Myocardial Infarction under Age 40: Risk Factors and Coronary Arteriographic Findings

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Objective: To evaluate risk factors and arteriographic findings in young patients under 40 year of age admitted with first acute myocardial infarction (AMI).
Design: A prospective descriptive study.
Place and Duration of Study: Cardiology Department, Allama Iqbal Medical College / Jinnah Hospital, Lahore from July 2002 to June 2003.
Patients and Methods: During the study period, 274 patients with first AMI were admitted in our coronary care unit and 52 (19%) were under 40 year of age. These 52 patients underwent pre-discharge coronary arteriography.
Results: Forty-five (87%) were male and seven (13%) were female. Risk factors in all study patients were smoking in 79%, systemic hypertension in 35%, diabetes mellitus in 31%, hyperlipidemia in 19% and family history of premature coronary artery disease in 17%. Risk factors were distinctly less frequent in patients without coronary atherosclerosis. Cigarette smoking was the main risk factor in male patients while diabetes and hypertension were main risk factors in female patients. Forty-six patients (88%) had significant CAD (greater than 50% diameter narrowing of at least one major coronary artery), 5 (10%) had normal coronary arteries and one patient (2%) had marked coronary ectasia. In patients with significant coronary artery disease, the prevalence rate of one, two and three vessel disease was 52, 28 and 20 percent, respectively. No patient had congenital coronary anomaly or significant left main CAD.
Conclusion: AMI in persons under the age of 40 years accounts for approximately 19% of AMI. In this age group, AMI is a disease of men who smoke & single vessel CAD predominates. Approximately half of the young patients have single-vessel coronary disease, and in up to 10%, the cause is not related to atherosclerosis. Coronary angiography may be warranted in young patients with AMI to define the anatomy of the disease and to permit optimal management.
Key words: acute myocardial infarction, coronary angiography, risk factors, age below 40

Coronary artery disease (CAD) is a devastating disease precisely because an otherwise healthy person in the prime of life may die or become disabled without warning. When the afflicted individual is under the age of 40, the tragic consequences for family, friends, and occupation are particularly catastrophic and unexpected. Whether the proportion of AMI patients under the age of 40 years is currently changing is uncertain. Studies in United States from 1970s and 1980s suggested that approximately 2% to 6% of AMI occur in young patients[1,2]. Series published in the 1990s suggest that young patients account for approximately 4% to 10% of myocardial infarctions[3]. In Iceland, the prevalence of AMI in young women increased almost threefold from 1968 to 1992[4].

Women have been thought to comprise only approximately 5% to 10% of all AMI patients under age 45 years[3]. However a more recent study found that women comprised 20% of AMI patients under age 55 years and 55% over age 75 years[5].

There are several risk factors for AMI in young adults, most of whom have coronary atherosclerosis[1]. As the number of atherosclerosis risk factors increases, so does the severity of coronary atherosclerosis in young adults. However, AMI in the absence of atherosclerosis, although uncommon in older patients, accounts for approximately 20% of cases in patients under age 45 years[6]. Cigarette smoking appears to be the most common risk factor in young MI patients. Between 76% and 91% of young patients with MI are smokers, compared with approximately 40% of older patients.[6, 7, 8] The prevalence of hyperlipidemia in young patients with MI ranges from 12% to 89%[8, 9, 10]. A positive family history of coronary artery disease is a major risk factor for MI in young patients[10]. The prevalence of positive family history among these patients ranges from 14% to 69%[2]. We conducted this study to evaluate risk factors and arteriographic findings in our population in young patients under 40 years admitted with AMI.

Methods

This prospective study was conducted at Cardiology Department, Allama Iqbal Medical College/Jinnah Hospital, Lahore between July 2002 to June 2003. During this period, a total of 274 patients with first AMI were admitted. Out of this, 52 (19%) patients were below 40 years of age. Myocardial infarction was diagnosed according to revised WHO Criteria AMI were classified into ST elevation and non-ST elevation infarctions. Eligible patients with ST elevation AMI were thrombolysed while non-eligible patients and non-ST elevation AMI were managed conservatively according to standard ACC/AHA recommendations[11].

The information relating to age, race, sex, height, weight, body mass index (BMI), waist/hip ratio for truncal obesity, typical risk factors for atherosclerosis, presence of pre-infarction angina and location of AMI was tabulated.

The recorded risk factors were:(1) smoking (any amount on a regular basis within the past year); (2) hypertension (blood pressure greater than 140/90 mm Hg); (3) diabetes (was considered present if insulin or oral hypoglycemic agents were being taken or if fasting blood glucose level was more than 110 mg/dl); (4) hyperlipidemia (diagnosed according to Adult Panel III guidelines)[28]; (5) family history of CAD in first degree relative before age 55 in males and before 65 in females; (6) oral contraceptive use in women. In the absence of classical risk factors, work up for novel risk factors such as hyper-homocysteinemia, elevated plasminogen activator inhibitor-1 (PAI-1), Lipoprotein Lp (a) or hypercoagulable conditions, was not done due to non availability. Pre-discharge left heart catheterization, including selective coronary arteriography and left ventriculography was performed using standard Judkins technique in all 52 study patients. All patients had detailed echocardiography with color flow imaging before undergoing cardiac catheterization and angiography. Left ventriculography was not done in case of even suspicion of left ventricular mural clot. A 50 percent luminal diameter narrowing was considered evidence of significant CAD. Before coronary angiography, exercise stress test was not done for risk stratification. The blood samples for fasting lipid profile were taken within 24 hours of hospitalization with overnight fasting.

Results

During the study period from July 2002 to June 2003, a total of 274 patients with first AMI were admitted. Out of this, 52 (19%) patients were below 40 year of age. Of 52 patients studied, 45(87%) were male and 7(13%) were female. (Table I). Risk factors in all study patients were smoking in 79%, systemic hypertension in 35%, diabetes mellitus in 31%, hyperlipidemia in 19% and family history of premature coronary artery disease in 17%. Risk factors were distinctly less frequent in patients without coronary atherosclerosis. Cigarette smoking was the main risk factor in male patients while diabetes and hypertension were main risk factors in female patients. Angina pectoris was present before AMI in about 30% of patients. The location of ST segment elevation AMI was anterior in 42 percent and inferior in 29 percent. The clinical characteristics, location of AMI and risk factor profile of all study patients are given in Table I. The risk factor profile of seven young females is given in Table II. No patient had clinical evidence of systemic lupus erythematosis (SLE) or other vasculitic disorder.

The most common cause of AMI in these young patients was coronary atherosclerosis. Forty-six patients (88%) had significant CAD (greater than 50% diameter narrowing of at least one major coronary artery), 5(10%) had normal coronary arteries and one patient (2%) had marked coronary ectasia. In patients with significant coronary artery disease, the prevalence rate of one, two and three vessel disease was 52, 28 and 20 percent, respectively. No patient had congenital coronary anomaly or significant left main CAD (Table III). No patient had coronary artery dissection or coronary artery aneurysms as in Kawasaki's disease.

Table I: Clinical Characteristics and Risk Factors (n= 52)

Gender	
Men	45(87%)
Women	7(13%)
Mean Age (yr)	33
Angina before AMI	15(30%)
Location of AMI	
Q - wave	
Anterior	22(42%)
Inferior	15(29%)
Infero-posterior	5(10%)
Lateral	2(4%)
Non – Q- wave	8(15%)
Risk Factors	
Smoking	41(79%)
Hypertension	18(35%)
Hyperlipidemia	10(19%)
Diabetes	16(31%)
Family H/o Premature CAD	9(17%)

Table II: Clinical Characteristics & Risk Factors in Seven Women Below 40 Admitted with AMI (n =7)

Mean Age (yr)	38
Angina before AMI	2 (28%)
Risk Factors	
Diabetes	4 (57%)
Hypertension	3 (43%)
Family H/o Premature CAD	2 (28%)
Smoking	0
Truncal Obesity	3 (43%)
Hyperlipidemia	3 (43%)
Oral Contraceptive use	0

Table III: Coronary Angiographic Finding (n = 52)

Coronary Artery Disease	46(88%)
Single vessel disease	24(52%)
Double vessel disease	13(28%)
Triple vessel disease	9(20%)
Left main disease	0
Normal Coronaries	5(10%)
Coronary Ectasia	1(2%)
Congenital Coronary Artery Anomalies	0
Coronary Artery Dissection	0
Coronary Artery Aneurysms	0

Discussion

There are several risk factors for AMI in young adults, most of whom have coronary atherosclerosis[1,3]. As the number of atherosclerotic risk factors increases, so does severity of coronary atherosclerosis in young adults. However, AMI in the absence of atherosclerosis, although uncommon in older patients, accounts for approximately 20% of cases in patients under age 45 years[6,8]. Risk factors in our study patients were smoking in 79%, systemic hypertension in 35%, diabetes mellitus in 31%,

hyperlipidemia in 19% and family history of premature coronary artery disease in 17%.

Cigarette smoking appears to be the most common risk factor in young MI patients. Between 76% and 91% of young patients with MI are smokers, compared with approximately 40% of older patients.[7, 8, 9]. The extent of smoking appears to be inversely related to the age at which the first MI occurs. A study of 11,483 patients found that 17% of patients with MI were under 50 years of age, and smoking was significantly more frequent in these patients than in older age groups[12]. Kannel et al[13] found in patients included in the Framingham Heart Study, the relative risk for CAD was about three times higher in smokers age 35 to 44, compared to nonsmokers. Repeated exposure to cigarettes and the resulting frequent catecholamine surges damage endothelial cells, leading to dysfunction and injury of the vascular intima.

The prevalence of hyperlipidemia in young patients with MI ranges from 12% to 89%[2,9]. Homozygous familial hypercholesterolemia, affecting approximately 1 in 1 million persons in the United States, appears to have the most consistent relation with premature atherosclerosis and AMI.[10] Premature coronary disease can also occur in patients with familial combined hyperlipidemia, which affects 1 in 100 persons in the United States[10]. It may partially account for the high prevalence of positive family history of coronary artery disease in young MI patients. Hyperlipidemia may be a more reliable predictor of MI in patients 30 to 39 years of age than in older age groups[14,15]. Increased triglyceride levels and decreased high-density lipoprotein (HDL) cholesterol levels have also been reported in MI patients under age 45 years[8]. A meta-analysis of 16 prospective epidemiological studies suggests that an elevated triglyceride concentration is an independent risk factor for coronary artery disease even after adjusting for HDL cholesterol level[10]. Isser et al[16] found significant elevation of triglycerides and lipoprotein (a) (Lp[a]) levels and depression of high-density lipoprotein (HDL) cholesterol in young patients presenting with their first MI compared with age & gender-matched controls.

A positive family history of coronary artery disease is a major risk factor for MI in young patients[10]. The prevalence of positive family history among these patients ranges from 14% to 69%[2]. Siblings of a young patient with MI have up to a 10-fold increased risk of developing coronary artery disease[14, 15]. How a positive family history increases the risk of MI in young patients is not known, although it may involve inherited disorders of lipid metabolism, blood coagulation, or other genetic factors.

Young women with CAD comprise an especially interesting group given the protective effect of estrogen, but which factors are predictive in this distinctly unusual cohort are poorly understood. Diabetes in women may have a more powerful role than in men[2]. Women who smoke have a quantitatively similar risk as men, but more than five times the risk of nonsmoking women[17]. Smoking in combination with oral contraceptives poses a 13-fold increase in CAD mortality[17,18]. Truncal obesity and increased body mass index (BMI) have recently been proposed as potential independent risk factors, particularly in young women with CAD[19]. In our study, about half of young women admitted with AMI, had diabetes, hypertension, truncal obesity and hyperlipidemia as risk factors. None of these seven women were smoker or using oral contraceptives. In the study of AMI in women by Memon and Samad[26], women were 6 years older than men and were significantly more likely to have diabetes and hypertension. Hassan et al[27] in their study of coronary angiographic findings and correlation with risk factors in Pakistani women concluded that pattern of CAD in females followed all or none phenomenon, severity of CAD correlated with presence of risk factors and diabetes was the single most predictive factor for CAD.

Hypertension is less common in young MI patients than in older patients. Hypertension is common in patients with left main coronary artery stenosis who are under age 45 years[12, 22]. Diabetes mellitus is also more likely to be associated with MI in older patients than in young patients less than 10% of whom have diabetes[2]. Approximately 30% to 58% of young patients with coronary artery disease are obese, a significantly greater proportion than in older patients[2].

In this study, none of our patient had congenital coronary anomaly. Only one patient had marked ectasia of both left and right coronaries without any flow- limiting lesion. Congenital coronary artery anomalies account for approximately 4% of MIs in young patients.[20] Of 48 patients with sudden cardiac death under age 35 years, 16(33%) had non-atherosclerotic coronary disease, of which coronary artery anomalies were the most frequent.[20] Several such anomalies, including a deep intramyocardial course, an origin from the wrong coronary sinus, or ostial obstructions, have been associated with MI and sudden death in young patients[21, 22].

Most young patients with MI, up to 82% in one study have typical atherosclerotic coronary artery disease[23, 24]. In our study, forty-six patients (88%) had significant CAD (greater than 50% diameter narrowing of at least one major coronary artery), 5 (10%) had normal coronary arteries and one patient (2%) had marked coronary ectasia. The prevalence rate of one, two and three vessel disease was 52, 28 and 20 percent, respectively. No patient had significant left main CAD. Chen et al[8] in their study of 100 men with premature coronary artery disease, found a preponderance of single-vessel disease (54% vs. 36%) and complex stenosis morphology (59% vs. 36%) in these patients than in 100 older male patients with coronary artery disease. Data from the Coronary Artery Surgery Study registry[7] show that the 504 patients under the age of 45 years more often had non-obstructive coronary disease and single vessel disease than did older patients.

Klein et al[15] reported a prevalence of 51% for single-vessel disease, 31% for two-vessel disease, and 19% for three-vessel disease in their study of 85 patients under age 40 years with coronary artery disease, 59 of whom presented with acute MI. One study of 1,041 patients found the prevalence of left main coronary stenosis was approximately 3% in men and 7% in women[22]. Multivessel disease is more likely to occur in young patients who have a history of diabetes[3]. However, approximately 20% of young patients with AMI do not have atherosclerosis. Most of these patients have one of the other causes of MI, such as cocaine use, oral contraceptive use, vasculitis, hypercoagulable states, cardiac embolism, coronary dissection or congenital coronary anomalies[24, 25].

Younger MI patients who undergo diagnostic coronary angiography are much more likely to have a major change in management than are older patients. For example, an aggressive risk factor modification program will be of limited benefit in a young person who sustained an AMI because of anomalous origin of a coronary artery. Young age at infarction is an independent predictor of good short-term prognosis. However, it also indicates relatively aggressive atherosclerotic process in approximately 80 to 90 percent of patients. In the long term, further progression of disease is likely unless risk factors can be controlled[23].

It is concluded that AMI in persons under the age of 40 years accounts for approximately 19% of AMI. In this age group, AMI is a disease of men who smoke & single vessel CAD predominates. The most important modifiable risk factor is cigarette smoking. Lipid abnormalities and a positive family history of premature CAD are also important. Approximately half of the young patients have single-vessel coronary artery disease. Multivessel disease is more likely in patients with multiple risk factors and diabetes. Because about 10% young patients with AMI have anatomically normal epicardial coronary arteries, it is reasonable to perform diagnostic coronary angiography in young patients with AMI to define coronary anatomy and pathophysiology of AMI to permit optimal management.

References

1. Choudhury L, Marsh JD. Myocardial infarction in young patients. Am J Med 1999; 107:254-61.
2. Jalowiec DA, Hill JA. Myocardial infarction in the young and in women. Cardiovascular Clinics. 1989; 20:197-206.
3. Fournier JA, Sanchez A, Quero J, Fernandez-Cortacero JA. A. Myocardial infarction in men aged 40 years or less; a prospective clinical-angiographic study. Clinical Cardiology. 1996; 19:631.
4. Jonsdottir LS, Sigfusson N et al. Incidence and prevalence of recognized and unrecognized myocardial infarction in women. Reykjavik Study Eur Heart J. 1998; 19:1011-1018
5. Goldberg RJ, McCormick D, Gurvitz JH, Yarzebski J, Lessard D, Gore JM. Age-related trends in short- and long-term survival after acute myocardial infarction: a 20-year population-based perspective (1975–1995). *Am J Cardiol*. 1998;82:1311-1317.
6. Berenson GS, Srinivasan SR, Bao W, Newman WP, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. NEJM. 1998;338:1650-1656.
7. Zimmerman F, Cameron A, Fisher L. Myocardial infarction in young adults: angiographic characterization, risk factors, and prognosis (Coronary Artery Surgery Study Registry). J Am Coll Cardiol 1995;26:654-61.
8. Chen L, Chester M, Kaski JC. Clinical factors and angiographic patterns associated with premature coronary artery disease. Chest 1995;108:364-9.
9. Uhl G, Farrell P. Myocardial infarction in young adults: risk factors and natural history. Am Heart J. 1983;105:548.

   9.a Meier MA, Al-Badar WH, Cooper JV, Smith DE, Eagle KA. The new definition of myocardial infarction. Arch Intern Med 2002;162:1585-1589.
10. Farmer JA, Gotto AM, Jr. Dyslipidemia and other risk factors for coronary artery disease. In: Braunwald E, ed. Heart Disease: A Textbook of Cardiovascular Medicine. Philadelphia: Saunders. 1997: 1126–1160.
11. Ryan TJ, Anderson JLet al. ACC/AHA guidelines for the management of patients with AMI: a report of the American College of Cardiology /American Heart Association Task Force on Practice Guidelines (Committee on Management of AMI). 1999 update; http:/www.acc.org/clinical/guidelines/ami.html.
12. Machete T, Malacrida R, Pasotti E, et al. Epidemiologic variables and outcome of 1972 young patients with acute myocardial infarction. Data from the GISSI-2 database. The GISSI investigators. Arch Int Med. 1997;157:865–869
13. Kannel WB. Update on the role of cigarette smoking in coronary artery disease. Am Heart J 1981;101:319-28.
14. Tuzcu EM, Kapadia SR. High prevalence of coronary atherosclerosis in asymptomatic teenagers and young adults: evidence from intravascular ultrasound. Circulation 2001;103:2705.
15. Klein LW, Agarwal JB, Herlich MB, Leary TM, Helfant RH. Prognosis of symptomatic CAD in young adults aged 40 years or less. Am J Cardiol 1987;60:1269–72.
16. Isser HS, Puri VK, Narain VS, Saran RK, Dwivedi SK, Lipoprotein (a) and lipid levels in young patients with myocardial infarction and their first-degree relatives. Indian Heart J 2001;53: 463–6.
17. Willett WC et al. Relative and absolute risks of CAD among women who smoke cigarettes. N Engl J Med 1987; 317: 1303.
18. Barbash GI, White HD, Modan M, et al. Acute myocardial infarction in the young—the role of smoking. The Investigators of the International Tissue Plasminogen Activator/Streptokinase mortality trial. Eur Heart J. 1995;16:313–316.
19. Nevas-Nacher EL, Colangelo L, Beam C, Greenland P. Risk factors for coronary heart disease in men age 18 to 39 years of age. Ann Intern Med 2001;134:433–9.
20. Cheitlin MD, McAllister LA, de Castro CM. Myocardial infarction without atherosclerosis. JAMA. 1975;231:951–959.
21. Corrado D, Thiene G, Cocco P, Frescura C. Non-atherosclerotic coronary artery disease and sudden death in the young. Br Heart J. 1992;68:601–607.
22. Crittin J, Waters DD, Theroux P, Mizgala HF. Left main coronary stenosis in young patients. *Chest*. 1979;76:508–513.
23. Cole JH, Miller III JI, Sperling LS, Weintraub WS. Long-term follow-up of coronary artery disease presenting in young adults. J Am Coll Cardiol 2003;41:521–8.
24. Warren SE et al. Historic and angiographic features of young adults surviving myocardial infarction. Chest. 1979;75:667–670.
25. Fournier JA, Sanchez-Gonzales A, Quero J et al. Normal angiogram after myocardial infarction in young patients: a prospective clinical-angiographic and long-term follow-up study. Int J Cardiol. 1997;60:281–287.
26. Memon MA, Samad A. Acute myocardial infarction in women. PJC 1999: 10:95-107.
27. Hassan MI, Rasheed SZ et al. Coronary angiographic findings and correlation with risk factors in Pakistani women. PJC 1992;3:26-33.
28. Expert panel on detection, evaluation and treatment of high blood cholesterol in adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP). JAMA 2001;285:2486-2497 11