ORIGINAL ARTICLE J. Med. Sci. (Peshawar, Print) October 2012, Vol. 20, No. 4: 159-164

HOSPITAL OUTCOMES OF ST- ELEVATION MYOCARDIAL INFARCTION IN PATIENTS WITH AND WITHOUT HYPERTENSION

Ibrahim Shah, Mohammad Faheem, Attaullah Khan, Hikmatullah Jan, Mohammad Hafizullah

Department of Cardiology, Postgraduate Medical Institute, Lady Reading Hospital Peshawar - Pakistan

ABSTRACT

Objective: To compare hospital outcomes of ST-elevation myocardial infarction (STEMI) in patients with and without hypertension.

Material and Methods: This observational cohort study was conducted in the department of Cardiology, Postgraduate Medical Institute, Government Lady Reading Hospital, Peshawar. A total of 569 patients with STEMI in which 348 patients were hypertensives while 221 were normotensives, were studied from December 2009 to December 2010. After enrolment in the study, patients were monitored for in- hospital complications of AMI.

Results: There were differences between both study groups in the prevalence of cardiovascular risk factors and baseline parameters on admission. Number of patients with Diuretics, hyper lipidimia, tachycardia and history of smoking were more in hypertensive group as compared to normotensive group. Complication rates were significantly higher in the hypertensive group as compared to normotensive group. Complication rates between hypertensive and normotensive groups were; atrial fibrillation (AF) 12.9% Vs 5.4%; P=0.002 while ventricular tachycardia/fibrillation (VT/VF) 11.8% Vs 11.3%; P=0.420, advanced AV block 14.4% Vs 5.4; P=0.001, acute heart failure (AHF) 18.4% Vs 10.0%; P=0.004, cardiogenic shock(CS) 13.8% Vs 6.3%; P=0.003, recurrent MI (Re-MI) 12.6% Vs 9.5%; P=0.155, acute renal failure 6.3% Vs 2.3%;P=0.019, hospital stay(days) 6.13 Vs 6.21; P=0.466 and in-hospital death 13.5% Vs 7.2%; P=0.013 respectively.

Conclusion: Hypertensive patients with an ST- elevation Myocardial infarction (STEMI) present with a greater prevalence of cardiovascular risk factors and have a higher rate of adverse hospital outcomes than patients without hypertension.

Key Words: Hospital Outcomes, Hypertension, ST-elevation myocardial infarction (STEMI).

INTRODUCTION

Myocardial infarction (MI) is the leading cause of death worldwide. Its annual incidence in the United States is estimated to be 600 000 new and 320 000 recurrent attacks. In 2004, it resulted in 695 000 hospital stays and $31 billion in hospital charges[1]. Similarly the South Asian countries of India, Pakistan, Bangladesh, Sri Lanka and Nepal contribute the highest proportion of the burden of cardiovascular diseases including MI compared with any other region globally[2,3,4]. In Pakistan it is estimated that one in five middle-aged adults may have underlying coronary artery disease (CAD)[5].

Myocardial infarction is complicated by a number of electrical and mechanical complications during its course. These complications are especially common in patients with hypertension[6]. It is an independent risk factor for the development of complications after AMI. The risk of cardiovascular disease doubles with each increase of 20/10 mm/Hg beginning at 115/75 mm/Hg[7].

Hypertension is also a major public health problem worldwide. It affected 15-37% of global adult population at present. The number of adults with hypertension is predicted to increase by 60% to a total of 1.56 billion people by 2025. It is estimated to account for 6% of deaths worldwide[8,9,10]. It affected 65 million adult in the United States. Its prevalence in the US population increased by 30% between the third National Health and Nutrition Examination Survey (NHANES III, 1988-1994) and NHANES 1999-2000[11,12,13]. In Pakistan its prevalence is estimated to be 23% and 18% in urban and rural areas respectively[8].

Few international studies conducted in Europe and United States have demonstrated that hypertension (HT) is associated with worse outcome

Address for Correspondence:
Dr. Ibrahim Shah
Resident, Department of Cardiology
Postgraduate Medical Institute,
Lady Reading Hospital, Peshawar - Pakistan
Cell No: 0333-9113365
E-mail: cardiol2011@yahoo.com

after AMI[14,15]. In the GISSI-2 study, in-hospital and 6-month mortality in hypertensive MI patients was significantly higher compared to normotensive, as was the rate of left ventricular failure, recurrent angina and recurrent MI[16]. However there are very few studies which look at the outcome of ST-elevation myocardial infarction (STEMI) in patients with hypertension in our population.The aim of this paper is to study the impact of hypertension (HT) on hospital outcome after ST-elevation myocardial infarction (STEMI) in our local set up.

MATERIAL AND METHODS

This observational cohort study was conducted in the department of Cardiology, Postgraduate Medical Institute, Government, Lady Reading Hospital Peshawar from December 2009 to December 2010 for a total period of one year. The sample size was calculated with the help of Casagrande, Pike & Smith calculator using 4% proportion of acute heart failure in normotensive and 12% proportion in hypertensives with 80% power and 5% significance level[17]. It estimated a sample size of 116 for normotensive group and a total sample of 464. However a larger sample of 569 patients was taken, in which 348 patients were in hypertensive group while 221 were in normotensive group. Purposive non probability sampling technique was used. Study population consisted of patients having hypertension and ST elevation MI. It included both genders of patients with age ranged from thirty to seventy-five years. Patients having preexisting congestive heart failure, valvular heart diseases, congenital heart diseases, cardiomyopathies of any cause and pulmonary artery hypertension either primary or secondary, ventricular tachycardia, atrial fibrillation, advance AV blocks, old left bundle branch block, permanent pacemakers (PPM) and implantable cardiac defibrillators (ICD) were excluded as these conditions make the diagnosis of in hospital complications of AMI complex. Patients with chronic renal failure (CRF), previous MI and coronary artery bypass graft surgery (CABG) were also excluded as in these patients the complications rate of MI is very high and can cause bias in the study results.

The hospital ethical committee approved the study protocol and informed consent was obtained from all participants. Patients fulfilling the above mentioned inclusion criteria were recruited from Coronary Care Unit. Patient's history and clinical examination were undertaken. Investigations including hemoglobin, serum creatinine, CK-MB level, lipid panel and random blood sugar (RBS) were obtained from hospital laboratory. Treatment variables (throbolysis or primary PCI) were recorded. Patients were hospitalized for five days until further needed. They were monitored for complications. Cardiac monitors (NIHON KOHDEN BSM-2301 K) and ECG (BTL 085-ECG) were used for the monitoring of electrical complications and recurrent MI. Mechanical complications were detected with the help of clinical examination and echocardiography using acuson CV 70 SIEMENS. If patients developed new chest pain during the course of admission, ECG and CK-MB were done to diagnose recurrent myocardial infarction. Acute renal failure was diagnosed when patient has a creatinine level of more than 2mg/dl on more than two occasions and progressively rising along with oliguria. All this data was recorded on a proforma.

Confounding variables mentioned in the exclusion criteria were controlled. Bias in the study was controlled by following strict inclusion criteria for patient's selection, measurable operational definitions for the diagnosis of complications and using the same ECG and echocardiography equipments for all patients.

OPERATIONAL DEFINITIONS

ST-elevation Myocardial infarction (STEMI) was diagnosed when patients has chest pain suggestive of myocardial ischemia lasting for at least 30 min and ST elevation of > 2 mm in > 2 contiguous precordial leads, or 1 mm in > 2 contiguous limb leads or when new left bundle branch block was found on the qualifying ECG.

Hypertension was defined as chronic use of antihypertensive drugs or a previously documented blood pressure > 130/80 mmHg from medical record.

Hospital outcomes were measured in terms of electrical or mechanical complications, recurrent myocardial infarction, acute renal failure, hospital stay and in hospital death.

STATISTICAL ANALYSIS

It was performed using statistical package for social sciences (SPSS) version 16. Numerical variables were presented as mean±SD. Categorical variables were presented as frequencies and percentages. Comparison between two groups was performed by using student-t test for numerical variables and Chi-Square test for categorical variables. P Value < 0.05 was considered significant. Results were presented as tables.

RESULTS

Patient characteristics and parameters on admission: Among 569 patients with ST-elevation myocardial infarction (STEMI), 348 patients were hypertensive and 221 were normotensive. Patient characteristics and parameters on admission to the coronary care units are shown in Table 1.

In-hospital complications: Complication rates were significantly higher in hypertensive group as compared to normotensive group as shown in Table

2. Complication rates between hypertensive and normotensive groups were; atrial fibrillation (AF) 12.9% Vs 5.4%; P=0.002 ventricular tachycardia/fibrillation (VT/VF) 11.8% Vs 11.3%; P=0.420, advanced AV block 14.4% Vs 5.4; P=0.001, acute heart failure (AHF) 18.4% Vs 10.0%; P=0.004, cardiogenic shock(CS) 13.8% Vs 6.3% ;P=0.003, recurrent MI (Re-MI) 12.6% Vs 9.5%; P=0.155, acute renal failure 6.3% Vs 2.3%; P=0.019, hospital stay 6.13 Vs 6.21 days; P=0.466 and in-hospital death 13.5% Vs 7.2%; P=0.013 respectively, is shown in Table 2.

DISCUSSION

The results of this observational study suggest that hypertensive patients with an ST- elevation Myocardial infarction (STEMI) present with a greater prevalence of cardiovascular risk factors and have a higher rate of adverse hospital outcomes than patients without hypertension.

Data on the effects of hypertension on in-hospital mortality are inconsistent. Rabin et al showed adverse short- and long-term outcome in hypertensive patients[18]. In the GISSI-2 study, in-hospital and 6-month mortality in hypertensive MI patients was significantly higher compared to normotensive, as was the rate of left ventricular failure, recurrent angina and recurrent MI[18]. In contrast to the above studies, elevated BP was not an independent prognostic factor for 30-day mortality among MI patients in the GUSTO-1 study[19]. However, patients with very high BP were excluded from the GUSTO-1 study due to the use of thrombolytic treatment, but despite this, systolic BP exceeded 180 mmHg in 602 patients. Ayward et al. evaluated all patients participating in the GUSTO-1 study and showed that the risk of an early death was higher in patients with elevated systolic BP[20].

In a study by Majahalme et al. in-hospital and 6-month mortality in hypertensive and normotensive MI patients was similar, while the rate of recurrent angina, paroxysmal atrial fibrillation and acute renal failure was higher among hypertensives[21]. Jonas et al. analyzed three groups of patients admitted due to MI (with normal, high normal or elevated BP) and found no significant differences in in-hospital mortality (5% among normotensives, 4% in patients with high normal BP and 1.9% among hypertensives)[22]. In our study, mortality was higher in hypertensive STEMI patients compared to normotensives (7.7 vs. 5.3%).

Data on the rate of hemodynamic and bioelectric complications of an AMI in hypertensive patients are also inconsistent. In a study by Abrignani et al. cardiogenic shock, ventricular fibrillation, atrioventricular conduction disturbances, intracardiac thrombus and cardiac rupture were significantly less common in hypertensive MI patients compared to normotensives, while atrial fibrillation was more common in hypertensives[23]. In contrast Magdalena Rembek et al. demonstrated that these in-hospital complications are higher in hypertensive patients as compared to nonhypertensive patients[17]. In our study, cardiogenic shock, acute heart failure, atrial fibrillation and advanced atrioventricular block were more common in hypertensive STEMI patients compared to normotensives. The risk of ventricular fibrillation in patients with hypertension was low in a study by Bertomeu et al[24]. In our study there was no significant difference between the two groups regarding this complication.

Renal function is an important prognostic factor in hypertensive MI patients. Al-Suwaidi et al. showed that reduced creatinine clearance was a significant adverse prognostic factor for mortality, including cardiovascular deaths[25]. Anavecar et al. also showed that even moderate renal dysfunction as assessed by glomerular filtration rate was associated with a higher rate of MI complications, in particular heart failure[26]. In our study, renal failure was also significantly higher in hypertensive STEMI patients compared to normotensives. Coronary flow reserve is reduced in hypertensive patients with left ventricular hypertrophy[27].

Prompt effective myocardial reperfusion results in reduced necrosis and lower rate of MI complications[28]. Regarding reperfusion, thrombolytic therapy was used more frequently in our patient population in both groups while primary PCI was used less frequently due to economic and logistic reasons.

Contrary to the above studies, our study also showed relatively higher in-hospital complications rate in both groups as compared to study done by Magdalena Rembek et al[23]. For example the frequency of cardiogenic shock was 10.6% and 6.8% in hypertensive and normotensive patients respectively in that study. In our study it is 14% and 10.4% in hypertensive and normotensive patients respectively. This higher complications rate in our study can be explained for a few reasons. Firstly poor control of the underlying risk factors like diabetes, hypertension, dyslipidemia and smoking in our patients, secondly late presentation to hospital for treatment due to unawareness about MI and poor logistic support, thirdly infrequent use of primary PCI in STEMI patients as primary PCI is superior to pharmacological reperfusion and fourthly the tendency of Asian people for higher mortality due to MI[29,30].

The clinical course of ACS is affected by risk factors for atherosclerosis including age, which is a significant negative prognostic factor[31]. Abrignani et al. found higher prevalence of diabetes, dyslipidemia, renal failure and chronic obstructive lung disease in patients with hypertension compared to normotensives[22]. In a study by Rosengre et al. the strongest risk factors in patients with ACS were

Table 1: Baseline characteristics of STEMI patients with and without hypertension

Baseline Characteristics	Hypertensive Group n+348	Normotensive Group n+221	P-value
Male (%)	207(61.1%)	135(59.5%)	0.12
Female (%)	141 (40.5%)	86 (38.9%)	0.12
Mean age (years)±SD	57.26±10.9	56.40±10.32	0.32
Diabetes Mellitus	174(50%)	51(23.1%)	0.001
Dyslipidemia	184(52.9)	89(40.3)	0.001
Positive FHx for CAD	97(27.9)	60(27.1)	0.42
Smoking	117(33.6)	47(23.1)	0.001
Anterior MI on ECG (%)	126(36.2)	82(37.1)	0.12
Heart rate(beats/min)± SD	99.06±23.2	82.94±18.5	0.001
Systolic blood pressure(mmHg)± SD	163.0±28.7	134.9±22.2	0.001
Diastolic blood Pressure(mmHg) ± SD	91.75±18.4	75.6±15.5	0.001
Mean blood glucose ± SD (mg/dl)	146.38±47.7	134.28±31.4	0.001
Hemoglobin level ± SD (g/dl)	11.86±2.15	11.76±2.15	0.61
Symptoms to thrombolytic time (hours) ± SD	3.07±2.21	2.59±1.49	0.05
Thrombolytic therapy (%)	272(78.2)	175(79.2)	0.49
Primary PCI (%)	4(1.1)	5(2.3)	0.36

Table 2: Hospital Outcomes of STEMI patients with and without hypertension

Complications of MI	Hypertensive Group = 348	Normotensive Group =221	P-value
Atrial fibrillation (%)	45(12.9)	12(5.4)	0.002
Ventricular tachycardia/ ventricular fibrillation (%)	41(11.8)	25(11.3)	0.004
Advanced AV blocks (%)	50(14.4)	12(5.4)	0.0005
Acute heart failure (%)	64(18.4)	22(10)	0.004
Cardiogenic shock (%)	48(13.8)	14(6.3)	0.003
Recurrent MI (%)	44(12.6)	21(9.5)	0.155
Acute renal failure	22(6.3)	5(2.3)	0.019
Hospital stay ± SD	6.13 ± 1.36	6.21 ± 1.08	0.466
In-hospital death (%)	47(13.5)	16(7.2)	0.013

hypertension, high BMI, diabetes (in men), and smoking[23]. In our study, the prevalence of diabetes, smoking and dyslipidaemia was also higher in hypertensive STEMI patients compared to normotensives. Family history for coronary artery disease was not significant between two groups. Abrignani et al. found no difference in the delay between the onset of pain and hospital admission between hypertensive and normotensive MI patients, while in the GREECS study, patients with hypertension presented late compared to normotensives[22,32]. A similar difference could be seen in our study, probably related to the higher rate of angina prior to MI in these patients, resulting in longer delay when patients with chest pain took their usual antianginal drugs and waited for their effect. Hypertensive patients presented with high heart rate and raised blood pressure as compared to normotensive patients. Jonas M et al. recently

studied hypertensive patients with AMI and found the same observations[6].

Blood pressure should be controlled up to recommended targets as proposed by the guidelines and not beyond that. This issue is recently addressed in ACCORD trail. Researchers randomly assigned 4,733 participants with elevated blood pressure to a target systolic blood pressure of either less than 120 mmHg (the intensive group) or to less than 140 mmHg (the standard group). After an average follow-up of about five years, researchers found no significant differences between the intensive group and the standard group in rates of a combined endpoint including nonfatal heart attack, nonfatal stroke, or cardiovascular death[33].

STRENGTHS AND LIMITATIONS

The strengths of this investigation include its prospective design, the use of standardized criteria for defining STEMI and hospital outcomes and the exclusion of patients confounding results.

Several limitations must also be kept in mind in interpreting the results of this study, however. Firstly the diagnosis of hypertension was based on the review of medical records alone and no information was available about hypertension control in the past. Secondly the present study included data on in-hospital complications only and no follow up data were taken. Hypertension is a chronic condition and long follow up period is needed to look its adverse outcomes.

CONCLUSIONS

1. Hypertensive patients with STEMI have more cardiovascular risk factors compared to normotensive patients.
2. The incidence of acute hemodynamic complications (cardiogenic shock and acute heart failure) and atrioventricular conduction disturbances is higher in patients with hypertension.
3. In-hospital mortality tended to be higher in the hypertensive patients with STEMI as compared to normotensive patients.

ACKNOWLEDGEMENTS

Amjid Khan, Statistical Officer CPSP (Peshawar Branch). Alamger Khan, Assist Professor, Department of Statistics, University of Peshawar. Waris Khan, Statistical Officer, Quid-e- Azam College of Commerce and Business Administration, University of Peshawar. Anayat Ullah, Statistical Officer, Department of Statistics, University of Peshawar.

REFERENCES

1. Russo CA, Andrews RM. The National hospital bill: The most expensive condition by Payer, 2004. Agency for Healthcare Research and Quality; 2006. HCUP statistical brief No.13. JAMA 2006; 4: 18-25.
2. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of diseases, part 1: general considerations, the epidemiologic transition, risk factors and impact of urbanization. Circulation 2001; 104: 2746-53.
3. Reddy KS. Cardiovascular diseases in non-Western countries. N Engl J Med 2004; 350: 2438-40.
4. Joshi P, Islam S, Pais P. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. JAMA 2007; 297: 286-94.
5. Jafar TH, Jafary FH, Jessani S, Chaturvedi N. Heart disease epidemic in Pakistan: women and men at equal risk. Am Heart J 2005; 150(2): 221-26.
6. Jonas M, Reiss HR, BoykoV, Behar S, Grossman E. Hospital and 1-year outcome after acute myocardial infarction in patients with diabetes mellitus and hypertension. Hypertension 2003; 17: 665-70.
7. Murray CJ, Lopez AD. Global mortality, disability and the contribution of risk factors: Global burden of disease study. Lancet 1997; 349: 1436-42.
8. Aziz K, Faruqui AM, Teri M, Davis CE, Abenathy J. Blood pressure and hypertension distribution in a lower middle class urban community in Pakistan. J Pak Med Assoc 2005; 55: 333-38.
9. Dobesh P P. Managing hypertension in patients with type 2 diabetes mellitus. Am. J. Health Syst. Pham 2006; 63(12): 1140-49.
10. Schrier RW, Estacio RO, Mehler PS, Hiatt WR. Appropriate blood pressure control in hypertensive and normotensive type 2 diabetes mellitus: a summary of the ABCD trial. Nat Clin Pract Nephrol 2007; 3: 428-38.
11. Ong KL, Cheung BM, Man YB, Lau CP, Lam KS. Prevalence, awareness, treatment and control of hypertension among United States adults 1999-2004. Hypertension 2007; 49: 69-75.
12. Wong ND, Lopez VA. L'Italien G, Chen R, Kline SE, Franklin SS. Inadequate control of hypertension in US adults with cardiovascular disease co morbidities in 2003–2004.Arch Intern Med 2007; 167(22): 2431-37.
13. Fields LE, Burt VL, Cutler JA, Hughes J, Roccella EJ, Sorlie P. The burden of adult hypertension in the United States 1999 to 2000: a rising tide. Hypertension 2004; 44: 398-04.
14. Thune JJ, Signorovitch J, Kober L,Velazquez EJ, McMurray JJV, Califf RM, et al. Effect of antecedent

hypertension and follow-up blood pressure on outcomes after high-risk myocardial infarction. Hypertension 2008; 51: 48-51.

15. Parodi G, Carrabba N, Santoro GM, Memisha G, Valenti R, Buonamici P, et al. Heart failure and left ventricular remodeling after reperfused acute myocardial infarction in patients with hypertension. Hypertension 2006; 47: 706-9.

16. Fresco C, Avanzini F, Bosi S, Franzosi MG, Maggioni AP, Santoro L, et al. Prognostic value of a history of hypertension in 11,483 patients with acute myocardial infarction treated with thrombolysis. GISSI-2 Investigators. Gruppo Italiano per lo Studio della, Sopravvivena nell'Infarto Miocardico. J Hypertens 1996; 14: 743-50.

17. Rembek M, Goch A, Goch J. The clinical course of acute ST-elevation myocardial infarction in patients with hypertension. Kardiol Pol 2010; 68: 157-63.

18. Rabkin SW, Mathewson FAL, Tate RB. Prognosis after acute myocardial infarction: Relation to blood pressure values before infarction in a prospective cardiovascular study. Am J Cardiol 1997; 40: 604-10.

19. Lee KL, Woodlief LH, Topol EJ, Weaver WD, Betriu A, Col J, et al. Predictors of 30-day mortality in the era of reperfusion for acute myocardial infarction. Results from an international trial of 41,021 patients. GUSTO-I Investigators. Circulation 1995; 91: 1659-68.

20. Aylward PE, Wilcox RG, Horgan JH, White HD, Granger CB, Califf RM, et al. Relation of increased arterial blood pressure to mortality and stroke in the context of contemporary thrombolytic therapy for acute myocardial infarction. A randomized trial. GUSTO-I Investigators. Ann Intern Med 1996; 125: 891-900.

21. Majahalme SK, Smith DE, Cooper JV, Kline-Rogers E, Mehta RH, Eagle KA, et al. Comparison of patients with acute coronary syndrome with and without systemic hypertension. Am J Cardiol 2003; 92: 258-63.

22. Jonas M, Grossman E, Boyko V, Behar S, Hod H, Reicher-Reiss H. Relation to early and one year outcome after acute myocardial infarction to systemic arterial blood pressure on admission. Am J Cardiol 1999; 84: 162-65.

23. Abrignani MG, Dominguez IJ, Bindo G. In-hospital complications of acute myocardial infarction in hypertensive subjects. Am J Hypertens 2005; 18: 165-70.

24. Bertomeu V, Cabadés A, Morillas P, Cebrián J, Colomina F, Valencia J, et al. Clinical course of acute myocardial infarction in the hypertensive patients in Eastern Spain: the PRIMVAC registry. Heart Lung 2006; 35: 20-26.

25. Al.Suwaidi J, Reddan DN, Williams K, Pieper KS, Harrington RA, Califf RM, et al. Prognostic implications of abnormalities in renal function in patients with acute coronary syndrome. Circulation 2002; 106: 974-80.

26. Anavecar NS, McMurray JJV, Veazquez EJ, Solomon SD, Kober L, Rouleau JL, et al. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. N Eng J Med 2004; 351: 1285-95.

27. Nemes A, Neu K, Forster T, Kovacs Z, Csanady M. Coronary flow velocity reserve is diminished in hypertensive left ventricular hypertrophy. Kardiol Pol 2005; 62: 1-5.

28. Hochman JS, Choo H. Limitation of myocardial infarct expansion by reperfusion independent myocardial salvage. Circulation 1997; 76: 299-306.

29. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: A quantitative review of 23 randomised trials. Lancet 2003; 361: 13-20.

30. Rashid S, Khandaker N. Risk factors for early myocardial infarction in south Asia. *JAMA* 2007; 297: 1880-81.

31. Sosnowski C, Janeczko-Sosnowska E, WoŸniak J, Jasiñski B, Dabrowski R, Sumiñski. Primary coronary intervention in diabetic octogenarians with acute ST elevation myocardial infarction. Kardiol Pol 2007; 65: 1181-86.

32. Pitsavos C, Kourlaba G, Pangiotakos DB, Stefanadis C. Factors associated with delay in seeking heath care for hospitalized patients with acute coronary syndromes: the GREECS study. Hellenic J Cardiol 2006; 47: 329-36.

33. The ACCORD Study Group. Effects of intensive blood-pressure control in type 2 diabetes mellitus. N Engl J Med 2010; 362: 1575-85.

The Journal of Medical Sciences, Peshawar is indexed with WHO IMEMR (World Health Organisation Index Medicus for Eastern Mediterranean Region) and can be accessed at the following URL.

http://www.who.int/EMRJorList/details.aspx?docn=4468