevant factors may be the remorbidity in psychiatric comorbidity among different physical illness and lack of understanding and rapport between psychiatrists and their non psychiatric professional colleagues.

The most common reason for referral was psychosomatic symptoms 42% similar figures were reported by Bhugale Creed et al and Fryne et al[1,5,7].

This is now well established that somatization is more common in developing countries which could be the reason for higher percentage of patients with psychosomatic symptoms[21]. Disruptive and agitated behaviour was the third most frequent reason for referral 11%. This was also responsible for urgent need for psychiatric consultation. This figure is similar to the one reported by Turbuck et al who called it management difficulty but Creed et al had a higher figure of 30%[1-3].

There were 10 cases of attempted suicide in this study which is in contrast to very high figure reported by Turbuck[3]. Suicide attempts are concealed and under reported on many occasions[5].

The most common psychiatric diagnosis on consultation in this present study was that of depressive disorder. This is a consistent finding in the literature[22,23] and may reflect the common occurrence of depression in association with different physical disorders. Symptoms simulating physical illness is a common presentation of depression[24]. Fryn et al and Creed et al reported depression as the commonest diagnosis in liaison psychiatry[1-7].

The second most common diagnosis was conversion disorder in our study. Creed et al had reported it in 4% of their cases only, while in Turbuck study it was only occasionally under the category of "Neurotic Stress related and somatoform disorder"[1-3]. These figures represent the fact that conversion disorder is still quite common in our region. Delirium was found in 11% of our cases. This figure is similar to the one reported by Creed et al 12%, while Fryne et al reported in 4% cases only[1-7].

Schizophrenia was found in only 4% of cases in the present study which is in line with the one reported by Nehall and Beharry in West Indies. In our study 64% patients were prescribed medication and advise was offered and relatively few patients were transferred to inpatient psychiatric care. This is in line with a similar figure reported by Turbuck et al[3].

CONCLUSION

Liaison psychiatry has an important role in multidisciplinary teaching hospitals. The reason for referral has to be understood, patients need to be engaged in a detailed interview, relevant information from informants arid ward staff need to be collected, new clinical signs and symptoms have to be elicited and the relationship between physical and psychological symptoms need to be understood.

The relatively poor referral rate indicate poor liaison between psychiatrists and physicians. There is greater need for better interaction between psychiatrists and physicians. Further links can be established

by participating in clinical seminars, case conferences and discussing and helping colleagues from other disciplines to understand the relationship between psychological factors and physical illness. A well organized consultation liaison service can minimize the economic burden on the over all health delivery system.

REFERENCES

1. Creed F, Guthric E, Black B, Tranmer M. Psychiatric referrals with in the general hospitals comparison with referrals to general practitioners. British Journal of Psychiatry 1993; 162: 204-11.
2. Gelder M, Gath DS, Mayou R, Comen P. Oxford Test book of Psychiatry 1996, 3rd edition Oxford University Press.
3. Turbuck AF. Liaison psychiatry in Addenbrooks hospital, six months experience. Psychiatry Bulletin 1990; 14: 668-70.
4. Aghwana HS, Makinyo, Anne OF. Consultation liaison psychiatry in a general hospital in West Africa. E Medical Journal 1996; 73 (2): 133-6.
5. Bhugale G, Katte SRM, Heble SP, Sinhaand UK, Pattil BA. Psychiatric referrals in a multi disciplinary hospital. Ind, Psychiat, 2; 212-26.
6. Dca K, Kar P. Psychiatric disorders in medical inpatients – a study in a teaching hospital. Ind J. Psychiat 1998; 40: 73-8.
7. Fryne A, Buckley P, Larkik, Walsh N. Consultation-liaison psychiatry with in the general hospital; referral pattern and management – Irish Med. J 1992; 85; 112-4.
8. Whyte A. Styles of liaison psychiatry; Discussion paper JR Soc Med. 1990; 83: 506-8.
9. Lipowski ZJ. An inpatient programe for persistent somatizers. Canad J Psychiat 1988; 33: 275-8.
10. Mayour R, Lloyd G. A survey of liaison psychiatry in United Kingdom & Eire. Bull R Col psych 1985; 9: 214-7.
11. Anderson HM. Liaison psychiatry in Scotland: the present service. Psychiatric Bulletin 1989; 13: 606-8.
12. Larkin C, Morgan R, Crmody R, Walsh N. Psychiatric consultation in Irish General Hospital. In: Proceeding of the 15th Europeon conference on psychosomatic research. Ed. JH Lacy & DA sturgeon. John Libby and Co Ltd. 1986.
13. Gous P, Gagiano CA, Weich DJV. Psychiatric disorders in internal medicine SAMJ 1992; 82: 441-2.
14. Chen CY, Yeh SS. Present state of psychiatric consultation in Chang Quang Memonal Hospital, Keelin of clinical characteristics Chang Qung Such 1996; 19 (4); 331-6.
15. Klienman A. Depression, somatization and the new cross cultural psychiatry SOU, Med 1997; 3-7.
16. Wellen J, Pincus HA, Macus SE. Psychiatric consultations in short term general hospital. Archives of general psychiatry, 1987, 44: 163-68.
17. Michalen M. Consultation liaison psychiatry – a perspective psychiatry in a general hospital Millier. Candal J Psychiat, 1993; 38 (3): 168-74.
18. Nihal J, Beharry N. The pattern of inpatients psychiatric referral in a general hospital. West Indian Med. J 1993; 42 (4); 155-7.
19. Mayour R, Hawton KE, Psychiatric disorders in the general hospital. British J of Psychiatry 1986; 149: 172-90.
20. Greed F, Liaison psychiatry for the 21st century: a review JR SOC Med 1991; 84: 414-6.
21. Harding TW, De Atiango MV, Battesar J, et al Mental disorder in primary health care: a study of their frequency and diagnosis in four developing countries. Psychological medical 1980; 10: 231-41.
22. Sharp MC, Hawton KE, Liaison psychiatry and psychological sequelae of physical disorders. Current opin psych 1990; 3: 199-203.
23. Vebroskey LA, Franko KN, Zrull JP. The relationship between depression and length of stay in general hospital patients, J. Clinical psych 1993; 54: 177-81.
24. Sharpe M, Hawton K, Seagoat V et al. Depressive disorders in long term survivors of stroke. Association with demographic and social factors. Functional status and brain lesion volume. Br. J. Psychiat 1994, 164; 380-6.

BIONIC ORGANS – THE FUTURE HUMAN IMPLANTS

Technological Advancements Blur The Line Between What's Human And What's Machine

***Sultan Mahmood, Ihsan Mahmood, Mohammad Humayun**

*Professor of Medicine, Khyber Teaching Hospital, Peshawar

One of the greatest challenges in medicine and bio-technology in the 21st century is the replacement of permanently lost function of human body organs - the replacement of organ failure- and one of the greatest breakthroughs that medicine and technology is going to see, hopefully in the near future, will be the development of "Bionic Organs" to replace the dysfunctional organs.

Most chronic progressive diseases of human body organs, unless successfully treated in time, ultimately results in partial or complete loss of function of mat organ, the organ failure like Blindness, Deafness, Renal failure. Heart failure, Liver failure, Paralysis of limbs, respiratory failure, Dementia, Joint destruction, Parkinsonism, Diabetes mellitus, Pancreatic insufficiency and so on.

In spite of tremendous technological advances, organ transplantation, except in few areas like renal transplantation, is unlikely to see major progress in future and therefore unlikely to solve the problem of growing need for human organ replacement, mainly because of donor organs availability. The number of patients requiring organ transplantation is increasing world wide. Take the example of heart transplant. About 2,000 people per year receive heart transplants. Yet 30,000 to 100,000 could benefit from a new heart. The problem is, there aren't enough donor hearts to go around. The available organs are rationed by transplant committees who must decide if the patient is young enough, healthy enough and compliant enough to take care of the donated organ[1,2]. There is the option of developing transplant organs by cloning but this does not seem to be a realistic option for the time being. The option of stem cell transplantation and gene therapy is not promising either. Therefore, the development and implantation of 'bionic organs' emerges as a logical and realistic approach to meet the growing challenge of increasing number of patients needing replacement of function of failing organs. Because of the tremendous advances and rapid developments in the field of bioengineering and Nano-technology, such a vision for the future of patients with organ failure is going to become a reality in the near future[3,4].

Artificial organs encompass a wide variety of anatomical and physiological parts with the possibility that every human organ may eventually be replaceable with artificial replicas for long-term implantation. The confluence of advanced computer systems, sophisticated microchips, and miniaturized electronic components coupled with today's much better understanding of the physical mechanisms of me human body has finally permitted medical researchers and scientists to develop the sort of practical implantable equipment that has the potential to afford persons with visual and physical disabilities a healthier, better, safer and much more independent life.

Bionics means the replacement or enhancement of organs or other body parts by mechanical versions. Bionic implants differ from mere prostheses by mimicing the original function very closely, or even surpassing it. Bionics are a common element of science fiction, with The Six Million Dollar Man as the probably best known example[4].

The era of bionic age has already begun, where man-made devices can replace damaged limbs and organs. Already on the market are 100 percent mechanical hearts and heart parts, mechanical arms, legs, hands and cochlear implants that can benefit the nearly deaf.

- On the near horizon are bionic eyes that restore at least partial vision, cochlear implants that allow hearing despite a damaged auditory nerve, and computer chips that permit the brain to control bionic limbs.
- In development are artificial blood, organs and other body parts, including the liver, pancreas, bladder, tendons and spinal cord. On the far horizon? Tissue engineering could make anything possible. In the field of pure bionics—the interface of human with machine—the focus has been on the heart, limbs, hands and eyes. Not only do they lend themselves to mechanical adaptation, they are also among the body parts most in demand. Advances in the field of bionics may provide a full body suit in which those with damaged spinal cords can walk upright, moving their arms and legs by using their thoughts[4,5,6].

1. **The Bionic Heart:** Artificial hearts are in great demand in the world today. They give heart disease patients, a higher chance of survival and also hope to potential heart disease sufferers. Total artificial hearts (TAH), are the greatest hope of replacing the need for scarce donor hearts but are also a tremendous mechanical challenge. A TAH must beat approximately 40 million times per year, and provide a reliable stream of blood that consists of 5 to 6 liters per minute. The current design goal for TAH is 90 percent reliability after five years, which is greater than the five-year survival rate for heart transplant patients[2,3,9]. The most popular TAH is made by Abiomed Corporation of Danvers, Massachusetts. It is a combination of equipment that fits entirely in the chest and is powered by an energy system that sends electricity through the skin. This helps avoid infection that could enter the body through an incision if the heart was joined to the power supply by a cable. The AbioCor heart, as it is called, consists of a one-kilogram pump that mimics the function of the heart's valves. Connected to mat pump is a small computer and a battery pack that allows the patient freedom from his external power supply[6,7,8,9].

The VADs (ventricular assist devices) are a thumb-sized pump that can be sewn inside a patient's ventricle to help it perform the work of pumping. One of these was installed in the left ventricle of Houghton, who was within days of death when the tiny pump was put in his heart. Now he, like many other VAD users, is enjoying a quality life. There is also an added plus. If their hearts become stronger, there is a possibility that the VADs can be removed.[9] Another type of artificial heart in the process of development is called the "StreamLiner" which is an artificial heart that can be permanently implanted into a person. As well, the device will be made so it will avoid the complications of infection and rejection, complications that usually occur after a transplant. This device will be suspended in the abdomen area using magnetic levitation[9].

2. **Bionic Ear:** A cochlear implant (Bionic Ear) is an artificial hearing device, designed to produce useful hearing sensations by electrically stimulating nerves inside the inner ear. The Bionic Ear was pioneered in 1978 by Professor Graeme Clark and his team. The present day multi-channel cochlear implants, consist of 2 main components: 1) cochlear implant package and electrode array (or receiver-stimulator) and 2) the speech processor and headset. Cochlear implants have shown steady improvement with the advance of electronics. Doctors at the House Ear Clinic in Los Angeles estimate success rate for cochlear implants at 99.6 percent and that deaf person can regain as much as 50 percent hearing.

Without a functioning auditory nerve, cochlear implants will not work. But the next generation of implants may change that. Doctors are looking always to connect a man-made device directly to me brainstem to eliminate the need to rely upon the auditory nerve. In the near future, bionics experts predict that surgeons will be able to plug into the brainstem with such precision that high-fidelity cochlear implants will be possible[10,11,12].

3. **Bionic Eyes:** Overcoming blindness with bionics has been a realistic goal for 50 years. In 2002, ophthalmologist Dr. Alan Chow with the approval of the FDA, implanted tiny microchips into the retinas of six blind patients. Those chips contained 5000 solar cells on a disc the size of a pinhead. When exposed to light, the cells generated electricity that stimulated the optic nerve. Chow's six patients reported substantial improvement in their vision. One went from seeing nothing to being able to see his porch light. Another went from barely being able to see his hands in front of his face to seeing a flock of geese in the sky. It was not the telescoping vision of the Six Million Dollar Man but it was a giant leap forward[13].

The Artificial Silicon Retina Chip: Optobionics' Artificial Silicon Retina microchip is a silicon device 2mm in diameter and 25 microns thick (less than the thickness of a human hair). The tiny ASR implant possesses approximately 5,000 microscopic solar cells called microphotodiodes, each with its own individual stimulating electrode. These microphotodiodes are designed to convert the light energy entering the eye into electrical impulses that stimulate the remaining functional cells of the retina in patients with retinitis pigmentosa and age-related macular degeneration types of conditions .Thus it can bring a blind person to the point where he or she can read, move around objects in the house, and do basic household chores[14].

Artificial Vision: Persons who have significant eye damage or who have lost their eyes entirely, even such hopeless and seemingly irreversible vision loss may be overcome with sophisticated computerized visual systems such as the innovative "Dobelle Eye." This artificial vision system, reflecting more than 30 years of developmental work by the Dobelle Institute in New York City and its affiliates on Long Island and in Switzerland, enables a totally blind person to achieve visual acuity of about 20/400 in a narrow "visual tunnel." The Dobelle Eye consists of a subminiature television camera and an ultrasonic distance sensor, both of which are mounted upon a pair of eyeglasses. The sensors connect through a cable to a small computer that is worn in a pack on a person's belt. After processing video and distance signals, the vision system's primary computer uses advanced computer-imaging technology, including sophisticated edge-detection algorithms, to eliminate any visual "noise." The first computer then activates a second microcomputer, which then transmits pulses to an array of 68 platinum electrodes implanted on the surface of the visual cortex of the user's brain[15].

4. **Bionic Kidney:** Kidney Transplantation is one of the most successful among the human organs transplant history and will continue as a treatment option for patients with chronic renal failure. But the biggest issue in transplantation is compatibility between the donor and the receiver. Even with many years of experience in kidney transplantation, the issue of compatibility and rejection of the organ has not been completely resolved. Since the availability of immunosuppressive drugs, the threat of rejection has minimized somewhat, but with great risk to the patient.

All patients while waiting for transplant are treated by artificial kidney which is also used in support for a kidney transplant. Therefore, as an alternative treatment option to transplantation, the present successfully used artificial kidney is continuing to be upgraded and miniaturized with new bioengineering innovations to make it suitable for implantation in the body for permanent replacement of renal function. With more development of better materials and cheaper technology, the artificial kidney can be made available as a treatment option to all patients[16].

5. **Artificial Pancreas:** For the millions of patients with diabetes, life is an endless routine of finger-sticking, glucose monitoring and, for some, insulin injections — and all are living with the fear of serious health consequences. Monitoring blood sugar levels is the best way to help guard against serious complications from diabetes such as kidney and heart disease, blindness, and vascular problems that can lead to stroke and lower limb amputation. But constant monitoring is not easy or convenient. While new tools for taking blood, measuring glucose, and administering insulin have helped somewhat, they still entail a loss of freedom and require a conscientious effort.

Insulin pumps are an attractive alternative to injections because they more closely match the natural action of the pancreas by releasing small amounts of shorter-acting insulin. The pumps currently on the market in the US are about the size of a pager, are worn externally, and deliver insulin through a catheter inserted under the skin. They must be pre-programmed and still require the user to draw blood several times a day.

An implantable device being developed by scientists at the Deptt. of Energy's (DOE) Lawrence Livermore National Laboratory in partnership with MiniMed, Inc. of Northridge, California, now offers hope for a more normal life style. Composed of a glucose sensor imbedded under the skin and an insulin pump implanted in the abdomen, the device will work like an artificial pancreas to signal when the body needs insulin and deliver it in precise doses. The new implantable pump, manufactured by MiniMed, is a 2.3-in.-diameter by 0.8-in.-thick titanium disk that includes a reservoir for the insulin. Unlike injections, which can pool insulin in the tissues before it slowly dispenses into the bloodstream, the pump infuses it directly into the abdomen where it is more quickly absorbed. The internal pump is approved for distribution in Europe and is undergoing clinical trials in the U.S. Livermore's new sensor mechanism automates the process by telling the internal pump when to administer the insulin. Adapted from technology used for fusion research at Livermore's Nova laser, the sensor uses fluorescent transducer molecules to measure light reflected in the tissues instead of measuring glucose in the blood. The detection mechanism uses a molecule that normally has low fluorescence because, once excited by light, electrons are transferred from one part of the molecule to another, preventing bright fluorescence from occurring. When bound to glucose, however, the glucose molecule prevents the electrons from interfering with the fluorescence, and the molecule becomes a bright fluorescent emitter. The more glucose that is present, the more molecules mat become bright emitters. The fluorescent molecules will be placed within a biocompatible polymer implant being developed by MinMed, and will transmit the information to the pump through a watch-like device worn on the wrist. The sensor components will work in conjunction with the pump, creating a "biomechanical" pancreas. The implant will monitor glucose levels for at least a year before it needs to be replaced[17,18].

The Livermore's research team has received two distinguished awards for their work: an Excellence in Technology Transfer Award from the Federal Laboratory Consortium and an Energy 100 Bright Light Award from the Department of Energy, which honors scientific and technological accomplishments[17].

6. **Bio-Artificial Liver:** The need for an artificial liver device that would remove toxins and improve immediate and long-term survival results for patients suffering from liver disease is more critical today than ever before. Millions of people suffer from liver disease as a result of viral hepatitis, alcohol abuse, drug overdoses and other factors. Limited treatment options, a limited supply of donor livers, and the high price of transplants and follow up costs all indicate that a strong need exists for an artificial liver device, now and into the foreseeable future. It is anticipated that an artificial liver device could be used as a temporary artificial liver for patients awaiting a liver transplant, thus lengthening the time they have available while an organ donor is located.

The greatest hindrance to the development of a therapeutically effective artificial liver device is the lack of a defined liver cell line that provides the functions of an intact liver. A leading candidate addressing this need is the PICM-19 cell line which is a liver stem cell line derived from porcine epiblast tissue (i.e., embryonic stem cells). The PICM-19 cell line is unique in its ability to form both functioning hepatocytes and bile duct cells, the two cell types that make up the bulk of the

liver and that are critical to its function. Thus, the PICM-19 cell line can be applied to the production and testing of an artificial liver device for treatment of human patients with liver failure.

In collaboration with USDA, HepaLife Technologies scientists Dr. Neil C. Talbot (cell biologist) and Dr. Thomas J. Capema (biochemist), co-inventors of the patented PICM-19 cell line and its patented application to an artificial liver device are optimizing the growth and functional performance of the PICM-19 cell line devising its use in an artificial liver device. These research findings mark an important cell engineering achievement for the development of bio-artificial Liver[19].

7. **Artificial Blood:** There is limited availability of fresh blood for transfusion due to the short-fall of donors and an increased number of surgical procedures which require blood. It is therefore becoming more important to consider safe and effective alternatives. BBC NEWS ON LINE reported on 23 October, 2003, that UK Doctors have for the first time successfully used artificial blood to treat patients. The product is a powder which can be stored for years. It is made from donated supplies of real blood, which normally has a shelf-life of just 42 days. The powder can then be mixed into liquid form when needed, and used immediately regardless of the patient's blood type. This is a molecule that the body's immune system gladly welcomes. Robert Winslow, founder of blood substitute company Sangart of San Diego has tested a new blood substitute called MP4. It contains haemoglobin molecules coated with polyethylene glycol to make them bulkier, so the resulting fluid is thicker, or more viscous, than normal blood. The coating also gives MP4 a higher affinity for oxygen than other substitutes. Studies have shown that MP4 releases oxygen in the capillaries, as intended[20].

Better than real: Tests in hamsters that had lost a lot of blood showed they actually fared better when given MP4 than real blood (Critical Care Medicine, vol 31, p 1824). The animals needed less MP4 than real blood to oxygenate their tissues. The researchers think this is because it releases oxygen only where levels are lowest.

8. **Artificial Larynx:** A fully functional tracheostoma valve for exhalation and inhalation has been produced, vocal cords have been produced and porous tissue connectors have been designed. Presently research is still being done for materials that will allow optimum soft tissue growth.

9. **Artificial Muscle:** Many machines can automate some functions of a human muscle. Recent research into polymer based artificial muscles may soon yield organs that work more like real limbs. Mo shahinpoor, an engineering professor at the University of New Mexico develops artificial muscles from polyacrylonitrile (PAN). Researchers discovered that PAN is a tough substance that is combination of a gel and a plastic. Shahinpoor's research documents state that the fibers are capable of holding 4 kg per square centimeter. A human biceps can lift a maximum of just over two kilograms per square centimeter. So far, models that effectively simulate muscle movement have been created. The artificial muscle has experimentally proven they are capable of moving limbs of a skeleton. Dielectric elastomers are still at a research level, but they have the potential to be produced at a low cost.

10. **Artificial Cartilage:** In one year, Americans cause 1 billion dollars in damage to the articular cartilage in their knee. This equals to approximately 500,000 operations. Cartilage replacement is imminent. Johnson & Johnson and Integra Life Sciences have developed a collagen matrix called Integra that will help the body naturally regenerate its cells. This innovation will reduce the number of surgeries and the cost of surgery. An operation is required to implant the matrix but it is less expensive and a less serious operation then all others available[21].

11. **Artificial Skin:** Every year, millions of people are severely burned. Artificial skin allows severely damaged skin to grow back and heal faster. Under normal conditions when the dermis is destroyed, it cannot regenerate. Usual methods of treating severe bums are skin grafting and harvesting from cadavers. There is a possible $130 million market for artificial skin in U.S and Europe. One such model of ARTIFICIAL SKIN, Integra allows immediate wound closure after a bum wound. There was no rejection in clinical trials. Integra provides a base for cells to grow.

Fantasy, Success and Failure: Is mere a completely bionic man in our future? Doubtful, say most bionics experts. Although technology has come a long way toward melding man and machine, it still has a long way to go. The major problem is in tissue-material interface. Machines need to interface with the organ of perception, the brain. Since our understanding of the brain has just begun, our understanding of how to connect mechanical devices to these workings is lagging even further behind.

"Continued research in neuroscience and bioengineering will no doubt lead to improvements," says William Jenkins, Ph.D., vice president for development at Scientific Learning Principles Corporation in an interview with Wired magazine. "But it will be a long, hard road filled with many failures and few successes."

REFERENCES

1. 2001 Annual report of the U.S. Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients. Vol. 1. Washington, D.C.: Department of Health and Human Services, 2001: 439-83.

2. Cardiac Replacement with a Total Artificial Heart as a Bridge to Transplantation. NEJM: No. 9, Vol 351: 859-867, August 26, 2004.

3. Experts discuss artificial organs and bionic technology at ASAIO's (The American Society for Artificial Internal Organs) meeting. Press briefings held on June 13, 14, 15, 2002, University of Michigan Health System.

4. Bionics (Science on the Edge) ~ Maxine Rosaler. 01 August, 2003. Blackbirch Press.

5. CCNmag-com .Technology And The Quality Of Life: Part One - A Vision Of The Future, by Kamil Z. Skawinski. www.ccnmag.com/storv.php?id=l 97

6. CHFpatients.com - Artificial Hearts-November 26, 2001 - Abiomed received permission from the FDA to implant its artificial heart in 5 more patients, www.chfpatients.com/implants/artificial_hearts.

7. AbioCor Implantable Replacement Heart - Texas Heart Institute, 1996-2006. Texas Heart Institute Journal.

8. ABIOMED AB5000 Circulatory Support System – Texas Heart Institute, 1996-2006. Texas Heart Institute Journal.

9. Frazier OH, Dowling RD, Gray, Jr. LA, Shah NA, Pool T, Gregoric I: The Total Artificial Heart: Where We Stand. *Cardiology 2004; 101: 117-121 (DOI: 1O.l 159/000075992.*

10. June 2004, John Huigen, The Bionic Ear Institute, University of Phoenix, webmaster@bionicear.org

11. Biology 202, 2004 First Web Paper On Serendip. Cochlear Implants: A Bionic Sensory Experience? By Lindsey Dolich.

12. Edmond Alexander. "The Coming Merging of Mind and Machine." Scientific American Inc. 1999.

13. Artificial Vision for the Blind, Try a brain implant, or opt for The voice auditory display? http://www.seeingwithsound.com/Artificial.htm.

14. *Progress In Artificial Vision. The Dobelle Institute's Artificial Eye allows the blind to see. Published in the June, 2002 issue./Eyes* Vision:www.crystalinks.com/eyes2.html.

15. CBC News: Sunday - Out of the Dark. Broadcast January 05, 2003 on CBC News.

16. BBC NEWS | Health | 'Biological' kidney implant hope. The first human trial of an artificial 'bio' kidney has shown encouraging results, offering hope of a working implant for patients.news.bbc.co.uk/2/hi/health/3985523.

17. Bright Light Award: Biomechanical Pancreas to Manage Diabetes - 1999: http://www.ma.doe.gov/energyl00/health/81.html.

18. Advances Toward the Implantable Artificial Pancreas for Treatment of Diabetes: http://www.diabetes.org/DiabetesCare/1998-03/pg444.html.

19. Vancouver, BC – October 5, 2005 – HepaLife Technologies, Inc. (OTCBB: HPLF) (FWB: HL1) September 19, 2005 press release. http://www.hepalife.com/Investor/PressReleases/20050919-l.html).

20. *Journal of Applied Physiology,* DOI: 10.1152/japplphysio.00530.2003).

21. McLean, Bethany, "The Billion Dollar Cartilage Market", Fortune, April 27, 1998.

INSTRUCTIONS FOR AUTHORS

Original articles, review articles, case report, special communication and quizzes pertaining to Health Sciences which have not been published elsewhere, are invited for publication in Journal of Medical Sciences. They are considered for publication on the understanding that they are contributed to this Journal solely.

Manuscript should be typewritten in duplicate on one side of the paper and double spaced, with wide margins. Manuscript prepared on MS Word 2000 or MS Word XP may be submitted on a floppy disk 2.5 along with the printed copy of the manuscript.

Begin each component on a new age in the following sequence.

Title Page – It should carry title of the article, which should be concise but informative, names of the authors, with their highest academic degree(s) and institutional affiliation; names of department(s) and institution(s) where work was carried out and name and address of the author responsible for correspondence.

Abstract – This should contain not more than 150 words and include a statement of the problem, the method of study, results and conclusion. The summary section should not be included in the main manuscript.

Introduction – State the purpose and rationale for the study with pertinent references. Do not include data or conclusions from the work being reported.

Research Methods – Describe selections of the subjects (inclusion and exclusion criteria) clearly. Identify the methods, apparatus, and procedures in detail.

Results – Present results in logical sequence in the text, tables and illustrations. Do not repeat in the text all the data in the tables or illustrations.

Discussion – Comment on the important results of the study; their implications and limitations. Compare the results to other relevant studies. Draw out conclusions and suggestions. Avoid unqualified statements and conclusion not completely supported by the data.

Avoid duplication of data given elsewhere in the text.

References – References should be numbered consecutively in the order in which they are first mentioned in the text. They should confirm to the style of Index Medicus e.g. Shahid A, Qureshi H, Nizami F. Electrolytes in Liver Disease: A preliminary study. JLO 1989 Vol. I: 1-10. References to books and monographs should include authors and editors, edition, year city of publication, name of publishing company and page number(s) e.g.: Burton JL, Lovell CR. Disorder of Connective Tissue. In: Champion RH, Burton JL, Burns DA and Breathnach SM, editors. Textbook of Dermatology 6th ed. Blackwell, 1998, 2003-2072. It is most important that authors should verify personally accuracy of every reference.

Tables are adjuncts to the text and should not repeat material already presented. Tables should be self-explanatory and have a brief title and numbered consecutively as they appear in the text.

Illustration (Figures) – Two sets of illustrations, one with each copy of the manuscript, must be submitted. They should be numbered consecutively as they appear in the text. Type l egend for illustration on separate page. Figure should be professionally drawn. Colored illustration will be charged to authors.

Case reports – Case reports should not exceed 1000 words. The introduction should be brief and the major part of it should give the pertinent details of the case with emphasis on the basis of the confirmation of diagnosis. Discussion including review of literature should be restricted to 2-3 paragraphs or so, but must include at least 3 to 4 key references. The significance of the case to justify its publication should be highlighted.

It is most important that authors should verify personally the accuracy of every reference. The reference should be recorded in the text by their number and in the order they appear in text.

Letter to the Editor – Send your comments, questions or criticisms about articles published in Journal of Medical Sciences in a short, crisp letter. Readers are invited to freely contribute to this column.

Meeting – If the manuscript was presented at a meeting, the place where it was held, and the date on which it was read must be included and should appear at the foot of the title page.

Each submitted paper takes 04-08 weeks for editorial review. Authors will be informed of decision of editorial board by post. Where the paper is submitted for peer review, confidentiality to the author and place of research will be maintained.