

Research Article

Coronary Artery Disease in Young Pakistanis: Risk Factors and Pattern of Disease

Muzaffar Ali¹, Usman Mahmood Butt², Rao Shahzad Abdul Tawwab Khan³, Mamoon Akber Qureshi⁴, Zubair Akram⁵

¹Associate Professor, Department of Cardiology, AIMC/ Jinnah Hospital, Lahore; ²Department of Cardiology, AIMC/ Jinnah Hospital, Lahore; ³Department of Cardiology, AIMC/ Jinnah Hospital, Lahore; ⁴Department of Cardiology, AIMC/ Jinnah Hospital, Lahore; ⁵Professor, Department of Cardiology, AIMC/ Jinnah Hospital, Lahore.

Abstract

Objective: To determine the distribution of risk factors and pattern of coronary artery disease among young Pakistanis presenting with acute coronary artery syndrome. A cross sectional study conducted from August 2018 to October 2019 at Department of Cardiology Jinnah Hospital Lahore.

Methods: Total of 150 young patients up to 40 years of age with acute coronary syndrome (ACS) was included in this study. Risk factors were evaluated on patient's current medication history for diabetes mellitus, hypertension, lipid lowering drugs and recent reports HbA1c, total body lipids. Data was entered and analyzed in SPSS version 21.0. Socio-demographic, clinical profile and risk factors were evaluated and presented as frequency and percentages. Cross tabulation was for ACS and risk factors. Statistical significance was assessed using Chi-square test with significant value of $p < 0.05$.

Results: Among 150 subjects mean age was 34.20 ± 4.246 with minimum age of 23 years and maximum age of 39 years. 92.0 % were male and 56.0% were having acute anterior wall STEMI, 36.0% had acute inferior Wall STEMI, 2.0% suffered from acute lateral wall STEMI, 2.7% had acute inferoposterior wall STEMI and 3.3% had NSTEMI-ACS. Risk factor analysis shows that 22.0% had diabetes mellitus, 20.7% had hypertension, 33.7% had a positive history of IHD in family, 71.3% were smokers, 44.0% had obesity, 66.0% had reduced HDL and 44.0 % had elevated LDL levels. Regarding pattern of coronary artery disease, 70.7% patients were having one vessel CAD, 28.0% two vessels CAD and 1.3% had three vessels CAD.

Conclusion: Mean age of acute coronary syndrome is low amongst young Pakistani population with male predominance and acute anterior and inferior wall STEMI being most frequent diagnosis. Smoking, dyslipidemia particularly low HDL, positive family history of ischemic heart disease, hypertension, diabetes mellitus, obesity, was identified as important risk factors. Most of the patients had one vessel CAD.

Corresponding Author | Dr. Muzaffar Ali, Associate Professor, Department of Cardiology, AIMC/ Jinnah Hospital, Lahore.
Email: muzcardio@gmail.com

Key Words: Acute Coronary Syndrome, Young Adults, Hypertension, Smoking

Introduction

Globally, cardiovascular disease (CVD) is an important cause of death.¹ There is ample amo-

unt of data available for coronary artery disease (CAD) across the world, while the literature highlighting premature CHD and myocardial infarction

(MI) in the “young” is still deficient.² The effects of MI predominantly in younger population can be distressing because of its possible impact on the patient’s mental health, functional capacity and the socioeconomic status. Myocardial infarction at a young age has a devastating effect on livelihood and affects the whole family.^{3,5}

Cardiovascular disease despite its declining trend in older age group, still causing adverse outcomes in younger population worldwide. The young age population is not vastly studied despite having inimitable risk profile in comparison to traditional risk factors in old age population.^{5,7}

The data is lacking in young population regarding history, clinical examination and prognosis of acute myocardial infarction. Although, acute myocardial infarction is less frequent in the young population, but major hazards like death and disability pose serious clinical implications.⁸ A number of studies have examined the frequency of CAD and coronary artery anatomy in younger population, while angiographic studies have established less extensive CAD than in older population.^{5,9-10}

The pattern and presentation of CAD in “young” patients and the difference that exist between “young” and older patients of MI still not well understood by the clinicians. There is a lot of discrepancy in the data on the exact definition of “young” in context to premature CAD and MI. The age limit for “young” varies from 40 to 55 by some researchers, other suggest a cut off age for “young” with respect to MI was taken 45 years of age.^{3,7-9} There is no consensus on single age cut-off for young throughout the world, this review will use a cut-off 40 years of age in Pakistani population. The data is lacking on MI in the “young” in comparison to literature on CAD without age limit.^{10,11} Perhaps the most well-known of all, The Framingham Heart Study, a landmark research work in the history of cardiovascular diseases, depicted a 10-year rate of “young” MI (<55 years of age) 51.1/1000 in males and 7.4/1000 in females.¹² While McManus et al. in their study found an incidence of 66/100,000 of MI in patients of age group 25 to 54 years.¹⁴ In comparison to these studies, McGill et al. presented a surprisingly increased prevalence of CAD in young males of age less than

35 years with 20% revealed to have advanced coronary artery disease on autopsy findings.¹⁵ Doughty et al. showed > 10% of MI patients presented to their hospital were “young”, the cut off value for “young” was 45 years of age for this study.¹⁶ One of the highest rates of MI in the “young” was reported by Loughnan et al. who conducted study on young MI patients (<55 years) admitted to hospitals in Melbourne, Australia over a span six-years found highest rates around 20%. This turned out to be 0.1% of the Melbourne population of age less than 55 years.¹⁷

In an analysis by World Health Organization, the global burden of CAD has an upsurge from 47 million disability adjusted life years (DALYs) in 1990 to around 82 million DALYs in 2020. At present, CAD burden is the 3rd common cause of DALY lost in females (5.3%) and 2nd common cause of disease burden (6.8%) in males.¹⁸ The largest cardiovascular Framingham study stated a 10-years CAD incidence of 12.9/1000 in men of age group of 30-34 years and 5.2/1000 in women of age group of 35-44 years.^{14,18}

The fact that clinically manifestation of CAD in the young adult is relatively infrequent and it indicates that these patients are atypical of the general population.^{13,19} Recently on top of the well-known cardiac markers of CAD, many novel markers, precisely related with CAD in young are revealed. The rationale of this study is to gauge the role of traditional and novel risk factors and pattern of CAD in young adults. Due to the growing incidence of the CAD in our part of the world, it is vital to measure these risk factors of CAD.¹⁹ As very limited local data is available regarding pattern of CAD & distribution of risk factors in young Pakistanis, hence present study is unique and innovative to look for pattern of disease and prevalence of risk factors simultaneously in young Pakistani to prevent increasing burden of disease in young generation.

Methods

A cross sectional study was conducted from August 2018 to October 2019 at Department of cardiology Jinnah Hospital Lahore. Young adult patients up to 40 years of age of either gender with acute coronary syndrome (ACS), those fulfilling the inclusion criteria were included through a non-probability / convenience sampling for the study. A sample of 150

cases was calculated to estimate sample size needed to find a case of acute coronary syndrome in young with confidence level of 95% and assumed rate of 51.1 per 1000 from The Framingham Heart Study.⁷ Young adults with history of congenital birth defects were excluded from the study. After approval of ethical committee and informed consent a detailed demographic profile was collected along with presence of risk factors among subjects. Data was entered and analyzed in SPSS version 21.0. Sociodemographic, clinical profile, risk factors and pattern of CAD were evaluated and presented as frequency and percentages. Cross tabulation was for ACS and risk factors. Statistical significance was assessed using Chi-square test with significant value of $p < 0.05$.

Results

Among 150 subjects mean age was 34.20 ± 4.246 with minimum age of 23 years and maximum age of 39 years. 82.1% were more than 30 years. 92.0% were male and 8.0% were females. 56.0% were having acute anterior wall ST-Elevation Myocardial Infarction (STEMI), 36.0% had acute Inferior wall STEMI, 2.0% suffered from acute lateral wall STEMI, 2.7% had acute infero-posterior wall STEMI and 3.3% had Non ST-elevation acute coronary syndrome (NSTE-ACS). (Table No: 1).

Table 1: Demography and diagnosis of study population.

Variables n = 150	Frequency	Percent
Age: Mean = 34.03, SD±4.221		
< 30 years	30	20.0
> 30 years	120	80.0
Gender		
Male	138	92.0
Female	12	8.0
Diagnosis		
Acute Anterior Wall STEMI*	84	56.0
Acute Inferior Wall STEMI*	54	36.0
Acute Lateral Wall STEMI*	3	2.0
Acute Infero-posterior Wall STEMI*	4	2.7
NSTE-ACS**	5	3.3

* ST-Elevation Myocardial Infarction ** Non ST-elevation acute coronary syndrome

Risk factor analysis shows that 22.0% had diabetes mellitus, 20.7% had hypertension, 33.7% had a positive history of IHD in family, 71.3% were smokers, 44.0% had obesity, 66.0% had reduced HDL and 44.0% had elevated LDL levels (Table no:2)

Table 2: Risk factors among study population. (Multiple response).

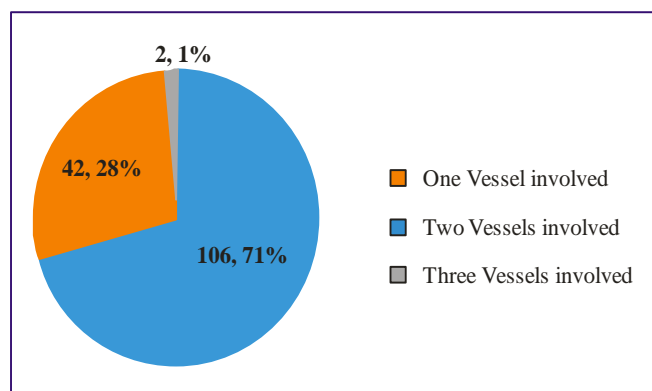
Risk Factors	Multiple Responses		Percent of Cases
	Frequency	Percent of responses	
Diabetes Mellitus	33	7.2%	22.0%
Hypertension	31	6.8%	20.7%
Family History	55	12.1%	36.7%
Smoking	107	23.4%	71.3%
Obesity	66	14.4%	44.0%
Low HDL	99	21.7%	66.0%
High LDL	66	14.4%	44.0%
Total	457	100.0%	304.7%

Risk factor cross tabulation showed that diabetes mellitus was risk factor in 48.5% of patients having acute anterior wall STEMI, 36.4% in acute Inferior Wall STEMI, 9.1% in acute lateral wall STEMI, while 0.0% acute infero-posterior and 0.0% who had NSTE-ACS. ($p = .009$). Hypertension was risk factor in 71.0% in patients having acute anterior wall STEMI, 25.8% who had acute Inferior Wall STEMI, while 0.0% in acute lateral wall STEMI, 3.2% with acute posterior wall STEMI and 0.0% had NSTE-ACS. ($p = .221$). Positive family history was risk factor in 61.8% having acute anterior wall STEMI, 29.1% who had acute Inferior Wall STEMI, 5.5% in acute lateral wall STEMI, 0.0% acute infero-posterior and in 3.6% who had NSTE-ACS. ($p = .027$). Smoking was risk factor in 54.2% having acute anterior wall STEMI, 78.0% who had acute Inferior Wall STEMI, 0.0% in having acute lateral wall STEMI, 2.8% with acute posterior wall STEMI and 3.7% had NSTE-ACS. ($p = .064$). Obesity was risk factor in 54.5% having acute anterior wall STEMI, 36.4% who had acute Inferior Wall STEMI, 4.5% in acute lateral wall STEMI, 0.0% with acute posterior wall STEMI and 4.5% had NSTE-ACS. ($p = .100$) (Table No: 3).

Table No 3: Risk Factors and differential diagnosis among subjects Cross-tabulation

Risk factors	Diagnosis					Total	P-value
	Acute Anterior Wall STEMI	Acute Inferior Wall STEMI	Wall STEMI	Acute Lateral Wall STEMI	Acute Inferior Wall STEMI		
Diabetes Mellitus	16 48.5%	12 36.4%	3 9.1%	0 0.0%	2 6.1%	33	.009
Hypertension	22 71.0%	8 25.8%	0 0.0%	1 3.2%	0 0.0%	31	.221
Family history of IHD	34 61.8%	16 29.1%	3 5.5%	0 0.0%	2 3.6%	55	.027
Smoking	58 54.2%	42 39.3%	0 0.0%	3 2.8%	4 3.7%	107	.064
Obesity	36 54.5%	24 36.4%	3 4.5%	0 0.0%	3 4.5%	66	.100
Total	84	54	3	4	5	150	

Regarding pattern of coronary artery disease, 70.7% patients were having one vessel CAD, 28.0% two vessels CAD and 1.3% had three vessels CAD. (Graph no: 1)

**Graph No 1: Vessel involved**

Discussion:

The term CAD in young is used for adults of age less than 40 years having CAD. In the previous studies the range of age used for young population having CAD was from 35 years to 55 years.^{14,18-19} According to recent data the frequency of CAD cases in this age group is found to be 1.2%. Different ethnic groups have different rates but South Asians especially Indians are more susceptible to have CAD in this age

group with a slightly higher occurrence of around 5% to 10%²⁰. Common risk factors like smoking, diabetes mellitus, elevated blood pressure, obesity and positive history of premature CAD in the family appear to be as crucial for CAD in young as in elderly patients. However, the distribution of these traditional risk factors appears to fluctuate in younger populations. The commonest most risk factor for CAD in young adults is found to be smoking.²¹ Similarly in our study smoking turned out to be the most frequent risk factor for CAD (71.3%) followed by low HDL (66.0%).

Previous data has revealed an augmented incidence of CAD in those young adults with positive family history than in those without family history (35% vs. 14%).¹⁶ In our study the frequency of family history of premature CAD was found to be 36.7%. The Framingham study data from 1880 to 2003 by National heart lung and blood institute (NHLBI's) showed a yearly incidence of CVD in men of age group 35-44 years of 3/1000.²² Our study revealed a mean age was 34.20 + 4.246 with least age of 23 years and extreme age of 39 years. 82.1% were more than 30 years and 92.0% were males. The data from Centre of disease control and prevention for the year 2010 exposed that frequency of CAD in the age

group of 18-44 years, 45- 64 years and >65 years was 1.2%, 7.1% and 19.8% correspondingly.¹⁸ In a Korean population study, the prevalence of occult CAD in young subjects (112 asymptomatic individual) of age <40 years was 11% (9 had one vessel CAD and 3 had two vessel CAD). Coronary CT angiography was used to define the occult CAD in young individuals.²³ In our data the pattern of CAD was 70-.7% having one vessel CAD, 28.0% having two vessels CAD and 1.3% having three vessels CAD.

In South Asians population particularly belonging to India is at higher risk of having CAD in young age (5%-10%) in comparison to other ethnic population (1%-2%). In a study from Indian population the reported prevalence of CAD in young (< 40 years) was 5% to 10%. This susceptibility of Indians to CAD may be linked to various factors related to their life style, environment and genetics.²⁰ Risk factor analysis shows that 22.0% had diabetes mellitus, 20.7% had hypertension, 33.7% had a positive history of IHD in family, 71.3% were smokers, 44.0 % had obesity, 66.0% had reduced HDL and 44.0 % had elevated LDL that are in accordance with other studies done in this region. The distribution of various risk factors like diabetes mellitus, elevated blood pressure, smoking, elevated blood cholesterol and obesity leads to incidence of premature CAD around 85% to 90%. Commonly young adults with CAD have several concomitant cardiac risk factors.²⁴ Smoking considered to be most common risk factor related to CAD in young. In our study the prevalence of smoking was found to be highest (71.3%). Those young individuals who smoke in the existence of further risk factors like diabetes mellitus, elevated blood pressure and obesity expose them to increased risk CAD in future.²⁵

The frequency of diabetes mellitus and hypertension appears to higher in young individuals with CAD than in healthy individuals. The frequency of hypertension in young individuals with CAD is 25% in comparison to 13% in healthy individuals. Similarly, in our study the frequency of hypertension is found to be 20.7%. The frequency of diabetes mellitus is 14.3% in young individuals with CAD in comparison to 5.4% in healthy individuals.²³ This

frequency of diabetes mellitus is 22.0% in our study. Although, frequency of these risk factors is quite higher in older patients of CAD.^{12,17-24} Several studies on younger individuals with CAD have proved a recent rise in the frequency of hypertension [8.86% (2001-2002) to 27.7% (2009-2010)] and diabetes mellitus [7.6% (2001-2002) to 36.15% (2009-2010)].^{24,25}

Our study findings are in accordance with other national and international studies on coronary artery disease among young population which include risk factors like unhealthy diet, obesity and tobacco use. The presence of behavioral risk factors in those young individuals led to hypertension, diabetes mellitus, dyslipidemia, overweight and obesity. These traditional risks factors indicate an increased risk of developing a myocardial infarction, stroke, congestive heart failure and other complications related to cardiovascular system.

Conclusion:

Mean age of acute coronary syndrome is low in our Pakistani population with male predominance and acute anterior and inferior wall STEMI being most frequent diagnosis. Smoking, dyslipidemia particularly low HDL, positive family history of ischemic heart disease, hypertension, diabetes mellitus and obesity were identified as important risk factors. Most of the patients had one vessel CAD. We need a larger data to implement these results on Pakistani population in future.

References:

1. Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, et al. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. *Circulation*. 2018; 137(12):e67-e492.
2. Gulati R, Behfar A, Narula J, Lerman A, Cooper L, Singh M. Acute Myocardial Infarction in Young Individuals. *Mayo Clin Proc*. 2020;95(1):136-156.
3. Safdar B, Spatz ES, Dreyer RP. Presentation, clinical profile, and prognosis of young patients with myocardial infarction with nonobstructive coronary arteries (MINOCA): results from the VIRGO Study. *J Am Heart Assoc*. 2018;7(13):e009174.

4. Aggarwal A, Aggarwal S, Goel A, Sharma V, Dwivedi S. A retrospective case-control study of modifiable risk factors and cutaneous markers in Indian patients with young coronary artery disease. *J-RSM Cardiovasc Dis.* 2012;1(3):012010.
5. Wiesbauer F, Blessberger H, Azar D, Goliash G, Wagner O, Gerhold L, et al. Familial-combined hyperlipidaemia in very young myocardial infarction survivors (< or =40 years of age). *Eur Heart J.* 2009;30(12):1073-1079.
6. Mack M, Gopal A. Epidemiology, traditional and novel risk factors in coronary artery Shah RV, Murthy VL, Colangelo LA, et al. Association of fitness in young adulthood with survival and cardiovascular risk: The Coronary Artery Risk Development in Young Adults (CARDIA) Study. *JAMA Intern Med.* 2016;176(1):87-95.
7. Awad-Elkarim AA, Bagger JP, Albers CJ, Skinner JS, Adams PC, Hall RJ. A prospective study of long term prognosis in young myocardial infarction survivors: the prognostic value of angiography and exercise testing. *Heart.* 2003;89(8):843-847.
8. Physical Activity Guidelines Advisory Committee. 2018 Physical Activity Guidelines Advisory Committee Scientific Report. Washington, DC: US Department of Health and Human Services. 2018. [Accessed: 12th August, 2020]. Available at https://health.gov/paguidelines/second-edition/report/pdf/PAG_Advisory_Committee_Report.pdf.
9. Das SR, Everett BM, Birtcher KK. 2018 ACC Expert consensus decision pathway on novel therapies for cardiovascular risk reduction in patients with type 2 diabetes and atherosclerotic cardiovascular disease: a report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. *J Am Coll Cardiol.* 2018;72 (24) : 3200-3223.
10. Piercy KL, Troiano RP, Ballard RM. The physical activity guidelines for Americans. *JAMA.* 2018; 320(19):2020-2028.
11. Ha EJ, Kim Y, Cheung JY, Shim SS. Coronary artery disease in asymptomatic young adults: its prevalence according to coronary artery disease risk stratification and the CT characteristics. *Korean J Radiol.* 2010;11(4):425-432.
12. Celik T, Iyisoy A. Premature coronary artery disease in young patients: an uncommon but growing entity. *Int J Cardio.* 2010;144(8):131-132.
13. McManus DD, Piacentine SM, Lessard D, Gore JM, Yarzebski J, Spencer FA, et al. Thirty-year (1975 to 2005) trends in the incidence rates, clinical features, treatment practices, and short-term outcomes of patients < 55 years of age hospitalized with an initial acute myocardial infarction. *Am J Cardiol.* 2011;108(21):477-482.
14. Aggarwal A, Srivastava S, Velmurugan M. Newer perspectives of coronary artery disease in young. *World J Cardiol.* 2016;8(12):728-734.
15. McGill Jr HC, McMahan CA, Zieske AW, Tracy RE, Malcom GT, Hedrick EE, et al. Association of Coronary Heart Disease Risk Factors with microscopic qualities of coronary atherosclerosis in youth. *Circulation.* 2000;102(23):374-379.
16. Doughty M, Mehta R, Bruckman D, Das S, Karavite D, Tsai T, et al. Acute myocardial infarction in the young-The University of Michigan experience. *Am Heart J.* 2002;143:56-62.
17. Loughnan ME, Nicholls N, Tapper NJ. Demographic, seasonal, and spatial differences in acute myocardial infarction admissions to hospital in Melbourne Australia. *Int J Health Geogr.* 2008;7 (3) :42.
18. World Health Organization: Cardiovascular diseases. [Accessed: 12th August, 2020] Available at: [https://www.who.int/news-room/factsheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/news-room/factsheets/detail/cardiovascular-diseases-(cvds)).
19. Malmberg K, Bavenholm P, Hamsten A. Clinical and biochemical factors associated with prognosis after myocardial infarction at a young age. *J Am Coll Cardiol.* 1994;24(8):592-599.
20. Aggarwal A, Aggarwal S, Sarkar PG, Sharma V. Predisposing factors to premature coronary artery disease in young (age > 45 years) smokers: a single center retrospective case control study from India. *J Cardiovascular Thorax Res.* 2014;6(3):15-19.
21. Ha EJ, Kim Y, Cheung JY, Shim SS. Coronary artery disease in asymptomatic young adults: its prevalence according to coronary artery disease risk stratification and the CT characteristics. *Korean J Radiol.* 2010;11(4):425-432.
22. Framingham Heart Study. [Accessed 16th, November 2020]. Available from: <https://www.nhlbi.nih.gov/science/framingham-heart-study-fhs>.
23. Centers for Disease Control and Prevention (CDC) Prevalence of coronary heart disease-United States, 2006-2010. *MMWR Morb Mortal Wkly Rep.* 2011;60(12):1377-1381.

24. Kang MK, Chang HJ, Kim YJ, Park AR, Park S, Jang Y, et al. Prevalence and determinants of coronary artery disease in first-degree relatives of premature coronary artery disease. *Coron Artery Dis.* 2012;23(6):167-173.
25. Ha EJ, Kim Y, Cheung JY, Shim SS. Coronary artery disease in asymptomatic young adults: its prevalence according to coronary artery disease risk stratification and the CT characteristics. *Korean J Radiol.* 2010;11(3):425-432.