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CONTENTS

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EDITORIAL

MANAGEMENT OF CHRONIC HEPATITIS B – ROAD MAP FOR THE FUTURE

Hepatitis B is a global health problem[1], consuming individual and national resources despite the fact that it is totally preventable. It is alarming to know that the prevalence of Hepatitis B is still on the rise in our country[2]. The world has moved on and is talking about cure of chronic hepatitis B when we are having failed attempts at the preventive stage. It is probably due to ineffective preventive strategies, unawareness and lack of interest of the public and malpractices of both qualified and unqualified health care givers.

Recent advances in its understanding have opened up new ways to deal with patients with hepatitis B. This virus and its activity can be monitored using biochemical markers (Alanine aminotransferase [ALT]), histological markers, serological markers (Hepatitis Be Antigen [HBeAg], Anti-HBe antibodies, Hepatitis B surface Antigen [HBsAg], Anti-HBs antibodies) and Hepatitis B viral DNA load (HBV viral load). Except for the last, all other factors are surrogate markers.

Not long ago, we used to ask for ALT levels in patients with chronic hepatitis B and select only those with high ALT levels for treatment. However, ALT is losing this screening status as there is evidence that the currently set normal range of ALT may not be accurate. This is because when ALT normal range was approved, we were unaware of the existence of Hepatitis C and Non-alcoholic fatty liver disease. The relative risk of dying from liver disease for ALT <20 IU/ml is 1 which is increased by 10-fold for ALT level up to 40 IU/ml[3]. That is why normal ALT levels have been revised: 19 IU/ml for women and 30 IU/ml for men[4]. Further, the pattern of rise in ALT is not always uniform in all patients. Some would have persistently high ALT, some may have persistently high ALT with flares while most of them would have flares in ALT levels with normal levels in the intervening period. Thus there is a chance of missing patients who may require treatment.

Though liver biopsy is important in bench medicine when comparing new therapies with old remedies, it is losing its status in bed side medicine. The various Scoring systems [Knodell histologic activity index (HAI), Ishak system, METAVIR system] speak for the inconsistency in reporting. Hepatitis Be Ag (HBeAg) is an important marker in the sense that its presence indicates active replication of the virus and its disappearance (spontaneously or with treatment) remains an important landmark in the management of chronic hepatitis B. However disappearance of HBeAg is no longer considered as an end point for therapy as we now know that 'e' seroconversion at the end of first year of therapy is around 20%, regardless of the drug potency.

HBV DNA viral load, compared to surrogate markers, is emerging as the most important marker in the diagnosis and management of chronic hepatitis B. Higher viral load is usually seen in 'eAg' positive patients and lowest levels are usually seen in healthy carriers while modest load is seen in 'eAg' negative patients. Thus it roughly suggests the phase of chronic hepatitis B. The relative risk of developing cirrhosis[5] and hepatocellular carcinoma[6] correlates with viral load and so does HAI[7], regardless of ALT levels. Further HBV DNA level can help monitor therapy, detect virological breakthrough and viral resistance, thus helping to confirm whether the current therapy is effective and when additional/switch therapy is required.

According to current 'Road Map Concept', HBV viral load should be assessed three months after starting oral therapy. A 10-fold reduction in viral load suggests 'Primary Response' while <10-fold reduction is called 'Primary Treatment Failure'. If primary treatment failure is not due to non-compliance, patients should be switched to another drug. Primary responders are assessed by viral load at six months after starting therapy. HBV viral load <60 IU/ml, six months after starting therapy, is called 'Complete virological response'; viral load $>10^3$ IU/ml is called 'Inadequate virological response' and viral load >60 IU/ml to $<10^3$ IU/ml is called 'Partial virological response'. Patients with complete response are continued with the same drug, those with inadequate response are switched to another drug. Those with partial response and taking drug with low resistance are continued with the same drug but monitored on three monthly basis with viral load, while those taking drug with high resistance are switched to another drug.

While previously it was thought that patients with chronic hepatitis B require life long treatment, it is now believed that therapy can be stopped if two consecutive PCRs (six months apart) are negative in 'HBeAg positive patients' and three consecutive PCRs (six months apart) are negative in patients with eAg negative chronic hepatitis B[8]. Thereafter patients have to be followed closely with serial HBV viral load to detect relapse. This new approach to achieve PCR negativity and stop therapy at a defined time has opened a new chapter in the management of chronic hepatitis B.

Treating patients with chronic hepatitis B is important, but far more important is prevention. This

becomes much more important in cash strapped countries like ours. Improving the standard of surgical/invasive medical procedures and blood transfusion services along with safe disposal of hospital waste would go a long way to prevent hepatitis B. Perinatal transmission can be prevented (at least in those having delivery in hospitals) by mandatory vaccination at birth of babies born to mothers infected with HBV. Currently Hepatitis B vaccination is included in EPI program, the first dose being given at the age of one month. This timing is wrong. It has to be given at birth along with hepatitis B immunoglobulin. Further, mass media campaign for public awareness regarding vaccination against HBV would also help reduce the disease burden. The right strategy, in our country, would be to invest in preventing HBV infection rather than spending millions on treating patients with chronic hepatitis B.

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OBITUARY

The patron and Editorial Board is deeply sorrowed by the sad demise of Maj Gen (R). Iftikhar Ahmad Malik, a distinguished pathologist, scholar and teacher. We offer our condolences to his family, friends and colleagues. May Allah rest his soul in peace. Aamin

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ACUTE RENAL FAILURE SECONDARY TO GASTROENTERITIS — DOES EARLY REFERRAL MAKE A DIFFERENCE ?

***Muhammad Abdul Mabood Khalil, Amer Azhar, Nisar Anwar, Faridullah Shah, Aminullah, Shahzad Haider, Shahzad Hussain**

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ABSTRACT

Objective: Gastroenteritis is one of the important causes of acute renal failure. Early referral and timely management is likely to improve the outcome of acute renal failure. This observational study was carried out to find whether early referral was associated with increased conservative management and decreased requirement for dialysis or not.

Material and Methods: It was hospital based observational study done at the department of Nephrology Khyber Teaching Hospital. A total of 50 adult patients with acute renal failure secondary to gastroenteritis were included. Their renal function tests, electrolytes and ultrasound for kidneys were done. Patients were either treated conservatively or with dialysis as per assessment of individual patient.

Results: A total of 50 patients were included in the study. Among them 34 were male and the rest were female. Twenty two out of 29 patients (75.86%) who were referred with in 24 hours were treated conservatively. Eighteen patients out of 21 (85.21%) who were referred after 24 hours required haemodialysis while only 3 out of 21 patients (14.28%) were treated conservatively in this late referral group. Thus the number of dialysis requirement increased enormously after 24 hours.

Conclusion: Early referral of the acute renal failure secondary to gastroenteritis leads to more conservative management with intravenous fluids and antibacterial therapy. However, the number of patients requiring haemodialysis increased in patients who were referred after 24 hours.

Key Words: Gastroenteritis, acute renal failure.

INTRODUCTION

Managing acute renal failure is still a major challenge for the nephrologists. Its incidence varies from 100 to 600 million per year[1]. In hospitalized patients, incidence of acute renal failure is 2.5%[2,3]. Acute renal failure can be community or hospital acquired. Hospital acquired acute renal failure usually complicates intensive care patients and is the end result of multi-organ failure[4]. Community acquired acute renal failure is usually secondary to volume depletion from hot environment, gastroenteritis or various infectious diseases like malaria and is more common in developing countries. Pakistan being a developing country has the problem of poverty, over-crowding and lack of clean water supply. Infectious diseases including gastroenteritis and respiratory tract infections are still common. Outbreaks of gastroenteritis usually occur in summer and rainy seasons[5]. Thus acute renal failure secondary to gastroenteritis is still a common problem in our country. Early referral and management of such potentially reversible cases can improve the outcome.

The aim of this study was to find out whether early referral to a nephrology unit in a tertiary care hospital leads to more conservative management and decreased requirement for dialysis or not.

MATERIAL AND METHODS

Due to increased referral of acute renal failure secondary to gastroenteritis to the department of Nephrology this observational study was carried out from 1st July 2006 to 31st December 2006 in the department of Nephrology, Khyber Teaching Hospital Peshawar.

All patients with acute renal failure secondary to gastroenteritis referred from out side and within hospital were included in the study. Patients with gastroenteritis having creatinine more than 1.5mg/dl were labeled as acute renal failure and were included in the study. Patients with history of chronic renal failure, diabetes, hypertension, urinary tract surgery, nephrolithiasis and small shrunken echogenic kidneys on ultrasound were excluded.

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Patients were treated either conservatively or with dialysis as per assessment of each patient. Conservative treatment included intravenous fluids and antimicrobial therapy. Early referral was defined as patients who were referred within 24 hours. Patients who were referred after 24 hours were labelled as late referral group. All information about referral time, hydration status, intake output record, renal function tests, serum electrolyte and renal ultrasound findings were recorded on a Performa. Patients with oligoanuria, hyperkalemia, fluid overload, pulmonary edema, pericarditis and encepahalopathy were dialyzed. After discharge they were then followed for a period of 3 months in Nephrology outpatients clinic for their final outcome. At the end T-test was applied to find the mean and standard deviation of various variables.

RESULTS

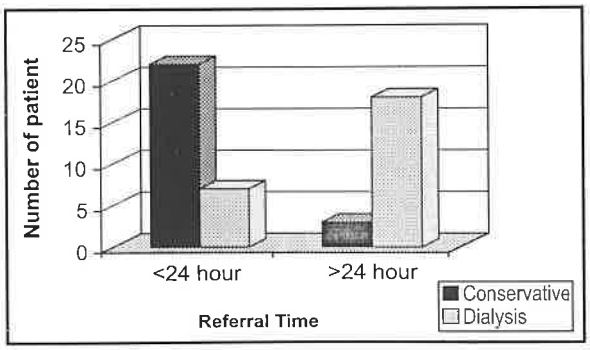
A total of 50 patients satisfying selection criteria were studied. Among 50 patients, 34 were male and 16 patients were female. Their ages ranged from 15-60 years and their mean age was 37±14 SD. Mean urea was 108.7±54.6 SD and mean creatinine was 5.33±3.028 SD. Twenty two patients out of 29 (75.86%) referred within 24 hours were treated conservatively. However the number of conservatively treated patient decreased to 3 out of 21 (14.28%) by late referral of more than 24 hours. In contrast 18 patients out of 21 (85.21%) who were referred after 24 hours required dialysis. Only one patient (2%) with coronary artery disease and shock died who was referred after 24 hours. On follow up all the patients had full recovery of renal function.

Table 1: General Characteristics

Sex	Male	34
	Female	16
Age	Range	15-60
	Mean	37±14 SD
Renal Function Tests	Blood Urea	108.7±54.6 SD
	Serum Creatinine	5.33±3.028 SD
Serum Electrolytes	Serum Potassium	4.5 ± 2.5 SD
	Serum Sodium	132 ± 3.5 SD
Urinary output	Normal urinary output	5
	Oliguria	30
	Anuria	15
Management	Conservative	25
	Dialysis	25

Table 2: Outcome according to referral time

Time of referral	Conservative	Dialysis	Total No. of patients
<24 hour	22 (75.87%)	7 (24.13%)	29
>24 hour	3 (14.28%)	18 (85.72%)	21



DISCUSSION

There is a greater understanding of pathophysiology and management of acute renal failure. Still its management is a challenging job for nephrologists. Mortality of acute renal failure is 50 to 80% in various studies[6]. Gastroenteritis is one of the leading causes of acute renal failure. Not much work is done on acute renal failure due to gastroenteritis alone. Rather majority of the studies are done on various etiologies of acute renal failure and its outcome unlike this study[7,8,9,10].

This study showed interesting trends. Out breaks of gastroenteritis still occur as evident by this study and another study in the country[5]. Early referral was associated with conservative management of acute renal failure due to gastroenteritis. Late referral was associated with increased requirements for dialysis. The mortality in this study was 2%.

In the developing countries diarrheal illnesses are still common. South Asia is no exception to this. Gastroenteritis is still an important cause of acute renal failure. In Pakistan various studies on acute renal failure showed that gastroenteritis is one of the common cause of acute renal failure[9]. Similarly in Nepal and India various studies reported gastroenteritis as a cause of acute renal failure in 22-44.5% of the cases[10]. Thus gastroenteritis is one of the important etiological agent of acute renal failure in our part of the world.

Gastroenteritis through volume depletion causes pre-renal failure. Failure to correct hypovolemia in gastroenteritis results in acute tubular necrosis and renal failure. This study showed that early referral of acute renal failure secondary to gastroenteritis led to conservative management. On the other hand late referral was associated with more requirement for dialysis. Hypovolemia due to any cause results in hypoperfusion. If hypovolemia persists it results in tubular injury and irreversible damage if not corrected in time. Earlier correction of hypovolemia has been shown to improve outcome. There is no study available on management of diarrheal illnesses leading to acute renal failure in context of referral time to compare with the results of our study. Rather majority of the studies are done on various etiologies of acute renal failure and its outcome unlike this study[11]. Blow and his colleagues found that detection of hypovolemia and hypoperfusion within 24 hours in major trauma improves the outcome[12]. Esson and Schrier found that delayed referral in cases of acute tubular necrosis affects the outcome of acute renal failure[13]. Similarly various other studies have shown that delayed referral and consultation in cases of acute renal failure leads to adverse outcome[14,15]. Thus early recognition and management of acute renal failure improves the outcome.

This study showed a low mortality of 2%. Community acquired acute renal failure has lower mortality than hospital acquired acute renal failure. The mortality in community acquired acute renal failure is 7 to 23% as compared to hospital acquired acute renal failure where mortality is 50 to 80%. A study in children showed full recovery in all cases of post diarrheal acute renal failure with no mortality at all[16]. In contrast hospital acquired acute renal failure, sepsis, multi-organ failure and acute renal failure in ICU set up has high mortality of 50 to 80%[17,18]. The low mortality in this study could be due to just simple hypovolemia, absence of sepsis and multi-organ failure. Thus this study gives a picture that gastroenteritis is associated with lower mortality as compared to other causes of acute renal failure. Moreover early referral decreases the need for dialysis and majority of the patients can be treated conservatively.

CONCLUSION

From this study it is concluded that early referral of acute renal failure secondary to gastroenteritis leads to more conservative management. However renal replacement therapy is needed in late referral group.

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EVALUATION OF 'MYCOBACTERIUM LEPRAE PARTICLE AGGLUTINATION' TECHNIQUE FOR THE SEROLOGICAL DIAGNOSIS OF LEPROSY

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ABSTRACT

Objective: This study is planned to determine the efficacy of a recently developed method called *Mycobacterium Leprae* Particle Agglutination (MLPA), which measures antibodies to Phenolic Glycolipid -1 (anti-PGL-1), especially in the sera of leprosy infected individuals and to compare the usefulness of this method with skin slit smear.

Material and Methods: The study was conducted at the Department of Microbiology, Hayatabad Medical Complex Peshawar, Pakistan from July 2001 to June 2002. A total of 147 cases were included; 72 histopathologically diagnosed cases, 25 open tuberculosis cases with positive IgG and IgM anti-tuberculosis antibodies (to evaluate the cross reaction) and 50 school children with age range of 10-15 years having no contact with leprosy and negative Antituberculosis IgG and IgM were included in the study as negative control. The serological diagnosis was compared with skin slit smear. Sera from all the cases were used for the detection of Anti bodies to Phenolic Glycolipid-1 (anti-PGL-1) antibodies by *Mycobacterium leprae* Particle Agglutination (MLPA) test.

Results: Of the 37 of lepromatous leprosy cases 25 (67.6%) were found to have positive skin smears and leprosy IgM anti-PGL-1 antibodies was positive in 29 (78.4%) mean having 0.78 ± 0.07 with p value of 0.044. Out of 25 tuberculoid leprosy only 3 (12%) cases positive by slit-skin smears and leprosy antibodies in 12 (48%) cases having mean 0.48 ± 0.10 with p value of 0.001. Among 10 intermediate / indeterminate leprosy cases 4 (40%) cases were positive with slit skin smear and leprosy serology in 5 cases (50%) with p value of 0.343. The overall leprosy serology had significantly better results than that of slit smear and in cases of open tuberculosis and normal non-exposed children with p value of < 0.0001. Slit skin smear in 25 tuberculosis cases and fifty school children were negative. However, 6 (24%) cases having mean 0.24 ± 0.09 cases of open tuberculosis cases were found positive for leprosy antibodies which may be due to cross reaction. There was only one case (2%) among the school children, which revealed positive reaction with leprosy serology. Sensitivity, specificity, positive and negative test and predictive values and efficacy of the serology test for Lepromatous leprosy demonstrated excellently in all values. However, intermediate type leprosy revealed very low value for predictive value of the test. Similarly sensitivity of tuberculoid and intermediate leprosy cases is low.

Conclusion: MLPA showed better results than slit skin smear in the diagnosis of different types of leprosy except indeterminate leprosy. It appears that this method is reliable, economical, and time saving especially for screening of contacts and for mass screening.

Key Words: *Mycobacterium leprae, Serology, Particle agglutination test.*

INTRODUCTION

Leprosy is considered to be a special public health problem, owing to the permanent disabilities it causes as well as its social consequences such as discrimination and stigma[1]. It currently affects over 1 million people in Africa, Asia, South America and the Pacific, and WHO estimates that between 2 and 3 million individuals are permanently disabled as a result of it. Although all the registered cases are on treatment, it is estimated that during the period 2000-2005, about 2.5 million people affected by leprosy need to be detected and treated[2].

Like other developing countries it is not uncommon in Pakistan and is endemic in many areas. In Pakistan the registered prevalence at the beginning of 2004, was 1062 and number of newly detected were 751; among them new children cases were 51 and number of cases with grade 2 disability were 169. Apart from Karachi, North West Frontier Province (NWFP) is contributing the maximum number of new admissions and thus attributing it as an endemic part as well[3].

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Due to the false positivity rates with slit-skin smears, the difficulties with histopathological assessments in developing countries including Pakistan[3] and inability of the organism to grow in artificial media coupled with the problems in culturing it in the foot-pad of armadillo[4], compelled the need of finding some new, rapid and accurate method for early diagnosis of leprosy.

This paper is presenting the efficacy of a recently developed method called *Mycobacterium Leprae Particle Agglutination (MLPA)*, which measures antibodies to Phenolic Glycolipid-1 (anti-PGL-1), especially in the sera of leprosy infected individuals. It determines the role of serology in the clinical and pre-clinical diagnosis of leprosy. The rising titre in the infected close contacts of leprosy patients can be used for pre-clinical diagnosis[5]. The test is easy to perform and has sensitivity and specificity comparable[6] to indirect Enzyme Linked Immunosorbent assay (ELISA). If found useful and effective, the test would be clinically useful for monitoring chemotherapy and screening high-risk individuals in leprosy endemic areas like Pakistan.

MATERIAL AND METHODS

The study was conducted at Department of Microbiology, Hayatabad Medical Complex Peshawar Pakistan from July 2001 to June 2002.

A total of 147 cases were included; 72 histopathologically diagnosed cases, 25 open tuberculosis cases with positive IgG and IgM anti-tuberculosis antibodies (to evaluate the cross reaction) and 50 school children with age range of 10-15 years having no contact with leprosy and negative Antituberculosis IgG and IgM were included in the study as negative control. The diagnosed cases were placed into different groups by their clinical, bacteriological, and/or histopathological findings according to Ridley and Jopling's classification of Leprosy. The relative distribution of different types of cases is given in the Table 1.

The history of every patient was taken on a specially designed proforma including age, sex, socio-economic status, relevant clinical details i.e. number, site, and morphology of lesions, clinical diagnosis, and classification noted at leprosy centre. All cases were individually dealt with for diagnosis by slit-skin smear and biopsy reported at National Institute for Leprosy Research (NILR) Tokyo, Japan.

Slit-skin smears were prepared from 4 sites i.e. Right ear, Left ear, forehead just above the right eye brow) and margin of an active lesion. In patients with diffuse infiltration the fourth site selected was dorsum of the middle finger. The technique described by Leiker and McDougall[8] was adopted for taking and processing of slit-skin smears.

For serology 3-4 cc of venous blood was collected and serum was separated. All sera were used for the detection of anti-PGL-1 antibodies by *Mycobacterium Leprae* Particle Agglutination (MLPA) test. In this test a semi-synthetic antigen (natural trisaccharide-phenyl-propionate bovine serum albumin (NT-P-BSA) reacts specifically with anti-PGL-1 antibody of patients serum on the surface of gelatin particle and aggregate in the form of a film. All serum specimens were first dealt with qualitative method and those found positive were further processed into higher dilutions for quantitative measurement of raised levels of antibodies according to the procedure described in the literature provided with the kits. The antibodies titre values are defined in terms of the highest dilution giving a reactive result, indicating the final specimen dilutions at which specimens remain reactive and beyond which they are no longer reactive. The dilution of more than 1:32 is taken as positive.

RESULTS

There were 72 cases of leprosy diagnosed histopathologically included in the study. Mean age of these 72 diagnosed cases was 38.78 ± 16.53 years and male to female ratio was 2.4:1. Among them range of age of lepromatous leprosy cases was 18-80 years with mean of 42.08 ± 2.87 years, age range for intermediate leprosy cases was 14-67 years with mean of 35.32 ± 5.25 years and age range of tuberculoid leprosy cases was 6-70 years with mean of 33.56 ± 2.85 years. The age range of open tuberculosis cases was 21-60 years with mean of 35.32 years ± 2.28 years and age range of normal school children was 10-15 years with mean of 12.24 ± 0.21 years. Results of slit skin smears, histopathological examination and serology by MLPA for different types of leprosy are given in the Table 1 & 2.

There were 37 biopsies, which were reported as lepromatous leprosy after processing with immuno-staining using special markers. Of the 37 lepromatous leprosy cases 25 (67.6%) were found to have positive slit skin smears, showing high enough BI to go into the lepromatous pole of leprosy spectrum. All these 37 sera were processed for the determination of IgM anti-PGL-1 antibodies by MLPA method. The frequency of positive cases was 29 (78.4%) having mean of 0.78 ± 0.07 cases, which significantly provided better results than that of slit-skin smears with p value of 0.044 (Table 3).

Twenty five biopsies, which revealed tuberculoid leprosy and only 3 (12%) cases, which were found positive by slit-skin smears. Out of 25 sera MLPA detected anti-PGL-1 (IgM) antibodies in 12 (48%) cases having mean 0.48 ± 0.10 cases, which also exhibited significantly better results than that of slit-skin smears with p value of 0.001 (Tables 1, 2 & 3).

There were 10 cases diagnosed as indetermediate leprosy. Slit-skin smear examination

Table 1: Distribution of age and sex among different groups of study population

Leprosy Type	No. of patients	Age Range (years)	Mean Age in years	Sex Ratio (M:F)
Lepromatous leprosy	37	18-80	42.08 + 2.87	3.5:1
Tuberculoid leprosy	25	6-70	33.56 + 2.85	1.5:1
Intermediate leprosy	10	14-67	39.60 + 5.25	1.5:1
Open tuberculosis	25	21-60	35.32 (+ 2.28)	1.5:1
Normal School Children	50	10-15	12.24 + 0.21	1.3:1

Table 2: Distribution of leprosy serology positive cases measured with *Mycobacterium leprae* particle agglutination (MPLA) test

Group	No. of patients	No. of positive cases	No of cases with Antibodies Dilution Titre				
			32	64	128	256	>512
Lepromatous Leprosy	37	29	5	8	3	5	8
Tuberculoid leprosy	25	12	2	3	5	—	2
Intermediate leprosy	10	5	3	1	1	—	—
Open Tuberculosis	25	6	3	2	1	—	—
School Children	50	1	1	—	—	—	—

Table 3: Comparison of Skin-slit smear and leprosy serology on cases of leprosy diagnosed by histopathology

Test Carried out	Lepromatous leprosy (n = 37)	Tuberculoid leprosy (n = 25)	Intermediate leprosy (n = 10)
Positive Leprosy Serology	29 (78.38%)	12 (48%)	5 (50%)
Positive Skin slit smear	25 (67.57%)	3 (12%)	4 (40%)
P-value	p = 0.044	p = 0.001	p = 0.343

Table: 4. Sensitivity, specificity, positive/negative predictive values and overall efficacy of serological tests by *Mycobacterium leprae* particle agglutination (MLPA) test in various types of leprosy

	Lepromatous leproty (n-37)	Tuberculoid leprosy (n=25)	Intermediate leprosy	Leprosy combined (n=10)
Sensitivity	78.38%	48%	50%	63.89%
Specificity	89.33%	89.33%	89.33%	89.33%
Positive Predictive Value	78.38%	60%	38.46%	85.19%
Negative Predictive Value	89.33%	83.75%	93.06%	72.04%
Efficacy	85.71%	79%	84.71%	76.87%

revealed positive in 4 (40%) cases and leprosy serology of 10 cases of indeterminate leprosy gave positive results in 5 cases (50%). However, there was no significant difference between the two (p=0.343) (Table 3).

The overall leprosy serology has significantly better results than that of slit smear and in cases of open tuberculosis and normal non-exposed children (p=<0.0001).

Twenty-five open tuberculosis cases and fifty school children were tested for nasal and slit-skin smears and for anti-PGL-1 antibodies by MLPA. Nasal and slit-skin smears were negative in all cases. The sera of 25 open TB cases were tested for 38 K. dalton protein and were positive, an integral component of the structure of M. *tuberculosis* and also present in the cell of M. *leprae* and 6 (24%) of open tuberculosis cases were found positive for IgM anti-PGL-1 antibodies by MLPA method. However, the antibody titre of one case was 1:128, suggestive of sub-clinical infection, while the antibody titre of other cases was below 1:128. This 24% positivity could be explained on the basis of a cross reaction with the antibody of 38 K. dalton protein present in the organisms of tuberculosis and leprosy. There was only one case (2%) among the school children, which revealed positive reaction with leprosy serology and that of with titre of 32, which negate for even sub-clinical infection.

Sensitivity, specificity, predictive value of positive and negative test and efficacy of the serology test for different types of leprosy and leprosy as whole is presented in Table 4. Lepromatous leprosy demonstrates excellently in all values. However, intermediate type leprosy revealed very low value for predictive value of positive test. Similarly sensitivity of tuberculoid and intermediate leprosy cases is low.

High false negative IgM determination in patients of tuberculoid and intermediate leprosy may be the limitation of this test.

DISCUSSION

Leprosy has a slow and insidious evaluation, which is present in all age groups, however most of the patients were in the middle age group[6]. Although the number of patients in this study was small but still one can speculate.

Data of this study presented only a small proportion of leprosy in children (3%), it is comparable to that found in other parts of the world[7]. Male to female ratio in most parts of the world is 2:1, which is almost similar to that found in this study. However in other parts of the world like Thailand, Japan, Uganda, Zambia, Gambia and Nigeria an equal distribution of the disease or an increased prevalence in the females has been reported[8].

Regarding the comparison of serology and skin-slit smear for the detection of different types of leprosy, the lepromatous leprosy was better diagnosed by MLPA serology than slit-skin smears. The findings of our work were consistent with Izumi, who found 78.9% positivity rates in active lepromatous leprosy and 42% in inactive lepromatous leprosy cases using MLPA method of testing.

Besides this, high-level expertise to describe the changes caused by tuberculoid leprosy in skin and AFB are important as well. The diagnostic capability of MLPA for the diagnosis of tuberculoid leprosy was contrary to that of lepromatous leprosy. The efficacy of MLPA for the determination of tuberculoid and intermediate leprosy was found less but still it was better than Skin-slit smear particularly in tuberculoid type. The general view is that the immunoglobulins are present in high concentrations in patients with lepromatous leprosy, whereas their frequency and activity is low in patients of tuberculoid leprosy causing more false negative results in this group of patients, thus the victims are more prone to nerve affection and we can't afford the delay in their diagnosis[9]. Less diagnostic efficacy of serology is also observed in a variety of other methods i.e. complement fixation, passive haemagglutination, gel precipitation techniques, and cross immunoelectrophoresis etc. In recent years highly sensitive techniques like radioimmunoassay and ELISA are in practice for the antibody estimation. Similar results have been reported by Izumi[10], who detected anti-PGL-1 antibodies in only one serum out of 86 tuberculoid leprosy specimens and this too was positive in the lowest of titres i.e. 1:32. In another study sera of borderline tuberculoid and tuberculoid leprosy patients were analyzed by very specific technique (ELISA), IgM D-BSA was detected in ratio of 57% and 40% respectively[11,12]. Furthermore, the positivity rates for titres of 32, 64, 128 and 512 were 2, 3, 5 and 2 respectively. This gross difference in the ratio of positivity and the presence of antibodies in higher titre in our patients could be due to late diagnosis when the bacterial antigen remained in the body for quite long to produce such high levels of antibodies. This is perhaps due to late reporting of patients to leprosy centres or delay in the diagnosis of the disease.

Contrary to the tuberculoid leprosy, indeterminate leprosy patients showed low antibody titre. This may be due to lower bacterial load in the skin. However the only case that showed relatively high antibody titre, showed high BI and MI on smear as well. Thus it can be presumed that in these cases the antibody titre is directly proportional to the bacterial load of the patient's skin. MLPA method will be of great benefit to the patients of this group of leprosy as the procedure is non-invasive. None of the studies so far on serology of leprosy has mentioned the statistical data relating to the diagnosis of indeterminate leprosy.

To fulfill our duties towards this most neglected infectious disease and to control its spread in the community and its eradication in future, MLPA could

help in screening of high-risk individuals in endemic areas. This study pointed out the efficacy of MLPA in finding out sub-clinical infections in the endemic areas. These cases need further follow up to know the exact proportion of emergence of leprosy in them, but still we can presume from our findings that those cases having high antibody titre in sub-clinical stage are more prone to develop leprosy at a later stage than those with positivity at low titres. Other studies carried out on household contacts pointed out considerable number of cases prone to leprosy[13,14,15].

The cross reactive antibodies due to the presence of 38 Kilodaltons protein was found in 14 cases in our study which is comparable to other studies. In a study carried out at Wayne State University School of Medicine, Michigan, it was 15%. Pessolani et al.,[16] found 10.5% false positive results due to cross reactive antibodies elicited by casual or deliberate contact with Mycobacteria other than *M. leprae*. It is another limitation of the MLPA method.

The specificity of control group is very high in present study which conforms to other studies[17].

CONCLUSIONS

MLPA showed better results than skin-slit smear used for the diagnosis of different types of leprosy except indeterminate leprosy. Another advantage of this method is screening of high risk individuals, like professionals, household contacts and mass screening of endemic areas to find out the suspected and prone cases by estimating their high antibody titres. Moreover MLPA is an easy, economical and time saving method.

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ORIGINAL ARTICLE

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PREVALENCE OF VARIOUS PATHOGENS AND THEIR SENSITIVITY PATTERN IN PATIENTS WITH BURNS AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: Objective of the study was to find out the prevalent micro flora and their sensitivity pattern in burn patients.

Material And Methods: The study was conducted at Burn unit of Fauji Foundation Hospital, Rawalpindi, from June 2004 to Dec 2006. The study included 100 patients of all age groups and either gender. Patients with perineal burns and those with chronic diseases like tuberculosis, diabetes mellitus were excluded from the study. All patients were started initially on ampicillin-cloxacillin combination. Burn wounds were dressed with silver sulfadiazine cream. Two serial swabs were taken at weekly intervals for 2 weeks and sensitivity was checked against commonly used antibiotics. Descriptive statistics were used to analyze the data.

Results: The incidence of burns was highest in the age group of 20-30 years. At the end of first week, 49 (49%) patients showed single isolate, while at the end of 2nd week, single isolate was obtained in 40(40%). Most prevalent agent was Staphylococcus aureus 77 (38.5%) followed by Pseudomonas 65 (32.5%), Proteus 37 (18.5%), Klebsiella 13 (6.5%) and Streptococcus 1 (0.5%). The pattern of sensitivity showed that staphylococci and streptococci showed resistance to commonly used antibiotics. Pseudomonas showed better sensitivity to penicillins and cephalosporins. It was also observed that antibiotic resistance to enterococci is rising.

Conclusion: The prevalent micro flora and their sensitivity pattern should be studied in each burn facility as micro flora of burn wound varies from place to place and from time to time.

Key Words: *Burns. Micro flora. Antibiotic Sensitivity. Antibiotic Resistance.*

INTRODUCTION

Burn injury is one of the major problems threatening public health in both developing and developed nations[1]. Individuals affected often require long periods of hospital stay, physical as well as psychosocial disabilities[2]. Scalds and fire burns are the most commonly occurring type. Most incidences of burn trauma are due to ignorance and social factors[3]. Sepsis is the commonest cause of death after burn injury[4]. Main source of bacteria which cause onset of sepsis is the burn wound itself. Patient factors such as, age, extent of injury and depth of burns in combination with microbial factors like number, type, motility, enzymes and toxin production determine the likelihood of invasive burn wound infection[5].

Sepsis may present with temperature >39 C° or <36.5 C°, azotemia, onset of respiratory distress or pulmonary oedema. Historically, staphylococci and beta hemolytic streptococci were the commonest organisms causing burn wound infection in early part of the century[6]. However, recently pseudomonas has emerged as the main pathogen causing infection. Burn wound may also be infected by E. coli, Klebsiella, Proteus, Candida and aspergillus. Recently (Methicillin resistant staphylococcus aureus (MRSA) has been isolated from burn wounds with rising resistance to vancomycin[7]. Systemic antibiotics are useful therapeutic modality in burn patients, however injudicious use may not only fail to be beneficial to the patient but can result in emergence of bacterial resistance[8]. Surveillance cultures are required to determine the emergence of colonization and aid in selection of antibiotic regimens.

The aim of the study was to find the prevalent micro flora and their sensitivity pattern in burn patients.

MATERIAL AND METHODS

The study was conducted at the Burns unit of Fauji Foundation Hospital Rawalpindi from June 2004 to Dec 2006. The unit uses ampicillin-cloxacillin combination initially as prophylactic antibiotic. However antibiotic regimens are changed according

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to culture reports. At first week we use cefuroxime for staphylococci , beta haemolytic streptococci and coliforms. In 2nd week we use penicillins, cephalosporins or a macrolide for Staphylococcus aureus, Coliforms and Pseudomonas aeruginosa according to culture and sensitivity results.

In this study, patients of all age groups and either gender were included. Adult patients with partial thickness burns less than 20% body surface area, children with partial thickness burns less than 10%, full thickness burns less than 5% burn of face, hands, feet, ears, inhalation injury or associated trauma were included in the study. Patients with perineal burns and those with chronic diseases like tuberculosis, diabetes mellitus were excluded from the study. The association of etiologic and social factors was recorded. All patients included in the study were initially started on ampicillin-cloxacillin combination as prophylactic antibiotic. Burn wounds were dressed with silver sulfadiazine cream on daily basis under aseptic conditions. Moist burn wound swabs were taken using the standard technique of collection of microbiological specimen and were processed under supervision of pathologist. The specimens were cultured under aerobic conditions and the sensitivity was checked with conventional methods. Two serial swabs were taken at weekly intervals for 2 weeks and sent for culture and sensitivity.

The sensitivity was checked against ampicillin, cloxacillin, gentamycin, erythromycin, tetracycline, ciprofloxacin cephradine, co-amoxiclav, aztreonam, fosfomycin, cefuroxime and cefotaxime.

All the demographic information and investigations were entered in structured Performa. Descriptive statistics were used to analyze the data.

Table 1: Organism cultured at the end of first and 2nd week

Organism	1st Week	2nd Week	Total No.
Staphy lococcus	39(39%)	38(38%)	77(38.5%)
Streptococcus	1(1%)	0	1(0.5%)
Pseudomonas	35(35%)	30(30%)	65(32.5%)
Proteus	16(16%)	21(21%)	37(18.5%)
E. coli	13(13%)	10(10%)	23(11.5%)
Klebsiella	9(9%)	4(4%)	13(6.5%)

Table 2: Antibiotic sensitivity pattern of different isolates

Antibiotic	Staph. Aureus		Strepto-cocci		Pseudomonas		Proteus		Klebsiella		E.coli	
	S	R	S	R	S	R	S	R	S	R	S	R
	%	%	%	%	%	%	%	%	%	%	%	%
Ampicillin	28.6	71.4	100	0	0	100	0	100	0	100	0	100
Cloxacillin	42.86	57.14	100	0	0	100	0	100	0	100	17.4	82.6
Erythromycin	16.8	83.2	0	0	0	100	0	100	0	100	0	100
Gentamycin	0	100	0	100	7.7	92.3	16.22	83.78	15.38	84.62	30.44	69.66
Tetrracycline	22	78	0	100	27.7	72.3	0	100	23.8	76.92	0	100
Ciprofloxacin	20.77	79.23	100	0	44.6	55.4	51.36	48.64	100	0	47.83	52.17
Cephradine	19.48	80.52	100	0	9.23	90.77	10.82	89.18	0	100	26.08	73.92
Co amoxiclav	61.04	38.96	100	0	78.46	21.54	54.06	45.94	69.23	30.77	47.83	52.17
Aztreonam	44.16	55.84	100	0	73.84	26.16	40.54	59.46	92.30	7.7	73.91	26.09
Fosfomycin	32.46	67.54	100	0	40	60	35.14	64.86	53.85	46.15	43.48	56.52
Cefuroxime	36.36	63.64	100	0	32.30	67.7	27.03	72.97	38.46	61.54	26.09	73.91
Cefotaxime	25.97	74.03	100	0	49.23	50.77	32.44	67.56	35.85	46.15	56.52	43.48

S= sensitive, **R**= Resistant

RESULTS

The age of patients ranged from 4 to 61 years. The incidence of burns was highest in the age group of 20-30 years i.e. 39 (39%) cases. The incidence was higher in females (63%) than males (37%) with male to female ratio of 1:1.7. Body surface area burnt varied from 8%-92%. In 35 (35%) patients, it ranged from 4%-30%, 46(46%) patients had 31%-60% burns, while 19 patients had 61%-92% burns. The burning agent was predominantly flame (66%) followed by scald (24%), contact (6%), electrical (3%), and chemical (1%). Six patients expired during 1st week and 10 patients during 2nd week of admission.

At the end of first week, 13 (13%) patients showed sterile culture, 49(49%) showed single isolate, and 32 (32%) patients showed multiple isolates. At the end of 2nd week, sterile cultures were obtained in 8 (8%) patients, single isolate in 40(40%) and multiple isolates in 36(36%) patients.

DISCUSSION

The study reaffirmed the concept that contamination of burn wound is a rule rather than exception. Infection control procedures, including scheduled surveillance cultures, utilization of cohort patient care methodology, strict enforcement of patients and staff hygiene, and patient monitoring have been effective in endemic resistant microbial strains.

The age group mostly affected by burn injury was between 20 and 30 years followed by age group between 10 and 20 years. This finding was consistent with the results of Ansari Lari M et al[9] who observed maximum number of patients between 20 and 30 years age. Incidence was higher in females with male to female ratio of 1:1.7. Nasreen A Siddiqui[3] also observed high incidence of burns in females of reproductive age groups. We observed maximum number of patients (18%) with total body surface area burnt between 5%-60%. Fire burn was the most common type of burn (78%) in our study while in the study by Chien WC et al[10] scald was the most common cause of burns. This may be due to socioeconomic reasons in our society.

At the end of first week 13.82% cultures were sterile, while 9.5% at the end of 2nd week. I Riaz et al[6] found 26.6% and 20% sterile cultures at 1st and 2nd week consecutively. Single isolate was obtained 52.12% and 47.61% cases at 1st and 2nd week while they found single isolate in 60% cases.

The ecology of organisms cultured showed that commonly isolated organisms are the same in different centers with one predominating the other in prevalence. Gram positive cocci were found in 36.40% and gram negative bacilli in 63.60% cases. Nasser S et al[11] found gram positive cocci in 40.3 % and gram negative bacilli in 55.7 % cases.

Staph. aureus was commonly found organism (38.5%), which was consistent with the findings of Komolafe OO et al[12] who found Staph. aureus in 37.6% cases. This was followed by Pseudomonas (32.5%) which was commonest organism in the study by Nasir Saleem et al[13]. Proteus was found in 18.5% cases while, in the study by Sharma G et al[14], it was found in 23.5% cases. E. coli and Klebsiella were found in 11.5% and 6.5 cases. Similar pattern was seen by Sandhir RK et al[15].

The pattern of sensitivity gives cause of serious concern as most of the organisms isolated from burn wound were resistant to commonly used antibiotics. Staph aureus showed poor sensitivity to ampicillin (29.48%) and cloxacillin (42.3%) as observed by Atoyebi et al[16]. This combination successfully prevented the streptococcal infection. It showed higher sensitivity to co-amoxiclav and aztreonam but poor sensitivity to cephalosporins which may be due to chromosome mediated type-1 beta lactamase. It was resistant to erythromycin, gentamycin and tetracycline as observed by Hussain MT et al[17]. Jiang HQ[18] reported infection with L-forms of staphylococci due to decreased host immunity and repeated administration of antibiotics.

Pseudomonas showed similar resistance patterns with low sensitivity to penicillin and macrolides and higher sensitivity to co-amoxiclav (78.46%) and aztreonam (73.84%). This was observed by Igumbor et al[19] who also concluded that newer drugs like tazobactam should be used in pseudomonas infection in resistant cases. Agnihotri N et al[20] found greater sensitivity of pseudomonas to pipercillin. Gentamycin and tetracycline showed poor sensitivity as observed by Shahid M et al[21] who found high resistance to aminoglycosides.

Proteus showed 100% resistance to ampicillin, cloxacillin, tetracycline and erythromycin as observed by I. Riaz et al[6]. However, sensitivity to ciprofloxacin and aztreonam was high as observed by Igumbour et al[19]. It showed poor sensitivity to cephalosporins[20].

Klebsiella were resistant to commonly used antibiotics but superior sensitivity was seen to ciprofloxacin, aztreonam and coamoxiclav. Similar pattern were seen by I. Riaz et al[6] and Agnihotri N et al[21].

E. coli were sensitive to most drugs except ampicillin, erythrocin and tetracycline.

This study has limitation as superficial culture was used as means of diagnosing burn wound infection. It does not provide information about the deeper layers of the burn wound and the actual status of the wound. It does not distinguish between colonization and infection and is also influenced by the use of topical antibiotics.

Current techniques of burn wound care have significantly reduced the incidence of invasive burn wound infection, altered the micro flora causing infection, increased the interval between injury and infection and reduced the mortality associated with infection. However antibiotic resistance to common pathogens, especially enterococci is rising. Therefore, injudicious use of antibiotics may not only fail to be beneficial to the patient but may produce harmful effects either through direct toxicity or through emergence of resistant strains of microorganisms.

CONCLUSION

The prevalent micro flora and their sensitivity pattern should be studied in each burn facility for the purpose of adopting preventive and therapeutic strategies as micro flora of burn wound varies from place to place and from time to time. A definitive policy of empirical antibiotic regimen can therefore not be devised.

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ORIGINAL ARTICLE

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ENDOPROSTHETIC PALLIATION OF MALIGNANT OESOPHAGEAL STRICTURE IN NORTH OF PAKISTAN

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ABSTRACT

Objectives: To evaluate the efficacy of endoprosthetic palliation of malignant oesophageal strictures in our local patients presenting with dysphagia.

Material and Methods: This study was conducted from 27th October 1999 to 12th December 2004, at Khyber Teaching Hospital and Al-Ibrahimi Hospital, Peshawar. All patients with inoperable malignant oesophageal stricture were included except those with stricture in the upper third of the oesophagus. All patients had their dysphagia graded, followed by endoscopic dilatation of their stricture and placement of endoprosthesis. Dysphagia grades were reassessed 12 hours and one month after the procedure.

Results: A total of 12 patients were included. There were 04 (33.33%) male and 08 (66.7%) female patients with mean age of 60.67 years (minimum 45 years and maximum 74 years). Squamous cell carcinoma was present in 08 patients (66.7%) and adenocarcinoma in 04 (33.33%). There were 07 (58.3%) patients with malignant stricture in the middle third while 05 (41.7%) patients had stricture in the lower-third of the oesophagus. Dysphagia grades improved from '3' to '0' in 12 hours and remained the same after one month of the procedure.

Conclusion: Endoprosthetic palliation is safe, effective and improves quality of life in patients with inoperable malignant oesophageal strictures.

Keywords: Oesophageal stricture, dysphagia, dilatation, oesophageal stents, oesophageal endoprosthesis.

INTRODUCTION

Dysphagia implies a sensation of mechanical difficulty with movement of food from mouth to stomach. Dysphagia with swallowing of hard boluses above a particular size is strongly suggestive of a fixed narrowing[1]. Oesophageal carcinoma (the 7th most common malignancy worldwide) commonly presents with dysphagia. Unfortunately most patients are no longer curable at the time of presentation with dysphagia as the oesophageal lumen has often reduced by at least 50–75% of its normal caliber[2]. That is why non-surgical palliative techniques are being developed, assessed and have an important role in improving the quality of life (QOL)[3] and often form the only realistic possibility[4] in patients who are not candidates for curative therapy. Oesophageal endoprosthesis is one of the many techniques used for palliation in such patients.

MATERIAL AND METHODS

This study was conducted from 27th October 1999 to 12th December 2004 at Khyber Teaching Hospital, Peshawar and Al-Ibrahimi Hospital, Peshawar. All patients with inoperable malignant oesophageal stricture were included except those with stricture in the upper third of the oesophagus. All patients had their dysphagia graded (using Cowling's modified version of dysphagia grades, Table. 1), followed by endoscopic dilatation of their stricture up to 54F and placement of plastic endoprosthesis (Atkinson's tube) in a single session. Dysphagia grades were reassessed 12 hours and then one month after the procedure. Dilatation was performed using KeyMed silastic dilators (Fig. 1) over a guide wire, followed by placement of Atkinson tube across the stricture, using Atkinson assembly (Fig. 2) under local pharyngeal anaesthesia and intramuscular Tramadol 50 mg. All patients were referred to oncologist after the procedure. Data regarding length of hospital stay, complications and 30-day mortality/morbidity was recorded.

Table 1: Dysphagia grades

Grade	Symptoms
0	No dysphagia
1	Semisolids
2	Liquids
3	Complete dysphagia

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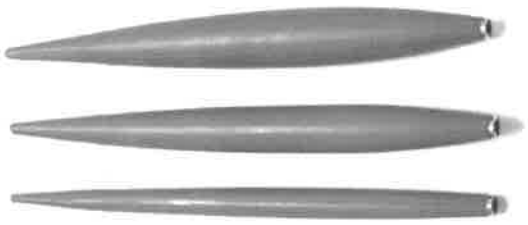

Fig. 1; KeyMed dilators

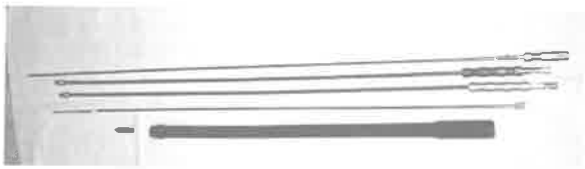

Fig. 2; Atkinson's assembly

Table 2: Type of Carcinoma

Type of carcinoma	No. of patients	%	Male	Female
Squamous cell carcinoma	8	66.7	02 (25%)	06 (75%)
Adenocarcinoma	4	33.3	02 (50%)	02 (50%)
Total	12	100.0		

Table 3: Site of oesophageal stricture

Site of oesophagus	No. of patients	%
Middle 3rd	7	58.3
Lower 3rd	5	41.7
Total	12	100.0

Table 4: Length of the Stricture

Mean	4.92cm
Minimum	3cm
Maximum	7cm

RESULTS

During the study period, 44 patients presented with inoperable malignant oesphageal stricture. Male patients were 24 (54.55%) and female patients were 20 (45.46%). Squamous cell carcinoma was present in 27 patients (61.36%) [16 female (59.26%), 11 male (40.74%)], Adenocarcinoma in 16 (36.36%) [04 female (25%), 12 male (75%)] and one (male) patient had Non-Hodgkin's lymphoma (2.27%).

Only 12 patients [04 male (33.3%) and 08 female (66.7%)] consented for the procedure. Mean age was 60.67 years with minimum age of 45 years and maximum age of 74 years. Histological distribution is given in Table. 2, oesophageal location in Table 3, and length of stricture in Table 4.

Dysphagia grades improved from '3' to '0' at 12 hours and remained so at follow up one month after the procedure. No mortality or serious complications occurred. Hospital stay was 12 hours in all patients. Transient chest pain was the commonest symptom, seen in all patients, after the procedure. One patient had recurrent dysphagia due to bolus impaction.

DISCUSSION

Non-surgical palliative techniques for oesophageal malignant stricture include endoluminal laser therapy[5], Photodynamic therapy[6], Argon beam or bipolar electrocoagulation therapy[7], Ethanol injection[8], Intracavity brachytherapy[9], External beam radiotherapy[10] and Combination chemoradiation[11]. In 1959, Celesti[12] described the palliation of oesophageal malignancy with a plastic endoprosthesis introduced at laparotomy. In the 1970s, Atkinson[13] introduced an endoscopically inserted plastic prosthesis. Oesophageal endoprosthesis, since then, has also been used for bridging tracheo-oesophageal fistulae, oesophageal perforation[14] and benign oesophageal stricture[15]. The number of patients in our series is small but it has been varying considerably in international literature, ranging from a small sample of six patients[16] to a larger selection of 70 patients[17]. The reasons for small number of patients in our study are the cost (as generally the public is poor and depends on subsidized health facilities) and lack of awareness among public and doctors regarding local availability of expertise in such palliative procedures. There was male preponderance overall (54.55%) but within the group of patients with endoprosthesis, there was female preponderance (66.7%). Maroju NK et al[3] and Ahmad S et al[18] reported female preponderance but Khokhar et al[19] and Khan IU[20] reported male preponderance i.e. 68.8% and 66.66% respectively. Patients with squamous cell carcinoma were largely female, both in general (59.26%) and within the group with endoprosthesis (75%). Such an observation was seen in a study from Karachi in which 75% patients were female[21]. Successful dilatation was done in all patients, ie in 100% of our patients. Successful dilatation has been reported in 100% patients by Khokhar et al[19], in 95% patients by Neyaz et al[22], in 93% patients by Cheema[23] while Ahmad S et al[18] have reported successful dilatation in only 25% patients. In our study, 07 (58.3%) patients had malignant stricture in middle third of the oesophagus, and 05 (41.7%) patients in the lower third. International literature reports up to 40% patients having malignancy affecting the middle-third[24] (usually squamous cell

carcinoma), and up to 45% affecting the lower third of the oesophagus (usually adenocarcinoma), This apparent high percentage of malignancy in the middle third in our series could be explained by the small number of patients and exclusion of cases with malignancy in the upper third of the oesophagus. Improvement in dysphagia from grade 3 to grade 0, 12 hours and one month after the procedure clearly reflects that placement of stent increases the dysphagia free interval and thus improves the quality of life. Siersems at al[25] confirms the same.

We used plastic (Atkinson's) tube. Though it is generally believed that self-expanding metal stents (first described by Frimberger[26]) are better than plastic stents, some series report little difference in the degree of palliation from dysphagia[27]. Alleviation of dysphagia is a major factor that improves quality of life (deemed more desirable[28]) in inoperable oesophageal malignancy.

Endoscopic dilatation of esophageal stricture is effective and safe with low rate of complications[21]. In our series, chest pain was the commonest symptom, seen in all patients after the procedure which settled during their hospital stay, requiring injectable Tramadol. Acunas et al[29] reported the same with prolonged chest pain occurring in <13% patients. The reduced duration and intensity of pain in our series could be due to the fact that we excluded patients with malignant stricture in the upper third of the oesophagus as stenting this part gives more severe pain[30]. Major complications such as bleeding, perforation, aspiration, fever and fistula, though occur in 10 – 20% of patients[31] were not seen in our study. There was no procedure related death in our study. Though it is uncommon, Adam A et al reported 7% mortality due to bleeding and aspiration[32]. Stent migration, though reported between 25 and 32%[33] specially when positioned across the cardia, was not seen in our patients probably because of short follow up. Recurrent dysphagia due to tumour over growing the stent, benign hyperplasia, granulation tissue and fibrosis[34] or food bolus impaction[35] has been reported. In our series one patient had recurrent dysphagia due to bolus impaction which was managed endoscopically.

CONCLUSION

The use of oesophageal endoprosthesis or stent is a reliable way to allay dysphagia, thus improving the standard of living for the sufferer. Stenting of malignant oesophageal obstruction and refractory benign strictures continues to evolve with the introduction of newer, anti-reflux anti-migration stents with an internal plastic coating. The determining factor as to which method is used to palliate patients with advanced oesophageal malignancy often depends on local expertise, availability of equipment and affordability. Atkinson's tube, while largely abandoned in the West, is still the standard stenting method in poor countries.

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ORIGINAL ARTICLE

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HYPERHOMOCYSTEINEMIA AND LOW VITAMIN B STATUS IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Objective: In this study the concentrations and possible correlation of serum homocysteine, vitamin B_6, B_{12} and folic acid were studied in the patients of acute myocardial infarction (AMI).

Material and Methods: A case control study, involving 400 acute myocardial infarction patients studied in two age groups of 25-45 years and 46-70 years, and an equal number of age, sex and socioeconomically matched controls. Serum homocysteine was analyzed by Fluorescence Polarization Immunoassay method on automated Abbott Immunoassay analyzer (IMX USA), and the determination of B vitamins was done by High Performance Liquid Chromatography (Hitachi HPLC Japan).

Results: There was moderate hyperhomocysteinemia in younger age patients as compared to controls [23.76 ± 2.08 vs 12.92 ± 1.36 μmol/L ($P < 0.001$) in male and 20.21 ± 4.17 vs 10.44 ± 2.28 μmol/L ($P < 0.001$) in female patients and controls] and intermediate hyperhomocysteinemia in older patients [44.62 ± 2.04 vs 18.89 ± 2.62 μmol/L ($P < 0.001$) in male and 29.84 ± 1.86 vs 16.62 ± 2.78 μmol/L ($P < 0.001$) in the female patients and controls]. Low B_6 concentrations were recorded in younger male and older female patients while vitamin B_{12} concentrations were low in older male and female patients. Significantly low folic acid concentrations were seen in female patients of both age groups and older male patients. Homocysteine correlated inversely with all the three vitamins. Homocysteine concentrations of control subjects in this part of the world were among the highest reported in the literature for control subjects.

Conclusion: Substantial nutritional deficiencies of vitamin B_6, B_{12} and Folic acid are highly prevalent in this population which results in moderate to intermediate hyperhomocysteinemia and the risk of acute myocardial infarction.

Key Words: Homocysteine; Vitamin B_6, B_{12}, Folic acid; Acute myocardial infarction.

INTRODUCTION

Hyperhomocysteinemia is one of the newly recognized risk factors for coronary artery disease (CAD). The mechanisms responsible for the atherogenic properties of homocysteine[1] and the causation of coronary artery disease are incompletely understood[2,3] but many hypotheses have been generated by experimental and in vitro studies, both in humans and in animals. These mechanisms include direct effects on the vascular endothelium by increasing oxidative stress and subsequently affecting its anti thrombotic properties,[4] which is an important factor in the pathogenesis of atherosclerosis[5]. Furthermore endothelial cell damage can cause increased uptake of low density lipoprotein cholesterol in the vascular wall[6,7]. Another proposed atherogenic mechanism involves inhibition of growth of endothelial cells and stimulation of proliferation of smooth muscle cells by homocysteine, finally leading to the thickening of arterial walls[8]. This association between hyperhomocysteinemia, endothelial dysfunction and atherogenesis may be explained by factors involved in homocysteine metabolism[9]. Homocysteine, a sulphur containing amino acid is an intermediate formed during transmethylation[10] and is either salvaged to methionine by a folate and cobolamin dependent remethylation reaction where cobolamin acts as a cofactor and folic acid as a substrate for methionine synthase (MS), or is directed towards degradation by the vitamin B_6 dependent enzyme cystathionine b synthase to form cysteine[11]. Genetic and acquired influences may interact in homocysteine metabolism and its removal from the circulation in important ways that are still being sorted out[12], but the deficiency of vitamin B_6, B_{12} and folic acid are considered as one of the important factors in the causation of hyperhomocysteinemia in ethnic groups. Therapy with these vitamins reduces blood homocysteine concentration, improves endothelial

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function and thrombolysis and in uncontrolled clinical observation leads to the regression of carotid plaque[13]. In this study concentrations of total homocysteine, vitamin B_6, B_{12} and folic acid were determined in the serum of the patients of Acute Myocardial Infarction (AMI) and compared with controls. Correlation studies of homocysteine with each of these vitamins were also done in all groups of subjects.

MATERIAL AND METHODS

This study was a non interventional, case control study carried out at Pakistan Medical Research Council (PMRC) Khyber Medical College Peshawar in collaboration with Cardiology Departments of Post Graduate Medical Institute Hayatabad Medical Complex and Lady Reading Hospital Peshawar and Abbott Laboratories Research Division Pakistan. The whole population was from the same geographic area, (general community of North West Frontier Province of Pakistan). The study population included 800 subjects, which included 400 fully diagnosed (by signs and symptoms, physical examination, electrocardiographic and laboratory findings) hospitalized patients of acute myocardial infarction (AMI) , presenting within twenty four hours of attack and an equal number of age, sex and socioeconomically matched control subjects. Subjects were studied in two broad age groups, (25-45 years, with Group A as patients and Group B as controls) and (46-70 years where Group C were patients and Group D were controls). The control subjects had neither history nor clinical or instrumental evidence of atherosclerosis in the past. The exclusion criteria for both patients and controls from the study was renal failure, thyroid disorders, psoriasis, malignancies and megaloblastic anaemia. An informed consent was taken from the patients and controls. Recording of demographic details, brief clinical history and physical examination was done and the information from each subject was recorded in a questionnaire which was designed with the help of a biostatistician. The study was approved by the Ethical Committee of the hospitals concerned.

A fasting venous blood specimen was collected in a plain tube (with out anticoagulant) avoiding haemolysis, from each patient and control and transported to the PMRC laboratory on ice. Serum was separated within one hour of sample collection by centrifugation at 1000 x g for ten minutes, and was divided in four separate plastic capped bottles and stored frozen at - 20° C until analyzed in batches, for serum homocysteine and B vitamins. The estimation of serum homocysteine was done by Florescence Polarization Immunoassay principle (FPIA method) on automated Abbott Immunoassay analyzer (IMX). The determination of B vitamins was done on High Performance Liquid Chromatogtaphy (Hitachi HPLC, Japan) using a standard solution of these vitamins and Intersil ODS column. All estimations were performed in duplicate.

The data was entered and processed on SPSS 10 software. The numerical and categorical data was presented as means. Means and Standard Deviation (SD's) of serum total homocysteine and B vitamins of the patients as well as controls were calculated and the differences were analyzed using the student's "t" test. All reported 'P' values less than 0.05 were taken statistically significant. Single linear univariate correlation analysis between serum homocysteine and individual B vitamins were performed by Pearson Product Moment correlation coefficient to evaluate the relationship between homocysteine and these vitamins.

RESULTS

Homocysteine

Total homocysteine concentration in the serum / plasma reflects cellular homocysteine metabolism and its normal concentration is usually taken upto 15μmol/ L. Moderate and intermediate hyperhomocysteinemia refers to homocysteine concentrations in the range of 16-30 μmol / L and 31-100 μmol/L respectively[14]. Figure 1 shows that the maximum percentage of patients in this study had moderate hyperhomocysteinemia and the percentage of patients showing intermediate hyperhomocysteinemia were comparatively less. Majority of the control subjects showed normal homocysteine concentration, which indicates that elevated homocysteine may have a role in the causation of myocardial infarction. Serum homocysteine concentrations in this study were higher in male patients as compared to female patients (Table 1), how ever an age related increase was also noted as younger patients revealed moderate

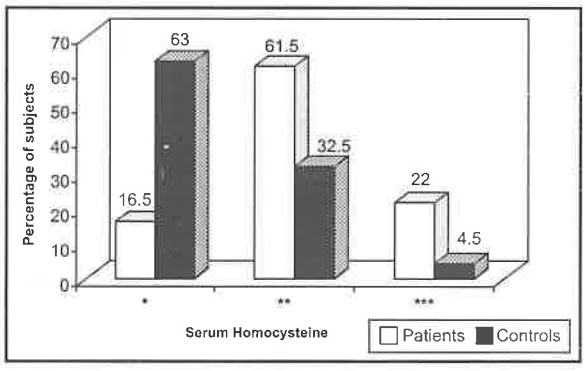

Fig.-1: Percentage Of Patients Of Acute Myocardial Infarction And Controls With Normal And Raised Serum Homocysteine

* Normal Homocysteine

** Moderate Hyperhomocysteinemia

*** Intermediate Hyperhomocysteinemia

Table 1: Serum Homocysteine by sex and age groups in the patients of Acute Myocardial Infarction and control subjects

Age Group	Group/Subjects	Sex	% Subjects	Serum homocysteine (mean + SD) (i mol/L)
25-45 years	A Patients (n=200)	Male (n=116)	58	23.76 + 2.08***
		Female (n=84)	42	20.21 + 4.17***
	B Controls (n=200)	Male (n=116)	58	12.92 + 5.04
		Female (n=84)	42	10.44 + 2.28
46-70 years	C Patients (n = 200)	Male (n=104)	52	44.62 + 2.04***
		Female (n=96)	48	29.84 + 1.86***
	D Controls (n=200)	Male (n=104)	52	18.89 + 2.62
		Female (n=96)	48	16.62 + 2.78

Number of subjects are given in parenthesis

***: P< 0.001: Highly significant

Normal serum homocysteine: 10-15 μmol/L

hyperhomocysteinemia and older age group (male patients only) showed intermediate hyperhomocysteinemia. A progressive increase in homocysteine concentration with age was also evident in the control subjects of group D of this study who showed moderate hyperhomocysteinemia, while controls in younger age group had normal homocysteine concentrations. The alarming situation is that the mean homocysteine concentration in normal healthy subjects (both male and female controls) of this population are among the highest reported in the literature for most eastern and western studies[1,7,8], which can be a future risk for cerebrovascular and cardiovascular events in these subjects.

Vitamin B: Compared with control subjects patients showed lower serum concentrations of B vitamins. The difference in mean vitamin B_6 concentrations of patients vs controls was markedly significant (P<0.001) in younger male patients of group A and the female patients of group C (P<0.01) (Table 2) which shows that vitamin B_6 concentrations in this study are related to age and sex. Table 2 also shows a significant decrease (P<0.001) in vitamin B_{12} concentration in the female patients as well as in the male patients (P<0.01) of group C as compared to controls. Normal vitamin B_{12} concentrations were noted in the younger male and female patients (Group A) but the levels were slightly low as compared to the controls of same age group. Vitamin B_{12} does not seem to be related to sex in our results as these concentrations were comparable in both sexes in two age groups, however there seems to be relationship with age as the patients in age group 46-70 years have shown below normal levels and the control subjects although have shown normal B_{12} levels but in the lower limits of normal. Low folic acid concentrations are noted in the majority of subjects (patients and controls) in this study (Table 2) but compared with control subjects, patients showed low folic acid concentrations in both age groups and the lowest concentrations were noted in younger female patients (Group A) (2.49 + 1.08 ng/ml) which were significantly low (P<0.001) as compared to controls (5.36 + 2.16 ng/ml) and the female patients of group C (3.16 + 1.54 ng/ml). Borderline normal folic acid concentrations of the male and female control subjects of group D shows an age related decline in this vitamin status.

Table 2: Serum Vitamin B_6, B_{12} and Folic Acid by sex and age groups in the patients of Acute Myocardial Infarction and Controls

Age Group	Group/ Subjects	Sex	Number of Subjects	Serum Vitamin B_6 (mean+SD) (ng/ml)	Serum Vitamin B_{12} (mean+SD) (pg/ml)	Serum Folic Acid (mean-SD) (ng/ml)
25-45 years	A Patients (n=200)	Male	116	8.57 + 2.36***	359.6+ 4.9	4.03 + 1.31***
		Female	84	11.38 +3.89**	308.43 + 2.7	2.49 + 1.08***
	B Controls (n=200)	Male	116	14.10 + 2.48	425.39 + 2.6	6.98 + 2.16
		Female	84	13.09 + 3.71	361.27 + 4.3	5.36 + 2.16
46-70 years	C Patients (n=200)	Male	104	12.28 + 3.26	92.37 + 1.6**	3.88 + 4.83
		Female	96	10.87 +3.71**	86.14 + 2.3***	3.16 + 1.54**
	D Controls (n=200)	Male	104	12.92 + 3.74	142.24 + 3.7	4.94 + 1.78
		Female	96	13.38 + 4.92	189.10 + 2.9	4.21 + 3.16

Number of patients are given in parentheses, ** $P < 0.01$ *** $P < 0.001$

Normal serum vitamin B_6: 13-16 ng/ml, Normal serum vitamin B_{12}: 100-700 pg/ml, Normal serum folic acid: 3-16 ng/ml

Table 3: Correlation coefficient of serum homocysteine with vitamin B_6, Vitamin B_{12} and Folic Acid in the patients of Acute Myocardial Infarction (AMI) and Control Subjects

Age group	Group/ Subject	Sex	Homocysteine VS vitamin B_6		Homocysteine VS vitamin B_{12}		Homocysteine VS Folic Acid	
			r value	P value of r	r value	P value of r	r value	P value of r
25-45 years	A Patient (n=200)	Male	-0.63	0.001***	-0.39	0.002***	-0.32	0.012**
		Female	-0.57	0.001***	-0.38	0.01**	-0.66	0.001***
	B Control (n=200)	Male	-0.20	0.02*	-0.06	0.64*	-0.14	0.001***
		Female	-0.37	0.04**	-0.21	0.35*	-0.52	0.001***
46-70 years	C Patient (n=200)	Male	-0.21	0.44*	-0.73	0.001***	-0.54	0.001***
		Female	-0.14	0.74*	-0.24	0.09**	-0.62	0.001***
	D Control (n = 200)	Male	-0.10	0.41*	-0.35	0.07**	-0.39	0.004***
		Female	-0.11	0.67*	-0.16	0.01**	-0.46	0.001***

*Non significant, **Markedly significant, ***Highly significant

CORRELATION

Levels of all vitamins correlated inversely with serum total homocysteine in a very similar way for cases and control subjects (Table 3). However the strongest and statistically significant ($P < 0.001$) inverse correlation of serum homocysteine in younger age group patients (Group A: age 25-45 years) was seen with serum folic acid in the female patients ($r = -0.66$,). Much more alarming was an almost similar strong ($P< 0.001$) negative correlation of serum homocysteine with serum folic acid in the female control subjects of same age group in our part of the world ($r = -0.5$).A comparable correlation of serum homocysteine with folic acid was seen in the female subjects (both patients and controls) of age group 46-70 years, which shows that low folic acid concentrations of this population especially females may be the commonest and most important cause of hyperhomocysteinemia leading to myocardial infarction irrespective of age group. A strong inverse correlation of serum homocysteine with serum vitamin B_{12} in the male patients of Group C (age group, 46-70 years) ($r = -0.73$, $P < 0.001$) shows that high homocysteine concentration is strongly associated with low vitamin B_{12} levels in the patients of acute myocardial infarction in age above 45 years of age as compared to younger age patients, Table 3 also shows that the strength of association of homocysteine with vitamin B_6 was more in younger male and female patients as compared to older patients in this study.

DISCUSSION

The primary finding of this study was that the patients with acute myocardial infarction had highly elevated homocysteine concentration compared to control subjects and this study is the first one in this part of the world to demonstrate that elevated homocysteine concentrations are positively related to the risk of myocardial infarction over a wide range of values. The correlation of homocysteine with three important B vitamins (vitamin B_6, B_{12} and folic acid) required for its removal from the circulation was also studied. Taken together our findings support the concept that components of homocysteine metabolism may affect vascular function and result in atherosclerosis which in turn modifies most ischemic heart diseases[15]. The connection between homocysteine and cardiovascular diseases was reported by McCully[16] about twenty nine years back when it was observed that people with a rare condition called homocysteinuria are prone to develop severe cardiovascular diseases in their teens and twenties. Following development of reliable methods for serum homocysteine analysis, many clinical studies[17-22] in subsequent years showed a positive association of serum homocysteine with coronary artery disease and myocardial infarction. According to a recent research work by Albert and colleagues[23] elevated blood homocysteine concentrations are as important as high blood cholesterol levels and can operate independently. In another study[24] some 10% to 20% cases of coronary artery disease have been linked to elevated homocysteine concentrations where both hereditary and dietary factors are thought to be involved. It has been reported[25] that IndoAsians (all those who trace their origin from India, Pakistan, Bangladesh and Sri Lanka) have the highest rates of acute and recurrent coronary artery disease and myocardial infarction events despite the fact that nearly half are life long vegetarians. The incidence, prevalence and mortality from coronary artery disease among these people have been 50% to 300% higher than Europeans, Americans and other Asians irrespective of gender or religion, and among IndoAsians younger than thirty years, the mortality from myocardial infarction is three fold higher than the whites in United Kingdom and ten fold higher than the Chinese in Singapore. This may result from nutritional deficiencies due to multiple causes rather than congenital enzyme deficiencies[26]. Similarly Pakistani people belong to an ethnic group which have the highest incidence of myocardial infarction. Serum homocysteine concentrations of acute myocardial infarction patients in our study show that there may be a relationship between this disease and hyperhomocysteinemia as maximum number of patients showed raised serum homocysteine with the incidence of moderate hyperhomocysteinemia being highest in both age groups. Over the past three decades, the association between elevated serum homocysteine and risk of cardiovascular diseases has grown from an obscure hypothesis to a major current topic. In a meta analysis of 14 case control studies Boushey and colleagues[27] found that an increase of 5μmol/L in basal total homocysteine concentration was associated with a 60% increase in the odds of myocardial infarction among men and an 80% increase in the odds of coronary artery disease among women. The meta analysis also estimated that approximately 10% of coronary artery disease in general population could be attributed to hyperhomocysteinemia. Spence and coworkers[13] have also reported that homocysteine concentrations above 10.2 μmol/L are associated with a 9.9 fold increase in the risk of myocardial events compared with concentrations below 9μmol/L. Results of serum homocysteine levels in our study indicate higher homocysteine concentrations in the male patients as compared to female patients in both age groups, but the effect was more marked in group C patients, which may be due to age related increase in serum homocysteine in both sexes. Moderate hyperhomocysteinemia in controls above the age of forty five years, especially male control subjects showing concentrations as high as 18.89 ± 2.62 μmol/L in this data suggest that in a general elderly population there is a considerable amount of risk of cardiovascular events, as hyperhomocysteinemia

results in hypomethylation[28,29], which may lead to impaired endothelial cell regeneration, endothelial dysfunction and atherosclerosis[30]. David. L. Wilcken[31] described moderate homocysteine elevation in both male and female elderly population almost a decade back and reported it to be associated with altered endothelial function potentially at an early stage of atherogenesis. The association between elevated homocysteine concentrations and occurrence of coronary, cerebral, peripheral and carotid vascular diseases was also described in the report. Similar reports were also given by Spirjkman and fellows[32]. Since the last many years more attention has been paid to dietary factors and the role of vitamins of B complex group in the causation of hyperhomocysteinemia and the resultant sudden premature heart attack. Like a few other recent studies[33] the results of this study have also shown that the deficiencies of folate, vitamin B_6 and vitamin B_{12} resulting in their low serum concentrations are frequent in the population and are associated with elevated homocysteine concentration. Percentage of patients showing low vitamin B_6 in our data were more in younger age group(Group A) (both male and female patients) and their B_6 concentrations were significantly low as compared to Group B (controls). An opposite trend was seen with vitamin B_{12} that the concentrations of this vitamin were significantly lower than normal in Group C and normal in Group A (younger patients). Serum folic acid concentrations in addition to showing a decreasing trend with age (in both male and female subjects), showed significantly low levels in the female subjects (patients and controls) of both age groups as compared to male subjects in our population. It has been suggested that the association between hyperhomocysteinemia and cardiovascular diseases may be explained by high homocysteine concentrations[34] and low concentrations of folate, vitamin B_6 and B_{12}[35,36]. An important observation of our study in relation to B vitamin concentrations compared to reports from other research workers was that much lower than normal concentrations of vitamin B_{12} were observed in group C patients[37], low vitamin B_6 in younger age patients (Group A)[38], and low serum folic acid concentrations in both age groups. An insufficient vitamin B_{12} status in elderly is sometimes due to low dietary intake especially in people above 60 years in addition to high prevalence of atrophic gastritis (type A and type B) in this age which results in less absorption of cobolamin than that in younger population[39]. Mechanistic studies are required to clarify the role of vitamin B_6 in the cascade of metabolic events related to coronary artery disease and myocardial infarction, however low vitamin B_6 concentration has been related to alteration of immunological function, including impaired T lymphocyte and macrophage differentiation and interleukin – 2 production[40]. In a previous study[41] higher risk of myocardial infarction was shown to be associated with reduced B_6 that defined a clear vitamin B_6 deficiency yet the results of present study provide evidence that even a mild impairment in B_6 status may confer higher risk of myocardial infarction. Such a vitamin status is apparently not a rare occurrence in population based studies[42]. Low folic acid concentrations in both age groups subjects (patients and apparently healthier controls) can be related to ethnic related dietary deficiencies in our population. Folic acid has been proved to have antioxidant properties[43] and is shown to interact directly with endothelial nitric oxide synthase[44] or has positive effects on tetrahydrobiopterin (BH4) the essential cofactor of endothelial nitric oxide synthase[45]. The ameliorative influence of folates on endothelial nitric oxide synthase suggests a more pronounced benefit of folate in the early phase of atherogenesis and less of a benefit on more advanced stage. Correlation studies of these vitamins showed that the levels of all these three vitamins correlated inversely with serum homocysteine in all the subjects (patients and controls), although it was statistically significant in the patients than in controls. Strong negative and statistically significant correlation of homocysteine in this study was seen with vitamin B_{12} in the male patients of Group C, followed by homocysteine vs vitamin B_6 in Group A patients (both male and female), and homocysteine vs folic acid in the patients of both age groups as well as controls. This shows a clear association of hyperhomocysteinemia and inadequate vitamin status in our population. With few exceptions[39,40], most other studies[46,47,48] of homocysteine and B vitamins in coronary artery diseases have shown a positive relation of serum homocysteine with these B vitamins.

CONCLUSION

In conclusion our data suggests that serum homocysteine concentrations were higher in patients as compared to controls but higher concentrations were recorded with increasing age and in male subjects as compared to females. The association between homocysteine and B vitamins existed over a wide range of homocysteine levels.The observation that in addition to the patients low concentrations of vitamin B_6, B_{12} and folic acid recorded in a good percentage of control subjects was unexpected, since the levels of these vitamins are important determinants of serum homocysteine. Further studies are therefore necessary to complement the growing evidence of the important role of elevated total homocysteine and low B vitamin status in the etiology of myocardial infarction and to further elucidate the role of other ethnic related factors like genetic, nutritional and life style factors in the causation of hyperhomocysteinemia and resultant cardiovascular events. In our opinion reduction of total homocysteine concentration in general population and not only those with clearly

abnormal homocysteine levels may protect against cardiovascular diseases, but this has yet to be proven in clinical trials.

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OUTCOME OF GALLSTONE ACUTE PANCREATITIS

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ABSTRACT

Objective: The objective of this study was to calculate the severity score for each patient with gall stone pancreatitis, because the presence of sepsis is an early indicator of the likely severity of acute pancreatitis.

Material and Methods: To find out the outcome of gallstone acute pancreatitis in terms of morbidity and mortality in a centre with limited intensive care and monitoring facility, a retrospective descriptive study was performed in the surgical department of Khyber Teaching Hospital Peshawar. 32 patients fulfilling the criteria and who were admitted between Jan 2005 and Feb 2008 were included in the study.

Results: Among the 32 patients 20 (62.5%) were females. Serum amylase was raised in 27 (84.3%) patients and among them 15 (46.8%) had the diagnostic rise which is three times normal. Ultrasound was the main tool for diagnosing biliary tract stones and showed gall stones or dilated bile ducts in all the 32 cases. Majority of the patients (71.8%) had Acute Physiology and Chronic Health Evaluation (APACHE) II scores of less than 8. Seven (21.8%) patients had severe acute pancreatitis (APACHE scores $\geq$ 8). These 7 patients had pancreatic necrosis on CT Scan and underwent surgery. Six (18.7%) of them died of sepsis. Twenty five (78.1%) patients developed some sort of complication and the overall mortality was 18.7%.

Conclusion: Gallstones pancreatitis has high morbidity and mortality. Proper assessment and doing the severity scores for every patient does affect the final outcome of these patients. Patients with high scores need close monitoring in the intensive care units. Limited intensive care leads to higher complication rate and increased mortality in our setup.

Key Words: Gallstone pancreatitis, APACHE II scores.

INTRODUCTION

Acute pancreatitis is a common surgical emergency. Biliary tract stones are responsible for the development of symptoms in majority of the cases in this part of the world. Obstruction at the sphincter of Oddi results in oedema and necrosis of pancreatic cells, causing the release of mediators of inflammation, which in turn causes an increase in the vascular permeability leading to haemorrhage, oedema and eventually pancreatic necrosis.[1]

When these mediators enter the general circulation, systemic complications arise, such as bacteremia, acute respiratory distress syndrome, pleural effusions, gastrointestinal and renal failure. Eventually the mediators can become so overwhelming to the body that haemodynamic instability and death ensue. Despite improvement in intensive care treatment during the past few decades, the rate of death has not significantly declined.[2]

Acute pancreatitis is relatively more prevalent in the West and other developed parts where there is an increased consumption of alcohol. In USA 220,000 patients with acute pancreatitis are admitted to hospitals each year.[3] In UK the incidence reported is 38 cases/ 100000 people/ year, in Germany it is 17.5/ 100000/ year and in Finland as high as 73.4 cases/ 100000 population reported in one year. In Pakistan the exact statistics are not available but we do see many patients admitted to the surgical and medical units suffering from acute pancreatitis.

Severe acute pancreatitis is defined as the presence of $\geq$ 6 Ranson criteria or an APACHE II score of $\geq$ 8. Twenty percent of patients with acute pancreatitis will have the severe form, resulting in sepsis, increasing organ failure and death[4,5]. In our circumstances with limited nursing and intensive care facilities, the mortality rate is expected to be high.

MATERIAL AND METHODS

This is a retrospective descriptive study conducted on patients admitted to surgical units of tertiary level teaching hospital within a span of three years. From January 1, 2005, to February 28, 2008, all patients who presented to Surgical units of Khyber Teaching Hospital Peshawar within 48 hours after the onset of acute gallstone pancreatitis, were evaluated. The diagnosis of acute gallstone pancreatitis was based on the presence of the following 5 criteria: 1)

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acute upper abdominal pain; 2) serum amylase 3 times or more the upper limit of normal for our laboratory; 3) biliary lithiasis on admission ultrasound (US); 4) evidence of pancreatic inflammation on computed tomography (CT) scan; and 5) absence of other causes of acute pancreatitis.

Patients in whom the diagnosis of biliary tract stones was not confirmed , those who came late after 48 hours and those diagnosed by chance at laparotomy were excluded from the study. The objective of the study was to find out the outcome of gallstone acute pancreatitis in terms of morbidity and mortality in our setup with limited intensive care and monitoring facility. Demographic data were collected from patients' medical records.

The aetiolology of pancreatitis, Ranson's scores, APACHE II scores, hospital and intensive care unit length of stay, results of abdominal ultrasound and CT scans, presence of pancreatic necrosis, complications and cause of death recorded. Variables for Ranson's and APACHE II scores including age of the patient, total leucocyte count (TLC), blood sugar, Serum LDH, serum ALT, blood urea levels, hematocrit levels, Po_2 levels, base deficits and serum calcium levels etc recorded.

RESULTS

Thirty two patients with confirmed biliary tract stones and acute pancreatitis were admitted between Jan 2005 and Feb 2008. Twenty (62.5%) of them were female. The average age was 50.6 years (range 34-78 years) for both sexes. Twenty (62.5%) patients were admitted through casualty, 8 (25.0%) patients through OPD and 5 (15.6%) patients taken over from the medical units. Serum Amylase levels and abdominal ultrasounds were performed on all 32 (100%) patients and were the main tools of diagnosis. Fifteen (46.9%) patients had serum amylase levels of more than 1000 International units which is more than three times normal, 12 (37.5%) patients had values between 250 and 1000 while 5 (15.6%) had normal levels. Ultrasound detected a swollen pancreas in 18 (56.25%) patients, gall stones and/or stones in the Common Bile Duct (CBD) in all the 32 (100%) patients. CT scans detected swollen pancreas in 100% of the patients. Ranson's and APACHE II scores were calculated for all patients. (Table 1 and 2). All patients (100%) received antibiotics, analgesia, H2 blockers and intra venous fluids during the course of their admission. Eighteen (56.2%) patients were treated in the ward, 14 (43.7%) patients had part of their stay in the surgical ICU. Seven (21.9%) patients required surgery for suspected pancreatic abscess formation. Over all 25 (78.1%) patients developed complications of acute pancreatitis (Table 3).

Surgical procedures performed in these patients are given in Table-4. Only 13 (40.6%) patients underwent cholecystectomy during the same hospital stay. Twelve (37.5%) patients were discharged home and came back for cholecystectomy with in two weeks of their discharge from the hospital. Seven patients (21.9%) had laparotomy for dealing with complication (necrosectomy/ abscess drainage) during the same admission. These seven patients did not undergo cholecystectomy during the same setting as it was not possible. Six of these (18.7%) patients died in the post operative course due to severe sepsis. One of these seven patients who survived was discharged home and had cholecystectomy with in a month. The average hospital stay was 9.5 days (range 5-24 days).

Table 1: Ranson's score at 48 hours

Ranson's score	Number of patients	%age
0-5	20	62.5
6-13	12	37.5

Table 2: APACHE II scores based on initial 12 parameters

APACHE II score	Number of patients	%age
0-4	07	21.8
5-7	15	46.8
8-12	10	31.4

Table 3: Complications

Complication	No. of patients	Percentage
Pancreatic Necrosis (on CT)	07	(21.9%)
Pleural Effusions	16	(50.0%)
Deranged renal function High urea/ creatinine	10	(31.2%)
Hypocalcaemia	13	(40.6%)
Multiorgan failure	07	(21.9%)

Table 4: Surgical procedures performed

Procedure	Number of patients	%age
Laparotomy+ necrosectomy	07	21.9
Cholecystectomy same admission stay	13	40.6
Cholecystectomy within a month of discharge	12	37.5

DISCUSSION

Acute pancreatitis is a potentially lethal disease and world wide there is a rise in the number of new cases admitted each year. The over all mortality has not decreased significantly over the years despite a greater understanding of the natural history of the disease and the recent advances in critical care.

Patients suffering from acute pancreatitis have typical symptoms of severe abdominal pain radiating to the back and relieved on sitting and stooping forward. Majority of our patients in the study had the classical history. Diagnosis of pancreatitis was based on the typical history of pain, physical examination, serum amylase and ultrasound/ CT scan reports. Serum amylase levels in patients with pancreatitis vary depending on the severity of the disease. On average, during uncomplicated cases, the serum amylase level starts increasing from two to 12 hours after the onset of symptoms and peaks at 12 to 72 hours. It usually returns to normal within one week[6,7]. Although it lacks sensitivity (75-92%) and specificity (20-60%), measurement of the serum amylase level is the most widely used method of diagnosing pancreatitis. The advantages of amylase testing are that it is quickly performed, easily obtained and inexpensive. However, a variety of nonpancreatic conditions cause increased amylase levels In studies where serum amylase levels are equivocal, 24 hrs urinary amylase levels and serum lipase levels are used for the diagnosis. Tests that are more specific for acute pancreatitis but less widely available are levels of trypsinogen activation peptide and trypsinogen.[8]

Radiography has a definite role in the diagnosis and management of acute pancreatitis. Plain x-rays contribute little but may show calcifications, dilated intestinal loops, detect prognostic signs like pleural effusions on chest radiographs. All of our patients underwent ultrasound scans, which has its value in detecting biliary tract stones, dilated biliary channels and pancreatic swelling. It is recommended in almost all the studies as an initial investigation for patients with suspected pancreatitis. Transabdominal ultrasonography is more sensitive than either CT or MRI for identifying gallstones and sludge and for detecting bile-duct dilatation but is insensitive for detecting stones in the distal bile duct.[9] We occasionally used CT scan for the diagnosis of pancreatitis when amylase levels were not diagnostically elevated and ultrasound could not show a swollen pancreas due to intestinal gases. This is true of most of the published series on acute pancreatitis. CT scans are mainly indicated for detecting pancreatic necrosis[10] and in such cases patients do not show improvement clinically with routine treatment and have symptoms of toxemia.

All of our patients included in this study had confirmed biliary tract stones. None of the patients had history of alcoholism. This is in contrast to most of the western studies where alcohol is the cause for acute pancreatitis in the majority of the patients. The recent rise in the incidence of the disease is directly attributed to increasing use of alcohol in different communities.[11]

All of our patients got admitted within 48 hours of their symptoms and thus Ranson scoring and APACHE II grading was done for all the patients. Patients with initial scores of ≥ 8 were kept in the high dependency surgical unit for better monitoring. It is critical to identify patients who are at high risk for severe disease, since they require close monitoring and possible intervention. Morbidity and mortality is high in patients with higher severity scores.[12] The Acute Physiology and Chronic Health Evaluation score (based on initial values of 12 routine physiological measurements, age, and previous health status) is among the best predictors of severity on admission, whereas elevated C-reactive protein levels are equally useful when measured 24 to 48 hours after the onset of symptoms.[13]

Majority of patients with acute pancreatitis are treated conservatively with nasogastric suction, intra venous fluids, pain killers and antibiotics. Use of antibiotics is controversial. Some studies state that prophylactic antibiotics do not prevent infected necrosis or death in acute necrotizing pancreatitis,[14] but others favor the use of antibiotics in severe acute pancreatitis.[15] Surgery is reserved for patients where pancreatic abscess formation is suspected.[16]

A few patients would be opened for necrosectomy but the mortality in such moribund patients is always high. We performed laparotomy on seven patients for pancreatic pus collection, six of them died after initial recovery. Majority of our patients did not under go cholecystectomy during the same hospital stay. This is in contrast to the Western countries where patients are encouraged to have their gall bladder removed once their pain subsides because a second attack of acute pancreatitis would prove fatal. None of the patients underwent endoscopic sphinterotomy as part of their treatment. This procedure is effective in reducing the over all incidence of recurrent pancreatitis.[17]

Most of the patients were discharged home with in ten days of their admission. Patients who developed complications had prolonged hospital stay.

Recent studies recommend minimally invasive procedures to be adopted for draining pancreatic abscesses.[18] The results of the open abdomen surgery are poor where as minimally invasive approach seems promising.[19,20]

CONCLUSION

All patients with acute pancreatitis should be properly evaluated and severity score calculated for each patient because the presence of sepsis is an early indicator of the likely severity of acute pancreatitis.

Patients with higher severity scores should be closely monitored in the intensive care unit. The higher morbidity and mortality rates in our setup are directly linked to the poor ICU facilities.

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ORIGINAL ARTICLE

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USING COMPUTER TECHNOLOGY IN TEACHING AND LEARNING

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ABSTRACT

Objective: To introduce a duplicate digital photo image record keeping system by replacing old conventional photo-slides and to avoid maintenance problems of conventional photo-slides library and establish a privacy policy to assure secure retrieval.

Material and Methods: This comparative study was conducted at ENT Department of Khyber Teaching Hospital Peshawar Pakistan from Jan 2003 to Dec 2004. In this project, the photo slides (chrome film transparency) captured by a conventional camera were converted into digital data format on a compact disc (CD) by a process called Digitalization. A total of 60 photo slides captured on chrome – file were selected from our photo graphic record library.

Results: The digitized photo image proved to be advantageous over conventional photo slide management in record keeping, being easily manageable via computer for easy retrieval . All the environmental and handling losses of the conventional photo slides can be avoided with this method of duplication.

Conclusion: It is concluded that digital photographs are useful tools for the evaluation of the patients pre operative photo images as a ready and reliable reference for the comparison.

Key Words: Medical Records, ENT Surgery, Digital Photography.

INTRODUCTION

For patient education, case presentation and documenting the medical photography is almost as old as photography itself.[1] Medical image libraries are a valuable source that can be used for education, research and maintaining of patients record. All the aesthetic ENT surgical procedures are rare and interesting procedures require good quality photographs to be taken in a standardized manner to establish records. Conventional photo prints (photographs) or conventional colour photo slides are still used by surgeons to keep or evaluate their records and judge the result outcome of the procedures. These methods have the advantages of wider density range, richer graduation, deeper color saturation than negative film/prints; no printing differences, which can affect color balance, sharpness and size. Some of the disadvantages of conventional photo record keeping are:

- High temperature can damage film transparency.
- Processed film storage temperature needs to be below 10 degrees centigrade (50 degrees Fahrenheit).
- Fading and discoloration especially to ultraviolet rays.
- Humidity and moisture control for processed film 30 to 50% RH,
- Repetitive handling can cause scratches and damage the quality of the photo-slide.
- Photo slides have limited shelf life and decreases if not managed properly.
- Larger file drawer cabinets are required to put them secure.
- They need to be kept in a sleeve, envelopes or mounts and placed in a dark environment with good ventilation.

Technological advancement has improved photographic equipment, techniques and materials. Digital imaging as well as videotaping are also on rise in record keeping of the patients. scanning of photographs and CD-Rom are powerful educational tools[2], and the evidence suggests that digital images under certain experimental conditions can be useful as slides.[3]

Digital photo images can be viewed with the help of computers, it has been shown that digital images can substitute for physical examinations; these images can be added in any database or any picture manipulation software.[4]

Because of the rapid advancement in technologies, the digital camera in future with high

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capturing option will be able to capture images, will be well comparable to conventional photo slides captured by conventional cameras. Digital camera image resolution still lags well behind that available with conventional film. Whereas on 35 mm film more than 100 million pixel are captured, a fairly high quality digital camera at present can capture just over 1 million (100×1280 resolution) or maximum 7.1 million pixel at 24 bit color (64 million colors).[5,6]

This study was undertaken to introduce a duplicate digital photo images record keeping system by replacing old conventional photo-slides to avoid maintenance problems of conventional privacy policy to assure secure retrieval.

MATERIAL AND METHODS

This study was conducted in ENT Department of Khyber Teaching Hospital, Peshawar Pakistan. In this project photo slides captured by a conventional SLR Camera were professionally converted into digital data format on a compact disc (CD) by a process called Digitization. A total of 60 photo slides were selected from our photoslides library, all captured by a conventional SLR camera on chrome film with 60mm lens using manual focusing techniques with a single flashlight attached. All the preoperative and postoperative slides were included that were routinely used for ready reference. The digital formats selected for scanning were JPEG (Joint Photographic Experts Group) and BMF (Bitman file, which is commonly used as window file system) Table 1. Each of the formats were scanned at 16 base and 4 base and stored in CD with 24 bit true color resolution. All the images were transferred and recorded on a compact disc (CD-R) using a CD writer so that they could be viewed on the computer monitor using computer software.

Compression of the images was done to reduce the file size, JPEG files were compressed with less amount of data loss to make the file size small for storage on the CD. The BMF format of 4-base and 16 base was in uncompressed form. For the purpose of easy access, the images were catalogued using serial number, date, patients registration number and anatomical view. The photo images were evaluated by visual perception and viewed on monitors by a team of surgeons and graphic designers. These images were classified into 4 grades, excellent, good, fair, and poor to rate the photo images.

Manipulation and editing of images were done in software Adobe shop 5.5 or ACD see version and saved in the hard disk of the computer. They were also used to improve the digital image color, contrast, brightness and visual transformation. When the desired image was achieved after transformation the duplicate image was saved in digital data format. These images were further transformed , augmented or mastered and used for consultation. A magnification (scale factor) of 25%, 50%, 70% or 100% was used to view these images.

RESULTS

The development of this new digital photo image database system proved to be advancement in the field of photograph-record keeping in the department of ENT. Joint photographic Experts Group (JPEG) format proved to be the best of all for the reason that it could compress image data in smaller size and stored more pictures on a single disc (CD having 600-MB space)and easy to access. The images which were saved on CD and its prints were well comparable with conventional photo slides (chrome file) prints. Imaging manipulation in software photo shop adobe was successful and the results were acceptable to modify the photo image and proved to be helpful and beneficial for image manipulation.

The compressed images on compact disc were categorized on the basis of outcome as excellent in 51(85%), good in 6(10%), fair in 2(3.3%) and poor quality in 1(1.6%) of all slides as shown in Table-2. The data loss in our study was 8% for the compressed disc images.

Table 1: Digital formats selected for scanning

Film	Recording type	Pixel dimensions	Dimension size (inch)	Compression ratio	color	Approx film size
135 mm	BMP 16 Base to CD	3360×2240	63×42.2	1.0	True color	22MB
135 mm	BMP 4 16 Base to CD	1840×1232	25.6×17.1	1.0	True color	6.6MB
135 mm	BMP 16 Base to CD	3360×2240	46.6×31.1	6-8	True color	2.3-3MB
135 mm	BMP 4 Base to CD	1840×1232	25.6×17.1	8-10	True color	600-800KB

Table 2: Quality of images on compressed disc, compared to conventional photographs

S. No.	Quality of image	No. of patients
1.	Excellent	51(85%)
2.	Good	6(10%)
3.	Fair	2(3.3%)
4.	Poor	1(1.7%)

DISCUSSION

The basic aim of photographic documentation of clinical cases is to compare these cases with each other, as well as to evaluate the pre operative and post operative outcome of skills. The photograph taken for the purpose of record should be sharply focused and of suitable quality display which may need enlargement to make the display better for evaluation.[8] Photography must be a regular part of theatre records as well as in every cosmetic and reconstructive procedure for teaching and clinical purposes and supplementing written operative notes but their medico legal use have been neglected.[9] The photo image quality depends on the type and resolution on which the images were saved.The scanned images in JPEG format seem to be the best resolution even with compression. There were certain data losses while compressing only initially when the photo slide were scanned and transferred to the CD. The gross appearance on the computer screen was unaffected. In a report by Schruddle et al[10], the deta loss while compresing was about 10% as compared to 8% loss in our results It is said that sensible compression for routine mean, the file size is down to below 10% of the original and the reduction in overall quality is barely perceptible to human eye.[10] Security of storage of CDs must be high considering the social, ethical and moral aspects. They should be kept in safe file cabinet. the compact disc (CD) is of polycarbonate with one or more metal layers capable of storing digital information on it and care must be taken while handling it to avoid image data loss. The JPEG format is easily manageable in any software available for manipulation/transformation. The duplicate image is saved in different digital data format e.g. JPEG(joint photographic expert group) or TIFF (tagged image file format). The images in the above format can be further transformed, augmented or mastered in many other soft wares successfully and can be used for consultation of the patient.

Surgeons can perform precise and predictable operative planning from this digital photograph and interactive simulation of the changes in the photograph which can make the patients understand the problem and their expectation with immediate aesthetic analysis. The important thing is to clearly explain to the patient the purpose of recording,[11] and ensure that the manipulation was just for the demonstration of an idea about the outcome of the results which would be near to it "NOT THE SAME". Bryson D et al[12] explained the results to the patients in 100% of cases as compareable to our results. In this study we overcame all the disadvantages of the conventional photographic, transparency and slides record which will further improve with more advancement in technology.

CONCLUSION

Medical workshops and appropriate training courses must be conducted for medical photography record keeping in ENT Surgery. The photo slides are still superior from digital camera image captured unless a standard comparable digital image capturing device is available in future development and research in digital technology.

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ORIGINAL ARTICLE

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INTRALESIONAL BLEOMYCIN THERAPY OF CYSTIC HYGROMA IN CHILDREN

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ABSTRACT

Objective: To Know the efficacy of intraleisional bleomycin injection (IBI) therapy in cystic hygroma.

Material and Methods: This was a prospective study which was conducted in Aman Hospital Peshawar from March 2003 to February 2006. A total of twelve (12) patients with cystic hygroma were treated with intralesional bleomycin injection (IBI) and followed prospectively. We performed an ultrasound study in all the cases to delineate the size, nature, location and the number of cysts in the lymphatic malformation. Under general anaesthesia the cysts were aspirated and bleomycin injected intralesionally in a dose of 0.5mg/kg body weight. The patients were followed monthly for 6 months. The second injection was made when the size of the cystic hygroma did not decrease by 50% after 03 months.

Results: Out of twelve patients, 8(66.67%) were male & 4(33.33%) were female. The age ranged from 7 days to 5 years. The localization of cystic hygroma was cervical in 7(58.4 %), submandibular in 3(25%), parotid in 1(8.3%) and axillary in 1(8.3%). Only 2 patients needed second injection. An excellent (complete clinical resolution) response was obtained in 9 (75%) patients, a good response (less than 50% decrease in size) in 2 (16.67%), while a poor response in 1 (8.3%) patient. There were no major deleterious side effects.

Conclusion: Intralesional bleomycin injection (IBI) therapy of cystic hygroma in children is a simple, safe and effective mode of treatment. In the majority of cases total healing may be achieved with a single injection.

Key Words: Cystic Hygroma, Lymphangioma- Bleomycin- Sclerosing therapy. Intra Leisional Bleomycin Injection. IBI

INTRODUCTION

Cystic hygroma is a large cyst or pocket of lymphatic fluid that results from blocked lymphatic vessels. A cystic hygroma may contain multiple cysts connected to each other by the lymphatic vessels. It may occur anywhere in the body but most frequently seen in the neck (75%), axilla (20%) and inguinal areas (2%).[1]

In 1828, Redenbacher is credited with describing a lymphangiomatous lesion and coined the term "ranula congenital." In 1843, Wernher reported the first case of cystic hygroma. This term comes from the Greek word "hygroth" meaning fluid and "oma" meaning tumor. In 1965, Bill and Summer proposed that cystic hygromas and lymphangiomas are variations of a single entity.[2]

Lymphatic vessels are small canals that lie near blood vessels and carry tissue fluids from within the body to the lymph nodes and back to the bloodstream.

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Embryologically the lymphatic channels are formed from a series of clefts that develop in the mesenchyme around the sixth week of gestation. From these channels, sacs are formed that establish drainage with the venous system. Failure to establish venous drainage results in dilated and disorganized lymph channels, the largest form present as cystic hygromas. Some lymphatic malformations can spread into the surrounding tissues and affect the proper development of the area.[3,4]

Most cystic hygromas are evident at birth (65%), while the remainder evident by the time the individual is aged 2 years.[5] The infection in cystic hygroma results in additional swelling, pain, fever, and localized erythema[6]. Hemorrhage in the cystic hygroma leads to sudden enlargement of the lesion with clinical evidence of acute blood loss.

Lymphatic malformations are sometimes seen in children with certain chromosomal and genetic abnormalities like Down's syndrome, Turner's syndrome and Noonan's syndrome.[7]

Most of the cystic hygroma are clinically obvious and require no imaging studies for diagnosis. The investigations done are to assess its extension into the surrounding structures. Chest radiography,

ultrasonography and computed tomography are necessary to determine the extension into the mediastinum in patients with cystic hygroma in the lower neck and axilla. Magnetic resonance imaging (MRI) is often required to determine the extent of invasion into the adjacent neurovascular structures.[8,9]

The mainstay of therapy is surgical excision. The goal of performing surgical therapy is to excise the lesion completely or to remove as much as possible, sparing all vital neurovascular structures. The exceptions to excision at the time of diagnosis are few and include premature infants of small size and those with involvement of crucial neurovascular structures that are small and difficult to identify (e.g facial nerve).[10,11,12]

The treatment of cystic hygroma with sclerosing agents is an alternative. Cystic hygromas may improve with use of sclerosing agents, such as bleomycin, OK-432, absolute alcohol, and steroid.[13]

Here we describe our experience with the intralesional bleomycin injection (IBI) for the treatment of cystic hygroma. This study was done to assess the results of IBI as it is simple, less expensive and requires no exhaustive technique and expertise as compared to the surgical excision.

Though the number of cases treated by IBI is small but we have noticed encouraging results with this simple technique for the treatment of cystic hygroma in children.

MATERIAL AND METHODS

All the patients of cystic hygroma were included in this study. The patients were admitted for twenty four hours. A standardized data collection sheet recorded the patient's details including age, sex, weight, size and location of lesion, clinical history, special investigations, bleomycin dose, clinical response, side effects and follow-up. Colour photographs were taken of every patient before, during, and after completion of treatment.

A through physical examination was done. The patients were screened for Hepatitis-B and C. Ultrasonography was done to know the extent, nature and number of cysts in lymphatic malformation.

The parents of the patient were counselled and results of the therapy explained to them. Informed consent was given to the use of bleomycin as injection therapy.

Intralesional bleomycin injection into the cystic hygroma was done under general anaesthesia. Bleomycin powder (15 mg) was reconstituted with 15 ml of normal saline (dilution 1 mg/ml). The calculated dose of bleomycin was taken from the reconstituted bleomycin and diluted in 20 ml normal saline. The cystic hygroma was aspirated and bleomycin injected in a dose of 0.5mg/kg body weight. A single dose of 15 mg per session was not exceeded. All the patients were observed for 24 hours to note and treat any immediate problems like fever and pain. The post injection course was uneventful in all cases. Mild swelling and pain at the injection site disappeared within 24 hours following IBI. Patients were discharged and asked to come after 4 weeks for follow up.

On follow up visit the size of the cystic hygroma was measured and compared with the pre-injection size. The improvement in the size of the cystic hygroma was noted. Second intralesional injection was given after 3 months if the size of cystic hygroma did not decrease by 50% of the initial size. Patients in whom the lesion did not decrease or decreased by 50% after two intralesional injections of bleomycin underwent surgical excision. There was no difficulty in excision of lesion after the IBI therapy.

RESULTS

There were twelve patients, 8 (66.67%) male and 4(33.33%) females. The age ranged from 7 days to 5 years. The localization of cystic hygroma was cervical in 7(58.4%), submandibular in 3(25%), parotid in one (8.3%) and axillary in one (8.3%) patient as shown in Table 1. In the cervical region the cystic hygroma were 4 (33.33%) on the right and 3 (25%) on the left side. In our study only 2 (16.67%) patients needed second injection. The criteria used to know the efficacy of IBI was as follows: Excellent (complete clinical resolution of the lesion) Good (less

(a) (b)

Fig. 1: A 9 months baby with left cervical cystic hygroma. (a): before (b) after IBI

Table 1: Sites of Cystic Hygroma (n=12)

Location	No. of patients	%age
Cervical	7	58.4
Submandibular	3	25
Parotid	1	8.3
Axillary	1	8.3

than 50% decrease in size of the lesion) Poor (no decrease in the size of the lesion) An excellent response was obtained in 9 (75%) patients as shown in figure 1. A good response in 2 (16.67%), while a poor response in 1 (8.3%) patient. There were no major deleterious side effects.

DISCUSSION

The treatment of cystic hygroma is a challenging problem both for the parents and surgeon as both expect an earlier and more effective treatment of this problematic pathological lesion[9,10,11]. Surgical excision offers the best opportunity for permanent cure of cystic hygroma. The goal is to excise the lesion completely sparing all vital neurovascular structures. Because of the close proximity of the lesion to the crucial neurovascular structures complete excision is sometimes difficult. If the lesion is not completely excised, then recurrence is common with a reported incidence of 10 to 30%[12].

The use of a sclerosant agent like bleomycin, OK-432, absolute alcohol and steroids is another therapeutic choice.[13]

We preferred bleomycin as a sclerosant because of its easy availability, low cost, and minimal side effects when used in low dose intralesionally in cystic hygroma.

Bleomycin was discovered as an antibiotic in 1965 by Dr. Umezawa. Interestingly, it has never been used as an antibiotic after it was found to cause incision of single stranded DNA. Since that time it has been used to treat malignancy. It was noticed that in the treatment of malignant pleural effusion, bleomycin caused fibrosis and scarring. So in 1977 Dr. Yura used it as an intralesional sclerosant in eight patients with lymphatic malformation and noticed good results.

Pulmonary toxicity is a potential side effect of bleomycin therapy. This risk is related to the dose, an increasing incidence being associated with the total dose of more than 400 units or a single dose exceeding 30mg/m^2 of body surface area. The pulmonary fibrosis of IBI therapy is not reported so far because of its low dose.

In our study intralesional bleomycin therapy was effective in complete resolution of cystic hygroma in 75% of the children. These results are in agreement with those reported by Tanaka (87%)[5], Okada (86%),[1] Baskin D (70%)[8], Muir T (80%)[4] and Zulfiqar (88%)[7].

Recently promising results have been reported with the use of OK-432. Ogita et al[10] reported favorable results without recurrence or significant side effects. Sanliap[3] has reported 80% resolution of cystic lymphangioma with the use of OK-432 as a sclerosant. The availability and cost of OK-432 are prohibitive factors and our results are the same by using bleomycin as a sclerosant in cystic hygroma.

The use of bleomycin as a sclerosant in the intrauterine fetus with cystic hygroma is under trial and some have noticed promising results.[14,15]

The most important factor in IBI is the concentration of the sclerosant available to the endothelial lining of the cystic hygroma. In lesions that are aspirated completely the bleomycin available per unit area of the lesion is higher and so is its sclerosing effect[16]. In lesions that are incompletely aspirated the drug would get diluted in the hygroma fluid and less drug per unit of the surface area would be available for the sclerosing effect.

Intralesional bleomycin therapy (IBI) is more effective for cystic lymphangiomas. Therefore, the patient selection for this mode of therapy is important. We suggest that the lymphatic malformation should be assessed by ultrasonography before going for IBI. Cervical, facial and axillary lymphangiomas are commonly of cystic type. These areas are also cosmetically important.

We suggest that the dose of bleomycin injected intralesionally should depend upon the size of the lesion rather than weight of the patient and bleomycin dose range of 0.3-0.6 mg/Kg body weight[6] needs to be revised. To achieve this goal more work needs to be done on IBI as the treatment option for cystic hygroma in children.

CONCLUSION

Sclerotherapy with bleomycin is effective and safe. It should be preferred as a primary mode of treatment in childhood cystic hygroma.

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MODIFIED RADICAL MASTOIDECTOMY *"LONG TERM PERSONAL EXPERIENCE"*

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ABSTRACT

Objective: The aim of current study is to present the long-term anatomical and functional results obtained in a group of patients, who underwent modified radical mastoidectomy.

Material and Methods: This is a descriptive study carried out at the department of ENT, Head & Neck surgery Khyber Teaching Hospital Peshawar, from June 1998 to May 2003. Fifty-three patients with discharging ears, having cholesteatoma who under went modified radical mastoidectomy were included in the study.

Results: Out of 53 patients, 37 (69.8%) were male & 16 (30.2%) were females with age range from 23 to 72 years. Average age was 43 years. In 38 (84.50%) cases dry, smooth cavity, free of complications were found, in one case (2.30%) residual cholesteatoma of the anterior epitympanic space was found, 2 (4.4%) patients had Attic retraction with epidermal debris & residual cholesteatoma and 2 (4.4%) patients had epidermal debris and granulations in mastoid cavity.

Conclusion: A modified radical mastoidectomy should always be considered in cases of epitympanic cholesteatoma with normal or near normal hearing.

Key Words: Middle ear, mastoid, Otitis Media, cholesteatoma.

INTRODUCTION

At the close of 20th century the surgical procedure used to treat chronic middle ear disease was treated by either simple or radical mastoidectomy, with no attempt to preserve the pre-operative hearing level[1]. In 1910, Bonday set forth the technique of, and indications for a modified radical mastoidectomy, in cases of chronic otitis media with epitympanic cholesteatoma in the presence of a defective pars flacida but with an intact pars tensa. The purpose of this operation was to obtain a "safe ear" while at the same time preserving the pre-operative hearing level. Varieties of surgical techniques are available for removing the lesions of middle-ear cholesteatoma and for treating the mastoid cavity & posterior canal wall following removal of the lesions[2,3,4]. One such procedure is the canal down technique in which the posterior canal wall is drilled out to secure a wide surgical field, thereby ensuring complete removal of the cholesteatoma lesions. Among the most important criteria in the surgery of the middle ear cholesteatoma is a complete exenteration of the lesion, and the above technique is advantageous in this respect. The primary aim of treatment of cholesteatoma is to attain a dry, safe, stable ear, free of disease[5]. Maintaining or improving hearing is important but the pursuit of a hearing result should not compromise this primary aim. Bondy's original procedure called for the cavities of the mastoid and epitympanum, while preserving the integrity of the pars tensa and ossicular chain. Removal of the posterior canal wall and lateral attic wall enable us to exteriorize the attic and antral cholesteatoma removed while leaving the matrix intact and creating a modified permanently accessible radical cavity that discharge through the external meatus. The main disadvantage of this operation stemmed from the incomplete removal of the perilabyrinthine air cells and leaving behind cholesteatoma matrix, which can continue to erode the bone and lead to formation of granulation tissue and cholesteatoma[6,7]. The aim of the current study is to present the long-term anatomical and functional results obtained in a group of patients who underwent a modified radical mastoidectomy.

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MATERIAL AND METHODS

This descriptive study was carried out at the department of ENT & Head & Neck surgery of Khyber Teaching Hospital Peshawar-Pakistan, from June 1998 to May 2003. Both male & female patients with age range from 23 to 72 years were included in the study. The criteria for the selection of patients was mastoid and epitympanic cholesteatoma without involvement of epitympanic space. In all these patients the parstensa was intact with ossicular chain and good

pre-operative hearing level (miled hearing loss). Patients who had cortical mastoidectomy or atticotomy were excluded. All patients had follow up for five years after modified radical mastoidectomy.

All patients underwent pre and postoperative audiological evaluation by pure tone audiometry (air and bone conduction), analyzing the mean threshold at the frequencies of 0.5,1,2,3kilohertz (KHz).

In comparing the pre and post operative air-bone gaps at (0.5, 1, 2, 3 KHz) the post operative gap was considered to be unchanged for PTA (Pure tone audiometry) if it was ± 10 Decibels(dBs). Improvement of hearing was noticed if air bone gap reduced by more than 10 dBS and worsened if the air bone gap was increased by more than 10dBS. Finally cochlear damage was diagnosed when a deterioration of 75dBs was detected in at least 2 frequencies of the bone conduction tests.

RESULTS

Total of 53 patients [37 (69.8%) male, 16 (30.2%) female] were included in the study. Age groups are given in Table-1 and complications of surgery are given in Table-2. Clinically the ears were free from complications, with a dry, smooth round cavity in 37 (84.5%) patients. One patient had residual cholesteatoma of the anterior epitympanic spaces one year after the operation requiring surgical revision. Two patients had posterior tympanic retraction. Two patients had retraction in the attic with epidermal debris, while other two patients had recurrent ottorhoea,epidermal debris or granulation in the mastoid cavities requiring cleaning and removing the pathologic tissue under local anesthesia. Three patients had insufficient meatoplasty.

With regard to functional features, 41 patients (91%) exhibited unchanged or improved hearing levels, while in four (9%) patients worsening of the air bone gap was observed (70dbs).

A high frequency sensorineural hearing loss, probably by acoustic trauma during drilling, was detected in four patients (9%). After 05 years, three patients had significant worsening of the air bone gap (70dbs) and two patients had tympanic retraction.

Table 1: Age Distribution of the Patients.(n=53)

Age in Years	No. of patients	%age
23 to 30	06	11.3
31 to 40	10	18.9
41 to 50	17	32.1
51 to 60	12	22.6
61 to 72	08	15.1

Table 2: Complications of the surgery. (n=53)

Type of complication	No. of cases	%age
No complication	38	71.6
Residual cholesteatoma	01	1.8
Posterior tympanic retraction	02	3.7
Epidermal debris	06	11.3
Granulation Tissue	03	5.6
Insufficient meatoplasty	03	5.6

DISCUSSION

Modified radical mastoidectomy is an extremely effective operation when performed on carefully selected patients.

If the cholesteatoma is located in the medial attic region, this operation is not recommended, because the malleus head and incus would have to be removed[8,9]. With improvements in surgical and anesthetic techniques and other advances, operations such as atticotomy may become popular in paediatric patients[10].

In day to day practice of ENT in our environment, acute mastoiditis with abscess formation developing from chronic otitis media and the cholesteatoma , the surgical procedures conducted in these cases should be at least modified radical mastoidectomy rather than simple incision & drainage of the pus[11].

Despite pre-operative audiological and otomicroscopic workup, all the anatomical features can be evaluated only during the surgical procedure[12].

Aggressive antibiotic therapy and combined management of cases by otologists and neurosurgeons are the key to reducing the morbidity and mortality of the serious complications of otitis media. Although the main indications are those stated earlier, there are other less critical factors that must be taken into account when making the choice between open or closed tympanoplasty; the degree of mastoid pneumatization, the age of the patient, the advisability or necessity of performing a single stage surgical procedure, the presence or absence of pathology in the contralateral ear if the otological disease is bilateral, and greater risk of a non-functioning Eustachian tube, which can cause recurrence of the disease after a closed technique.[13]

In the patients in this study treated via the modified radical mastoidectomy, post-operative healing was rapid and the ear was stable during follow-ups. These results correspondes to the study of Kinney SF, who studied 200 cases and showed 85% of smooth post-operative cavities[14].

In our study, we only performed modified radical mastoidectomy without tympanoplasty. Our results matches with the functional improvement of hearing in 92% of cases reported by Smith JB et al.[15]

Residual cholesteatoma also occurred in a low percentage of cases, and recurrent cholesteatoma was not seen. Performing only one surgical procedure offers great practical advantages over closed techniques.

The disadvantages of the modified radical mastoidectomy to patients are very limited and essentially stem from the problem caused by getting water in to surgical cavity, especially during water sports. Lastly the risk of sensorineural hearing loss from the acoustic trauma during drilling must always be taken into account although this risks closed tympanoplasty.[16]

CONCLUSION

Modified radical mastoidectomy should always be considered in cases of epitympanic cholesteatoma with normal or near normal hearing, even if the precise choice of surgical technique can only be made inter-operatively.

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THE ROLE OF AMNIOTOMY ON DURATION OF LABOUR & ITS EFFECTS ON NEONATAL OUTCOME

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ABSTRACT

Objectives: To describe the effects of amniotomy on post-partum maternal and neonatal morbidity including Apgar score at 5 minutes and admission to Neonatal Intensive Care Unit (NICU).

Material and Methods: This study was conducted in Gynae "A" ward Khyber Teaching Hospital, Peshawar from January, 2003 to June, 2003. A total of 60 primarygravidas women; 30 women in intervention group and 30 women in control group were studied.

Result: Duration of labour was significantly longer in the conservative management group; 9 hours (Relative Risk 0.787, P <0.01) as compared with amniotomy group; 8 hours. There was no difference in Neonatal outcome with respect to the Apgar score or admission to Neonatal Intensive Care Unit (NICU). Maternal febrile morbidity was lower in conservatively managed women. Half of the patients wanted analgesia. Abnormal Fetal Heart Rate (FHR) was seen in 3% pregnant women in amniotomy group as compared to 13% in non amniotomy group.

Conclusions: Amniotomy leads to quick labour with no adverse effect on neonatal outcome.

Key Words: Labour, partogram, amniotomy.

INTRODUCTION

It would seem that a relatively simple question "does amniotomy have an important effect on the course of labour at term? – should be relatively easy to answer, but this has not proved to be the case, Artifical rupture of the amniotic membranes (amniotomy) either after spontaneous labour has been diagnosed, or as a part of process of induction of labour[1], with the intention of accelerating the progress of labour is among the most commonly performed procedures in obstetrics[2].

Early amniotomy has recently been advocated to prevent dystocia in women in spontaneous labour[3].

Active management of labour has been proposed as an alternative to the high rate of Lower Segment Cesarean Section[4] (LSCS). Over the past several years a number of randomized clinical trials have assessed the effectiveness of these measures, either alone or in combination. Trials which assessed the effects of early amniotomy as an isolated intervention has been previously reported[5]. This protocol also minimizes the rate of LSCS for dystocia among nulliparous women[6] and dysfunctional labour[7].

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Although a shorter labour may be an important outcome for women and clinicians on busy delivery suites, the main aim of intervention in dysfunctional labour should be to reduce the LSCS rate with out adverse effects on the mother or infant. It is also important that women feel 'in control' because this is a major contributor to their satisfaction, during childbirth[8,9].

All previously published studies were conducted in the United States and New Zealand, whereas a few studies were conducted here in Pakistan regarding the issue of timing of obstetrical intervention during spontaneous labour.

MATERIAL AND METHODS

This study was conducted in Gynaecology and Obstetrics Department Khyber Teaching Hospital, Peshawar, from January, 2003 to June, 2003. Primigravidae presenting with spontaneous labour, singleton fetus, Cephalic presentation at 37 weeks Gestation, were consented after explaining the procedure. Women with diabetes, requiring high dependency intrapartum care, Unsatisfactory Cardiotocography on admission were excluded. Women in the amniotomy group under went the procedure as soon as possible while those in the control group had membranes conserved. Amniotomy during labour was permissible in the control group if there was a Foetal Heart Rate (FHR) abnormality, arrest of cervical dilatation for > 2 hours, or when full

dilatation was achieved. It was requested not to augment labour with oxytocin unless there had been an arrest of cervical dilatation for > 2 hours.

While performing amniotomy, the woman was advised to empty her bladder spontaneously and then put in lithotomy position. Parts cleaned and drapped. During cervical examination, Bishop score was assessed, the inferior pole of the membranes was ruptured by the Kocker forceps. The amount and colour of liquor drained was noticed. FHR was checked.

All labours were recorded on partogram, with an alert line representing cervical dilatation of 1cm/hour and an action line drawn four hours to the right of alert line. If cervical dilatation was proceeding at satisfactory rate, the women's labour would be managed according to initial allocation. If progress was still slow after four hours or there was evidence of fetal distress, management of labour was changed according to the standard protocol. Access to analgesia was freely available in the form of 50-100mg Tramadol intra muscular.

RESULTS

Sixty women with advance pregnancy were included in the study with 30 in amniotomy group and 30 in control group. Charcteristics of participants are given in Table-1, charcteristics of liquor drained in Table-2, charcteristics of labour in Table-3 and modes of delivery in Table-4. Mortality was zero in both groups.

In our study, oxytocin was given in the second stage to 3 (10%) patients in the amniotoy group and to 2(6.6%) patients in the control group (Relative risk 1.03). LSCS for which fetal distress was an indication were comparable in both the groups.

Neonatal complications are given in Fig.-1 and partogram in Fig.-2 Amniotomny did not show any adverse effect on the Fetal heart rate.

The proportions of women with dystocia in the amniotomy and conservative management groups were 6.66% (2/30) & 13% (4/30) respectively.

DISCUSSION

It has been suggested that rates of cesarean section could be reduced by more active management of labour according to protocols designed to prevent and treat functional disorders of labour[10]. Impressively low rates of cesarean section have been reported in series in which active management has been used.[11]. This study was designed to assess only one element of active management, early amniotomy while attempting to minimize differences between the groups in other variables that could influence the progress of labour.

There was one hour reduction in the length of labour, but this was not associated with reduced maternal infection. The reduced duration of labour found in other trials[12] ranging from 60 minutes in the

Table 1: Characteristics of study participants according to group

Bishop score	Amniotomy group (n=30)	Control group (n=30)
< 8	14(46%)	16(53%)
> 8	16(53%)	14(46%)

Table 2: Among women in the study group, the Characteristics of Liquor Drained

Characteristics	Amniotomy group (n=30)	Control group (n=30)
Clear liquor	22(73.3%)	24(78.3%)
Meconium Stained Liquor	8(26.7%)	6(21.7%)

Table No 3: Incidence of Dystocia and other Characteristics of Labour in Amniotomy and control group. Means are compared by T-test & proportions by Chi-square Test

Variable	Amniotomy Group N=30	Control Group N=30	Relative risk	t-value	χ2-Value	P-Value	Result
Dystocia	2 (6.66%)	4 (13%)	0.5	—	0.185	>0.05	N.S
Total Duration of Labour (hrs)	8	9.4	0.787	4.71	—	<0.01	HS
First stage (hrs)	7 [0.936]	9 [0.66]	0.72	9.6	—	<0.01	H.S
Second stage (min)	31.7 [3.36]	40 [1.88]	0.73	11.81	—	<0.01	H.S
Labour > 12 hours	2 (7%)	4 (16%)	0.46	—	0.2858	>0.05	N.S

N.S = Not Significant, H.S = Highly Significant, hrs = hours, min = minutes

Table No 4: Mode of Delivery values are given as N %. Proportions are compared by χ^2- test.

Variables	Amniotomy Group		Control Group		Relative Risk	χ^2 Value	P-Value	Result
Mode of Delivery	No. of patients		No. of patients					
Vaginal Delivery	27	(90%)	25	(83.3%)	1.08	0.144	>0.05	N.S
Spontaneous	20	(66.6%)	22	(73.3%)	0.91	0.848	>0.05	N.S
Forceps	6	(20%)	3	(10%)	2	0.368	>0.05	N.S
Vacuum	1	(3.3%)	0	(0%)	0.033	0.0015	>0.05	N.S
Caesarean Section	3	(10%)	5	(16.6%)	0.6	0.0144	>0.05	N.S
First Stage	2	(6.66%)	3	(10%)	0.6			
2nd Stage	1	(3.33%)	2	(6.66%)	0.5			

N.S = Not Significant H.S = Highly Significant

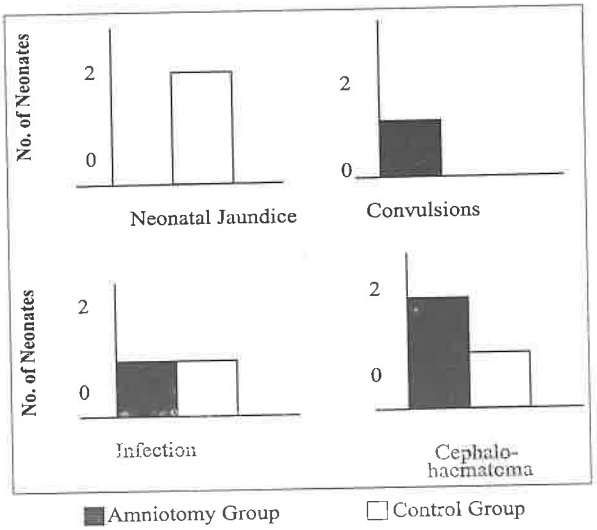

Fig.1: Neonatal Complications

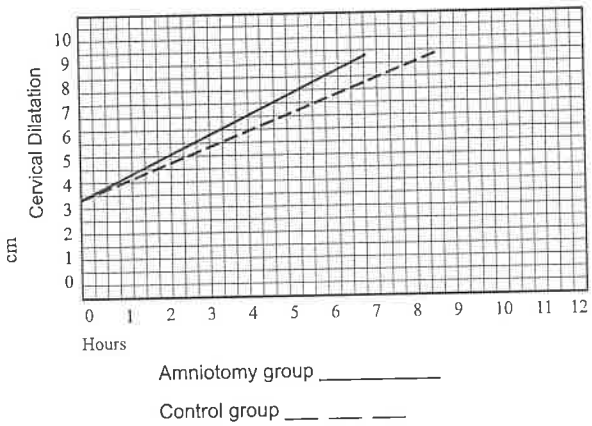

Fig.- 2: Partogram For 60 Nulliparous Women in Spontaneous Labour At Term

current study to 102 minutes in the study by Rogers et al[3], may be important to some women who as a result may wish to make an informed choice to have their labour actively managed.

The shorter duration of labour in this study was the result of early amniotomy. So by performing early amniotomy the incidence of prolonged labour can be reduced[13].

The results of this analysis indicate that a policy of early amniotomy reduces disorders of progress in the active phase of labor. On international data increasing evidence exists that many women prefer early intervention in dystocic labours[14].

Seven percent of women in amniotomy group and 16% of women in control group (RR=0.5) had prolonged labour. This pattern corresponds with the three North American trials of active management, in which the prolonged labour rates were reduced from 26% to 9%, from 19% to 5% & from 42% to 25%.

Twenty percent of women in control group underwent amniotomy for delay in progression of labour. Despite the reduction in the frequency of dystocia for women assigned to routine early

amniotomy, the frequency of LSCS was also reduced, though statistically not significant. The results were comparable to the study conducted at Holy family Hospital Rawalpindi[14].

Of the three large randomized trials[15,2,3] only one reported a significant reduction in LSCS rate with active management of labour.

The rate of LSCS in the 2nd stage of labour in this study [5% (3/60)] is similar to that found in three North American studies.[15] compared with 0.2% of nulliparous women at the National Maternity Hospital in Dublin, Ireland[16].

CONCLUSION

Amniotomy when performed at favourable Bishop score is associated with a reduction in the duration of labour with no adverse effect on neonatal outcome.

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PATTERN OF COMMON EYE DISEASES IN CHILDREN ATTENDING OUTPATIENT EYE DEPARTMENT, KHYBER TEACHING HOSPITAL, PESHAWAR

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ABSTRACT

Objective: The objectives of the study were to find out the pattern of eye diseases their early diagnosis, and early treatment to avoid high morbidity and mortality associated with such diseases.

Material and Methods: It was a descriptive cross sectional study carried out in the Eye department of Khyber Teaching Hospital Peshawar from 1st January 2005 to 31st December 2007. In this 3 years study, 6060 children in the age group of upto 16 years were examined and treated. A questionnaire was designed for recording personal history, clinical examination and treatment given.

Results: A total of 31894 patients attended the Eye out patient department during these 3 years period. Children between the age upto 16 years were 6060 (19%). Mean age of children was 7.2 years. 3692 (60.93%) were male and 2368 (39.07%) were female. Conjunctivitis was the most common disorder affecting 2160 (35.6%) children. It was followed by refractive errors involving 774 (12.77%) children. Disorders of Lens accounted for 709 (11.69%) and ocular motility was affected in 489 (8.06%) children. 3638 (60.03%) children needed medical treatment, 1676 (27.66%) required surgery and 746 (12.30%) required glasses and orthoptic correction.

Conclusion: Conjunctivitis was the most common disorder followed by refractive errors. Males were more affected than females. Cataracts were the most common disorder requiring surgical treatment followed by squints. Most children needed medical treatment.

Key Words: Children, Eye diseases, Conjunctivitis, Refractive errors.

INTRODUCTION

Pediatric ophthalmic disorders are important because of the impact on child's development, education, future work, opportunities and quality of life. Pediatric ophthalmic disorders may be due to causes that operate in prenatal period, neonatal period and childhood. The site of lesion can be in the orbit, eyelids, whole globe, conjunctiva, cornea, sclera, lens, vitreous, retina, uvea optic nerve and refractive system. Strategies to manage pediatric ophthalmic disorders include intervention at all three levels primary, secondary and tertiary prevention. Possible measures include optical, orthoptic, medical and surgical interventions.

There are about 1.5 million blind children in the world and more than one million children in Asia alone[1,2]. Approximately half of all blindness in children especially in poor countries is avoidable[3]. Cataract is the leading cause of preventable blindness[4,5]. Globally 190,000 children are blind from cataract alone[4]. These facts and figures are alarming and as healthcare providers, parents and teachers, we need to come together to identify the childhood eye diseases early enough in-order to give the child a more happy and productive life. We wanted to identify pattern of eye diseases in children, determine age and sex distribution and find out treatment given for these disorders.

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MATERIAL AND METHODS

This hospital based descriptive cross sectional study was done in outpatient department of Ophthalmology Khyber Teaching hospital from 1st January 2005 to 31st December 2007.

All the children between the age of upto 16 years were included in the study. Children above 16 years and those admitted in Eye department were excluded from the study.

A questionnaire was designed to include the disorders of conjunctiva, whole globe, cornea and sclera, lens, uvea, retina, optic nerve, ocular muscles,

nasolacrimal duct system, lids, orbit and refractive system. Detailed ocular examination was done for diagnostic, teaching and training purpose. Refraction was performed routinely under cycloplegia. Anterior segment examination was done with slit lamp, binomac and torch. Posterior segment examination was performed after dilating pupil using direct and indirect ophthalmoscope and fundus examination. Intraocular pressure was checked with Perkins Tonometer. Squint assessment was done, using prisms and tests for steropsis. Treatment was divided into medical, surgical and optical/orthoptic treatment.

RESULTS

Total of 6060 children were examined in out patient Eye department Khyber Teaching Hospital Peshawar with 3692 (60.92%) male and 2368 (39.08%) female. Age distribution is given in Table 1.

Conjunctiva was involved in 2580 (42.57%) patients. In conjunctival disorders; Bacterial conjunctivitis was present in 2152 (83.41%), Vernal catarrah in 158 (6.12%), follicular conjunctivitis in 88 (3.41%), sub conjunctival haemorrhage in 66 (2.56%), Vitamin A deficiency in 54 (2.09%) and pterygium in 62 (2.41%) patients. Cornea and Sclera was involved in 296 (4.88%) patients. In corneoscleral disorders corneal foreign body was present in 86 (29.05%), corneal ulcer in 148 (50%), corneoscleral repairs in 62 (20.95%) patients. Disorders of whole globe were present in 82 (1.35%) patients, with whole globe phthisis in 23 (28.05%) and glaucoma in 59 (71.95%). Disorders of Lens were seen in 709 (11.69%) patients. They were pre and postoperative cataracts. Uveitis was seen in 30 (0.50%) patients. Disorders of vitreous and retina were seen in 120 (1.98%) patients, including retinoblastoma (Fig.-1) in 61 (50.85%), maculopathy in 28 (23.33%), retinal detachment in 17 (14.16%) and hereditary vitreoretinal degeneration in 14 (11.66%) patients.

Ocular motility was affected in 489 (8.06%) children. Among these, 311 (63.6%) were convergent squints, (Fig.-2 and 3) 149 (30.48%) were divergent squints, 17(3.48%) were oblique while 12 patients had (2.45%) dissociated vertical deviation.

Lids and orbit was involved in 525 (8.66%) patients. In disorders of lids and orbit blepharitis was present in 214 (40.76%), chalazion in 66 (12.57%), stye in 34 (6.47%), ptosis in 46 (8.76%), lid repairs in 23 (4.38%), congenital malformations of lids and orbit in 14 (2.66%) and proptosis in 29 (5.52%) patients. Nasolacrimal duct was involved in 330 (5.4%) patients. Refractive errors were present in 774 (12.77%) patients, with 358 (46.25%) having astigmatism, 243 (31.39%) having Hypermetropia and 173 (22.36%) having myopia.

Table 1: Age wise distribution of Paediatric ophthalmic disorders

Age group (in years)	Numbers	Percentage
0-6	2386	39.38%
7-12	2796	46.13%
13-16	878	14.49%

Fig.-1: 2½ years old child with enucleation for left retinoblastoma.

Fig.-2: Left convergent squint (60 prism diopters) of partially accommodative type in 10 years old child (Pre-operative).

Fig.-3: Child in Fig.-1, one day after surgery.

Medication was given to 3638 (60.03%) of patients. Medication and surgery was performed in 1676 (27.66%) of the patients. Optical and orthoptic correction was performed in 746 (12.30%) of the children.

DISCUSSION

The occurrence of pediatric ophthalmic disorders in our sample of 6060 patients was 19.2% with 60.9% male and 39.1% female. These findings also resemble a study done at Mayo Hospital Lahore with 63.6% male and 36.4% female. In this study males i.e. 490 (81%) were predominantly affected than females i.e. 116 (19%)[6].

In our study, bacterial conjunctivitis was the most common disorder; 35.6%. In a prospective study of 275 cases in the Eye OPD of CMH Bahawalpur, Pseudomonas aeruginosa was the most frequent causative organism, present in 35.6% of acute bacterial conjunctivitis, followed by Staphylococcus aureus in 15.6%[7] Pediatric conjunctivitis often has a benign etiology and a self-limited course. It is common in childhood and may be infectious or noninfectious in nature and acute or chronic in presentation. Infectious causes include bacterial and viral conjunctivitis. Noninfectious causes include congenital nasolacrimal obstruction, ocular allergies, congenital glaucoma, and uveitis[8] Managing the infected or traumatized eye in the outpatient or emergency setting presents a diagnostic and therapeutic challenge to the physician; the causes and prognoses range from benign, self-limited illness to blindness. A careful history with knowledge of the complete ophthalmologic examination is important. Much of the morbidity is avoided with prompt therapy.

Corneal diseases accounted for 4.9% of paediatric ophthalmic disorders. This is much less in comparison to other reports. In blind schools in Pakistan and India the corneal diseases accounted for 12% and 26.4% respectively of all children with severe visual impairment / blindness.[10,11] In our study trauma accounted for half of the corneal disorders. Large families and lack of proper care put children at risk of sustaining trauma. In a study conducted at Hayatabad Medical Complex Peshawar showed that childhood ocular trauma accounted for 49% of the total ocular trauma admissions[12].

In our study lens disorder accounted for 8.9% of the paediatric ophthalmic disorders. Cataract is a leading cause of treatable blindness.[13,14] Bilateral congenital cataract is the most common cause of treatable childhood blindness. Nuclear cataract is usually present at birth and is non progressive where as lamellar cataract usually develops later and is progressive[15] The major causes of bilateral cataract in South Asia are rubella (25%), heredity (25%), and idiopathic (50%)[16]. In our study refractive errors were seen in 12.7% of patients. Refractive errors which account mostly for low vision and visual handicap are the third largest cause of curable blindness in Pakistan.[17] In one study it was found out that refractive errors account for 8% cases of uniocular blindness in North West Frontier Province[18]. In a study conducted at Jinnah Postgraduate Medical Centre Karachi refractive error accounted for 2% of ocular morbidity[19].Errors of refraction are cause of one quarter of blindness and half of low vision. Astigamtism was most common and accounted for 46.25% of refractive errors in our study. This is different from other studies where hypermetropia was more common during childhood.[20] In our study squints were seen in 8.06% of pediatric ophthalmic disorders. A study from Kathmandu reported that the prevalence of squint was 1.6%[21] Determinants of strabismus diagnosis are important because of the amblyogenic nature of certain concurrent amblyopia[22] Esotropia is more likely to be amblyogenic than exotropia.[23,24] Congenital glaucoma in our study accounted for 0.99% cases. The incidence of congenital glaucoma varies among different geographic locations and ethnic groups, with the highest recorded incidence found in the Gypsy population of Slovakia (1:1250), followed by the general populations of the Middle East (1:2500) and the western nations (1:10,000). The inheritance pattern for congenital glaucoma is most commonly autosomal recessive with incomplete penetrance[25]. In our study, there were 61 cases of retinoblastoma. Free treatment is provided to children with retinoblastoma in this hospital that's why there was a big referral from district hospitals to this hospital. Some were new while the remaining were follow up cases. In a study done at Karachi Cancer Registry Department of Pathology, Aga Khan University, 101 cases of retinoblastoma were reported between 1998-2002[26] In order to detect retinoblastoma as early as possible, health education for parents and health providers and improved training for ophthalmologists is essential. Genetic testing of siblings and children for retinoblastoma and identification of high-risk children would be helpful, but lacks financial feasibility in developing countries.

The pattern of underlying causes of childhood blindness varies considerably between developed and developing countries. The aetiological pattern seen today in industrialized countries have so evolved that factors operating in prenatal period are now the most important. By contrast, in the developing countries, factors operating postnatal continue to predominate. In industrialized counties the main cause of childhood eye diseases are cataract, glaucoma, retinopathy of prematurity, genetic diseases and congenital anomalies. In developing countries, the children usually get conditions, which cause scarring of the cornea such as vitamin A deficiency, measles, infections such as trachoma and bacterial conjunctivitis, conjunctivitis of newborn, cataract, trauma, refractive errors and harmful traditional eye practices.

CONCLUSIONS

The most common eye problem was conjunctivitis. Refractive errors presented the second most common cause of paediatric ophthalmic disorder. Males were more affected than females. The most common age group affected was 7-10 years. Most of the children required medical treatment. Cataracts were the most common disorder after squints requiring surgical intervention. Future health care planning should focus on capacity building for neonatal ophthalmologic screening, opportunities for education, occupational training and cosmetic rehabilitation for surviving retinoblastoma patients.

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No. 1	1-52	January - June 2008
No. 2	53-105	July - December 2008

AUTHORS INDEX

SUBJECT INDEX

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