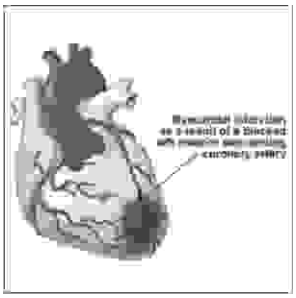
ORIGINAL PROF-930

ACUTE MYOCARDIAL INFARCTION;
EVIDENCE FOR A SEX-AGE INTERACTION



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ABSTRACT... drabdulrehman@hotmil.com Women with acute myocardial infarction have higher in-hospital mortality than men mainly due to greater age on presentation. **Objective:** To evaluate the age specific sex difference in in-hospital mortality of acute myocardial infarction. **Design:** Descriptive study. **Place and duration:** Coronary Care Unit and cardiology ward of Nishtar Hospital Multan from 15th of September 2002 till 30th of April 2003. **Material & Methods:** Four hundred and fifty patients of acute myocardial infarction who fulfilled our inclusion criteria were studied while they were admitted to the hospital. Patients were divided into four groups according to age and sex i.e. Group I (male <45 years), Group II (male ≥45 years), Group III (female <45 years) and Group IV (female ≥45 years). In-hospital mortality was compared between different age groups by Chi-square test. **Results:** The total in-hospital mortality was 76(16.9%).In Group III none of the patients expired. In Group I in-hospital mortality was 6(7.1%) patients followed by Group II 50(18.3%) patients and Group IV 20(23.3%) patients p<0.019. In-hospital mortality was greater in Group IV than in any other group. Group IV patients were more frequently diabetic and hypertensive than patients in any other group. Group IV patients presented late to the hospital. There was no significant difference in site of myocardial infarction in different groups. Higher Killip class was observed in Group II and IV p<0.05. Streptokinase injection was given less frequently in Group IV than in any other group p <0.012. Only 34(39.5%) patients in Group IV had no complication during hospital stay while more patients in other groups had uneventful hospital stay p<0.001. **Conclusion:** Female sex is associated with higher in-hospital mortality in older age group as compared to the male patients of same age group.

Key Words: Acute Myocardial Infarction, Female, Age, Mortality.

INTRODUCTION

Each year in the United states, there are 1.5 million hospitalizations for acute coronary syndromes[1]. Coronary artery disease is the leading cause of death among women 65 years of age[2-4]. In 1992 it accounted for more than 45 percent of all deaths in women which is more than the proportion due to all forms of cancer combined[2,3].

Age is an obvious factor that may account for sex differences in coronary artery disease incidence and outcome[5]. Women with acute ischemic syndromes tend to be 5-10 years older than men with such syndromes because the premenopausal state protects against coronary artery disease[5]. Because of loss of hormonal protection after menopause, the proportion of women among patients with myocardial infarction rises thus the epidemiological significance of myocardial infarction is greater as age advances[3,5].

The mortality rate among women younger than 75 years of age has been reported twice that among men in that age group[6-8]. Women hospitalized with an acute myocardial infarction have higher short-term and long term mortality rates than men a difference mostly explained by the greater age of women, prior coronary artery disease, diabetes and hypertension[1,4,5,8-16].

A significant interaction between sex and age has been documented with younger but not the older women having higher rates of death during hospitalization than men of the same age[17-21].

Studies have shown a higher reinfarction rate in females but other reports have not found a significant difference[2,4,12,13,22,23].

Studies analyzing thrombolysis and invasive coronary procedures have found a less invasive approach in women than in men which may explain of their excess mortality[24,25].

An interaction between sex and age has been described that suggests that the effect of sex on coronary artery disease prognosis may be different according to the age group analysed[3,5-7,9,11,21,24]. This study was designed to evaluate the age-specific sex difference in the in-hospital mortality of acute myocardial infarction.

MATERIAL AND METHODS

Four hundred and fifty consecutive patients of acute myocardial infarction hospitalized in coronary care unit and cardiology ward of Nishtar Hospital Multan from 15th of September 2002 till 30th of April 2003 were included in this descriptive study.

Patients presenting with acute myocardial infarction were examined and included in the study on the basis of any two of the following criteria.1) Chest pain consistent with acute myocardial infarction. 2) Electro-cardiographic changes either a) ST-Segment elevation >0.2 mv in at least two contiguous chest leads or >0.1 mv in at least two contiguous limb leads. Or b) New or presumably New Left Bundle Branch Block on electrocardiogram. 3) Raised levels of cardiac Enzymes CPK-MB more than double of the reference value or Positive Troponin T test done by commercially available kits of Trop T (Boehringer Mannheim Germany Distributed by Roche Pakistan Pvt. Ltd.).
Patients were divided into four groups.

1. Group I comprising of male patients <45 years of age.
2. Group II of male patients $\geq$45 years of age,
3. Group III female patients <45 years of age and
4. Group IV $\geq$45 years old female patients.

A detailed history was taken particularly age, sex, occupation, address, history of smoking, diabetes mellitus, hypertension, ischemic heart disease and family history of ischemic heart disease were inquired. Time from onset of symptoms till arrival at the hospital was noted. Complete physical examination was done with

emphasis on pulse, blood pressure, precordial examination and signs of congestive cardiac failure. ECG and X-ray chest was done in all patients. Site of myocardial infarction, Killip class[27] and medications given especially Streptokinase were noted for all the patients. All patients were treated according to the treatment protocol of the Cardiology Unit.[28] Patients were followed up daily and pulse, blood pressure, ECG changes and complications if any were monitored till death or discharge of the patient.

In-hospital mortality was our primary endpoint while complications occurring during hospitalization were our secondary endpoints. Complications were broadly divided into mechanical and electrical complications. Mechanical complications consisted of LVF and MR. While electrical complications were Ventricular Tachycardia, Ventricular Fibrillation, Complete Heart Block and Asystole.

STATISTICAL ANALYSIS

All the data was analyzed by SPSS (Statistical Package for Social Sciences) Version 12.0 for Windows. Patient characteristics and in-hospital mortality for different groups were compared using Chi-square test. 5% level of significance was used. All tests applied were two tailed.

RESULTS

During the study period 450 patients met our inclusion criteria. The whole study population was divided into four groups according to sex and age of the patients. Group I (male <45 years) consisted of 84(18.6%) patients, Group II (male $\geq$45 years) consisted of 273(60.6%) patients, Group III (Female <45 years) of 7(1.5%) patients and group IV comprised of 86(19.1%) patients. The mean age of the study population was 54.7±12.2 years.

Epidemiological characteristics of the study population are presented in table I. Overall 375(79.3%) patients were males and 93(20.6%) were females. Diabetes Mellitus was observed more commonly in Group IV patients as compared to other groups. Similarly hypertension was present in 47(54.7%) patients of group IV which was more than in any other group. Young male patients in Group I were more commonly smokers. Previous history of Ischemic Heart Disease was present in 79(28.9%) in Group II and 20(23.3%) patients in Group IV.

The presenting complaints observed were chest pain, pain epigastrium and shortness of breath. Among these chest pain occurred most commonly. Table II shows the clinical features on presentation of acute myocardial infarction. Group I patients reported earlier to the hospital with a minimum time from onset of symptoms till arrival at the hospital while Group IV patients took maximum time to arrive to the hospital.

Anterior wall myocardial infarction was observed more frequently followed by Inferior wall myocardial infarction in all the groups except Group III where Inferior wall myocardial infarction occurred in 5(71.4%) patients while Anterior wall myocardial infarction occurred in only 2(28.6%) patients. Higher Killip class was observed in Group II and Group IV patients. Overall 206(45.8%) patients received Streptokinase. Group I had the maximum number of Streptokinase recipients followed by Group III and Group II. Group IV had minimum Streptokinase recipients with only 30(34.9%) patients receiving this injection $p<0.012$.

Table III shows the in-hospital complications of the study population. In group I 55(65.5%) patients had no complication during their hospital stay while 34(39.5%) patients in Group IV had no complications during hospital stay. Electrical complications occurred more frequently in young patients as compared to old patients while mechanical complications occurred more commonly in old patients as compared to young $p<0.001$.

The total in-hospital mortality was 76(16.9%). Overall in-hospital mortality was 20(21.5%) in female patients and 56(15.7%) in male patients. None of the patients expired in Group III. In Group I in-hospital mortality was minimum as only 6(7.1%) patients expired followed by Group II 50(18.3%) patients and Group IV 20(23.3%) patients

p<0.019. (Table IV). Left ventricular failure was the most common cause of death followed by Complete Heart Block and Asystole p=0.303. In total 57(12.7%) patients died in first 24 hours of hospital admission p<0.035.

Table-I Epidemiological Characteristics of the Study Population

Characteristics	Total n=450	Group I (Male < 45 y) n = 84	Group II (Male ≥ 45 y) n = 273	Group III (Female < 45 y) n = 7	Group IV (Female ≥ 45 y) n = 86	P Value
Mean age in years	54.74±12.2	37.5±4.7	58.5±9.2	38.8±2.34	61.7±9.5	
Diabetes	121(26.9%)	12(14.3%)	69(25.3%)	2(28.6%)	38(44.2%)	0.001
Hypertension	148(32.9%)	25(29.8%)	75(27.5%)	1(14.3%)	47(54.7%)	0.001
Smoking	226(50.2%)	51(60.7%)	161(59%)	0	14(16.3%)	0.001
H/O IHD	112(24.9%)	12(14.3%)	79(28.9%)	1(14.3%)	20(23.3%)	0.046
Family H/O IHD	65(14.4%)	14(16.7%)	38(13.9%)	2(28.6%)	11(12.8%)	0.633

Table-II Clinical Features on Presentation of Acute Myocardial Infarction

Clinical features	Total n=460	Group I (Male < 45 y) n = 84	Group II (Male ≥ 45 y) n = 273	Group III (Female < 45 y) n = 7	Group IV (Female ≥ 45 y) n = 86	P Value
Time from onset of symptoms till arrival at hospital						
< 6hours	256(56.9%)	48(57%)	162(59.3%)	5(71.4%)	41(47.7%)	0.492
6-12 hours	122(27.1%)	21(25%)	70(25.6%)	2(28.6%)	29(33.7%)	
> 12 hours	72(16%)	15(17.9%)	41(15%)	0	16(18.6%)	
Mean time	8 Hours	7 Hrs 10 Min	7 Hrs 50 Min	7 Hrs 35 Min	9 Hrs 30 Min	
ECG on Admission						
Anterior wall MI	255(56.7%)	43(51.2%)	164(60.1%)	2(28.6%)	46(53.5%)	0.015
Inferior wall MI	165(36.7%)	30(35.7%)	98(35.9%)	5(71.4%)	32(37.2%)	
Lateral wall MI	12(2.7%)	4(4.8%)	7(2.6%)	0	1(1.2%)	
Posterior wall MI	7(1.6%)	4(4.8%)	2(0.7%)	0	1(1.2%)	
LBBB	11(2.4%)	3(3.6%)	2(0.7%)	0	6(7%)	
KILLIP Class						
I	100(22.2%)	10(11.9%)	62(22.7%)	1(14.3%)	27(31.4%)	0.05
II	27(6%)	3(3.6%)	18(6.6%)	0	6(7%)	
III	10(2.2%)	0	8(2.9%)	0	2(2.3%)	
IV	17(3.8%)	1(1.2%)	14(5.1%)	0	2(4.2%)	
Streptokinase	206(45.8%)	50(59.5%)	122(44.7%)	4(57.1%)	30(34.9%)	0.012

LBBB = Left Bundle Branch Block.

Table-III In-Hospital Complications						
	Total n=460	**Group I (Male < 45 y) n = 84**	**Group II (Male ≥ 45 y) n = 273**	**Group III (Female < 45 y) n = 7**	**Group IV (Female ≥ 45 y) n = 86**	**P Value**
No Complication	216(48%)	55(65.5%)	124(45.4%)	3(42.9%)	34(39.5%)	0.001
Electrical Complications	92(22%)	21(25%)	58(21.2%)	3(42.9%)	17(19.8%)	
Mechanical Complications	70(15.6%)	5(6%)	51(18.7%)	0	14(16.1%)	
Both Mechanical & Electrical Complications	65(14.4%)	3(3.65%)	40(14.7%)	1(14.7%)	21(24.4%)	

Table-IV In-Hospital Mortality With Cause Leading to Death.						
	Total n=460	**Group I (Male < 45 y) n = 84**	**Group II (Male ≥ 45 y) n = 273**	**Group III (Female < 45 y) n = 7**	**Group IV (Female ≥ 45 y) n = 86**	**P Value**
In-Hospital Mortality	76(16.9%)	6(7.1%)	50(18.3%)	0	20(23.3%)	0.019
Cause of Death LVF,	42(9.3%)	4(4.8%)	27(9.9%)	0	11(12.8%)	0.303
VT, VF	6(1.3%)	1(1.2%)	5(1.8%)	0	0	
CHB	16(3.6%)	0	11(4%)	0	5(5.8%)	
Asystole	12(2.7%)	1(1.2%)	7(2.6%)	0	4(4.7%)	
Time of Death After Admission						
1st 24 hours	57(12.7%)	4(4.8%)	40(14.7%)	0	13(15.1%)	0.035
24-48 hours	4(0.9%)	0	4(1.5%)	0	0	
> 48 hours	15(3.3%)	2(2.4%)	6(2.2%)	0	7(8.1%)	

LVF=Left Ventricular Failure.: VT, VF=Ventricular Tachycardia, Ventricular Fibrillation : CHB=Complete Heart Block.

DISCUSSION

Women hospitalized with acute myocardial infarction have higher short term and long term mortality rates than men a difference mostly explained by the greater age of women, prior coronary artery disease, diabetes and hypertension. Furthermore higher reinfarction rates have been observed in women. Women have been reported to be less aggressively treated than men as lesser number of female patients receive thrombolysis and invasive coronary procedures. Because of pre-menopausal protection, the proportion of women among patients with myocardial infarction rises with advancing age and older women have higher rates of death during hospitalization than men of the same age.

In the current study the total in-hospital mortality was 16.9%. Mortality was higher in females 21.5% as compared to males 15.7%. In male patients in-hospital mortality was 7.1% in Group I (male <45 years) and 18.3% in Group II (male ≥45 years), while it in female patients in-hospital mortality was none in Group III (female <45 years) and 23.3% in Group IV (female ≥45 years) p<0.019. In-hospital mortality was more in older age female patients as compared to male patients of the same age group. Our results are consistent with previous studies [1,2,4,5,7,9-13,24,25]. All these studies have shown overall increased mortality in females as compared to males suffering from acute myocardial infarction.

Marrugat et al[7] have reported increased mortality in women aged 65 to 74 years as compared to men of the same age, while women younger than 65 years had

lower mortality risk than their male counterparts. In our study we divided the patients into <45 and ≥45 years because we observed a steep rise in female patients after the age of 45 years. Our results are consistent with this study. Hochman et al[1] in a trial of 12,142 patients similarly reported that women had a higher 30 day mortality and were older than men on presentation to the hospital. A smaller percentage of women than men had ST segment elevation myocardial infarction. We only studied in-hospital mortality in contrast to 30 days mortality reported by Hochman et al and further more we included only patients suffering from ST segment elevation myocardial infarction. Chandra et al[13] while reporting data from the National Registry of Myocardial Infarction-I concluded that in comparison with men women were substantially older, i.e. 55.7% were older than 70 years. However for similar age and treatment groups, the mortality rate was higher in women. The overall in-hospital mortality rate was higher for women whether treated with thrombolytic therapy or not. Gottlieb et al[24] 2867 consecutive AMI patients and reported that women had worse fatal and non-fatal outcomes and were older than men.

Few studies have suggested a diverging effect of female sex on myocardial infarction in different age groups.[6,17-22] All found a significant interaction between age and sex but in the opposite direction to our. It is difficult to compare our results because of considerable differences in study designs. Studies differed in age range, some included patients enrolled in clinical trial (non-consecutive), or only patients admitted to coronary care units and some included a large proportion of patients with Non-Q wave myocardial infarction. Particularly to mention are the differences between our results and those from Vaccarino et al [6,18,21]. Vaccarino et al [6] in her large cohort study of more than 380,000 patients noted increased in-hospital mortality among women compared with men aged 30 to 89 years (16.7% versus 11.5%) respectively. Sex based differences in mortality varied according to age. Among patients aged <50 years, the mortality among women was more than twice that of men. The difference in the rates decreased with increasing age and was no longer significant after the age of 74 years. Vaccarino et al[6] in this study excluded 21% of candidates because of transfer to another hospital. This may have introduced a selection bias because it is probable that transferred patients were more severely diseased. In fact the mortality observed could be considered low taking into account that patients upto 89 years of age were included. The low mortality observed in Vaccarino's cohort may also be related to the high proportion of Non Q wave AMI (50%), which is known to have lower early mortality but we excluded patients having Non-Q wave AMI.

We observed that women especially in old age group were more likely to suffer from complications after AMI. Left Ventricular Failure was more commonly observed. This is consistent with other studies who have reported more occurrence of Cardiogenic shock and Congestive cardiac Failure in females[1,7,11-13,24].

Worse outcome was associated with presence of multiple risk factors like Diabetes and Hypertension in female patients of older age group. Other studies have also reported a higher incidence of diabetes and hypertension in female patients as compared to their male counterparts[1,7,24].

We observed that women were less likely to be treated with thrombolysis as compared to men of the same age group. Marrugat et al[12] reported in another study that women presented to the emergency department approximately 1 hour later than men which might explain their lower thrombolysis rate. An explanation for this study could be the fact that women were older than men and may have been less sensitive to symptoms than younger people. Grace et al[25] reported that females had a significantly longer interval between diagnostic electrocardiogram and administration of athrombolytic than males. Tjandrawidjaja et al[23] extracted data from the ASSENT-2 trial of 16,949 patients reported that women with early reinfarction following fibrinolysis for AMI had more frequent early death and were managed less aggressively than men.

CONCLUSION

Female sex is associated with higher in-hospital mortality in older age group as compared to the male patients of the same age. The increased mortality can be explained on the basis of presence of diabetes, hypertension, more occurrence of congestive heart failure and less aggressive thrombolytic therapy in female patients as compared to male patients of same age.

REFERENCES

1. Hochman JS, Tamis JE, Thomson TD, Weaver WD, White HD, Van de werf F, et al. **Sex, clinical presentation and outcome in patients with acute coronary syndromes.** N Engl J Med 1999;341:226-32.

2. Gan SC, Beaver SK, Houck PM, Maclehose RF, Lawson HW, Chan L. **Treatment of acute myocardial infarction and 30 day mortality among women and men.** N Engl J Med 2000;343:8-15.

3. Rosengren A, Wallentin L, Gitt AK, Behar S, Battler A, Hasdai D. **Sex, age and clinical presentation of acute coronary syndromes.** Eur H J 2004;25:663-670.

4. Hanratty B, Lawlor DA, Robinson MB, Spasford RJ, Greenwood D, Hall A. **Sex differences in risk factors, treatment and mortality after acute myocardial infarction: an observational study.** J Epidemiol Community Health 2000;54:921-916.

5. Borzak S, Weaver D. **Sex and outcome after myocardial infarction.** A case of sexual politics? Circulation 2000;102:2458-2459.

6. Vaccarino V, Parsons L, Every NR, Barron HV, Krumholz HM. **Sex based differences in early mortality after myocardial infarction.** N Engl J Med 1999;341:217-25.

7. Marrugat J, Gil M, Masia R, Sala J, Elosua R, Anto JM, et al. **Role of age and sex in short-term and long term mortality after a first Q wave myocardial infarction.** J Epidemiol Community Health 2001;55:487-493.

8. Tustall-Pedeo H, Morrison C, Woodward M, Fitzpatrick B, Watt G. **Sex differences in myocardial infarction and coronary deaths in the Scottish MONICA population of Glasgow 1985 to 1991.** Circulation 1996;93:1981-1992.

9. Gottleib S, Goldbourt U, Boyko V, Harpaz D, Mandelzweig L, Khoury Z, et al. **Mortality trends in men and women with acute myocardial infarction in coronary care units in Israel.** A comparison between 1981-1983 and 1992-1994. Eur Heart J 2000;21:284-295.

10. Roger VL, Jacobsen SJ, Weston SA, Goraya TY, Killian J, Reeder GS, et al. **Trends in the incidence and survival of patients with hospitalized myocardial infarction, Olmsted County, Minnesota, 1979 to 1994.** Ann Intern Med 2002;136:341-348.

11. Bueno H, Vidan MT, Almazan A, Lopez-Sendon JL, Delcan JL. **Influence of sex on short-term outcome of elderly patients with a first acute myocardial infarction.** Circulation 1995;92:1133-1140.

12. Marrugat J, Sala J, Masia R, Pavesi M, Sanz G, Valle V, et al. **Mortality differences between men and women following first myocardial infarction.** JAMA 1998;280:1405-1409.

13. Chandra NC, Ziegelstein RC, Rogers WJ, Tiefenbrunn AJ, Gore JM, French WJ, et al. **Observations of the treatment of women in the United States with myocardial infarction.** A report from the National Registry of Myocardial Infarction-I. Arch Intern Med 1998;158:981-988.

14. Graham MM, Ghali MA, Faris PD, Galbraith PD, Norris CM, Knudston ML for the APPROACH Investigators. **Sex differences in the prognostic importance of Diabetes in patients with Ischemic Heart Disease undergoing coronary angiography.** Diabetes Care 2003;26:3142-3147.

15. Raza MA, Azeem M, Barlas N, Mehfooz I, Ali Z. **Acute myocardial infarction: comparison of clinical characteristics, treatment and early outcome among women and men.** Pak J Med Sci 2000;16(4):207-215.

16. Lundblad D, Eliasson M. **Silent myocardial infarction in women with impaired glucose tolerance.** The Northern Sweden MONICA study. Cardiovascular Diabetology 2003;2:9.

17. Rosengren A, Spetz CL, Koster M, Hammar N, Alfredsson L, Rosen M. **Sex differences in survival after myocardial infarction in Sweden.** Data from the Swedish National Acute Myocardial Infarction register. Eur Heart J 2001;22:314-322.

18. Vaccarino V, Krumholz HM, Yarzebski J, Gore JM, Goldberg RJ. **Sex differences in 2-Year mortality after hospital discharge for myocardial infarction.** Ann Intern Med 2001;134:173-181.

19. Kam R, Cutter J, Chew SK, Tan A, Emmanuel S, Mak KH, et al. **Gender differences in outcome after an acute myocardial infarction in Singapore.** Singapore Med J 2002;43(5):243-248.

20. Ayanian JZ. **Increased mortality among middle aged women after myocardial infarction: Searching for mechanisms and solutions.** Ann Intern Med 2001;134:239-241.

21. Vaccarino V, Horwitz RI, Meehan TP, Petrillo MK, Radford MJ, Krumholz HM. **Sex differences in mortality after myocardial infarction Evidnce for a sex-age interaction.** Arch Intern Med 1998;158:2054-2062.

22. Conti RAS, Solmene MC, Lemos da luz P, Benjo AM, Lemos neto PA, Ramires JAF. **Comparison between young males and females wtih acute myocardial infarction.** Arq Bras Cardiol 2002;79(5):518-25.

23. Tjandrawidjaja MC, Fu Y, Goodman SG, Van de werf F, Granger CB, Armstrong PW for the ASSENT-2 Investigators. **The impact of gender on the treatment and outcomes of patients with early reinfarction after fibrinolysis:** insights from ASSENT-2. Eur Heart J 2003;24:1024-1034.

24. Gottlieb S, Harpaz D, Shotan A, Boyko V, Leor J, Cohen M, et al. **Sex differences in management and outcome after acute myocardial infarction in the 1990s.** A prospective Observational Community-Based study. Circulation 2000;102:2484-2490.

25. Grace SL, Abbey SE, Bisaillon S, Shnek ZM, Irvine J, Stewart DE. **Presentation, delay and contraindication to thrombolytic treatment in females and males with myocardial infarction.** Women's Health Issues 2003;13:214-221.

26. Killip T, Kimbal JT. **Treatment of myocardial infarction in coronary care unit: A two year experience with 250 patients.** Am J Cardiol 1967;20:457-464.

27. Ryan TJ, Antman EM, Brooks NH. 1999 update: **ACC/AHA guidelines for the management of patients with acute myocardial infarction:** Executive summary and recommendations; a report of the American College of Cardiology/American Heart Association Task Force on Practice guidelines. Circulation 1999;100:1016-30.

GENIUS IS ONE PERCENT INSPIRATION AND NINETY-NINE PERCENT