International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 9; Issue 04 (C); April 2020; Page No.22001-22005
DOI: http://dx.doi.org/10.24327/ijcar.2020.22005.4333

Research Article

EVALUATION OF THROMBOPHILIC AND ATHEROSCLEROTIC MARKERS IN YOUNG PATIENTS (<45 YEARS) WITH ST-SEGMENT ELEVATED MYOCARDIAL INFARCTION

Rakesh Tumula, *Jenny Madhuri Gudivada and Malladi Srinivasarao

Assistant Professor, Andhra Medical Collage Dr NTR University, Dept of Cardiology

A R T I C L E I N F O

Article History:
Received 12th January, 2020
Received in revised form 23rd February, 2020
Accepted 7th March, 2020
Published online 28th April, 2020

Key words:

Coronary artery disease, STEMI, tissue plasminogen antigen, plasminogen activator inhibitor-1

A B S T R A C T

Objective: The present study was designed to evaluate the clinical profile, thrombophilic and atherosclerotic markers in young patients with ST-segment elevated myocardial infarction (STEMI)**.**

Methods: This was an observation, hospital-based study which included 46 young (≤45 years)and 46 elderly (≥60 years) patients with STEMI. Electrocardiogram, echocardiogram, carotid intima media thickness (CIMT), ankle-brachial pressure index (ABPI) were assessed. The serum tissue plasminogen antigen (TPA), plasminogen activator inhibitor-1 and antithrombin-III were analyzed and compared with elderly STEMI patients, and then patients are subjected to coronary angiography to know vessel involvement.

Results: Among 46 young patients, 38 (82.6%) were males. Total 65.2%patients were smokers and28 (60%) had dyslipidemia and 17.4% had obesity (17.4%).Chest pain was most common symptom (91%). Mean time to thrombolysis was 41.5min. Among all, 31.7% had normal coronary angiograms and 43.5% patients had single vessel involvement (43.5%). Mean CIMT increased as the severity of coronary artery disease increased. Serum TPA in the young group was statistically significant compared to elderly group (p=0.006).

Conclusion: In young STEMI patients, CIMT and ABPI do not appear to be useful surrogate markers of atherosclerosis unlike elderly patients. Thrombophilia whether inherited or acquired seems to have a role to play in the young STEMI patients however, larger studies are required in further to prove this.

INTRODUCTION

Coronary artery diseases (CAD) especially myocardial infarction is an important public health problem in developing countries like India. According to Registrar General of India Report 2009, CAD is the primary cause of death for all economic classes and in all regions of India. Furthermore, CAD accounts for greater than1/3rd of all deaths in individuals aged>35 years. Atherosclerosis and hypercoagulable states are the two major causes of myocardial infarction in young patents. Other non-athermanous causes of CAD such as coronary artery anomalies, coronary bridging, osteal stenos is and coronary dissection play minor role in younger patients.

Anti-phospholipid syndrome is associated with recurrent thrombosis of both arterial and venous territories that usually affect young patients in their thirty. These patients tend to have increased platelet adhesiveness and premature atherosclerosis. Coagulation Factor-V Leiden mutation is linked to a procoagulant state and has been reported to result in myocardial infarction in young people. Moreover, bedside non-invasive surrogate markers of atherosclerosis are ankle brachial pressure index (ABPI) and carotid intima media thickness (CIMT). Various emerging risk factors of CAD in young people include higher baseline concentrations of tissue plasminogen activator (TPA) antigen, plasminogen activator activity(PAI-1), antithrombin-3, homocysteine, lipoprotein (a), fibrinogen, CIMT and ABPI. Therefore, the present study was designed to study the clinical profile, thrombophilic and atherosclerotic markers in young patients (<45 years) with ST segment elevation myocardial infarction (STEMI). This study also compared the values of various thrombophilic and atherosclerotic markers in younger (<45 years) and older (>45 years) STEMI patients.

Corresponding author:* **Jenny Madhuri Gudivada
Assistant Professor, Andhra Medical Collage Dr NTR University, Dept of Cardiology

METHODS

This was an observational, hospital-based and physician-initiated study conducted at a tertiary care center in India between October-2017 and July-2019. The study was approved by institutional ethic committee and was performed as per Declaration of Helsinki. The written inform consent was obtained either from patient or from patient's family member before the conduct of the study.

The population was divided into two groups 1) Test group: included 46 patients of age <45 years who were presented STEMI and 2) Control group: included 46 patients of age <60 years who were presented with STEMI. The patients satisfying at least two of the three elements such as: i) history of ischemic chest discomfort, ii) serial electrocardiogram (ECG) changes suggestive of STEMI iii) elevated cardiac enzymes; and presenting within 48 hours of symptoms were included in the study. However, patients taking atorvastatin for >6 months and anticoagulants, patients with chronic liver disease, chronic kidney disease, connective tissue disorders, coronary anomalies, gout, psoriasis, bad obstetric history, and polycythemia vera were excluded from the study.

A detailed evaluation of demographic parameters and coronary risk factors was obtained from all the patients. The waist was measured at the level of the umbilicus in men, and midway between the lowest rib and the top of the hipbone in women. To measure the hips, measurements made at the tip of the hipbone in men, at the widest point of the hips/buttocks in women. ECG, 2D echocardiogram, and ankle-brachial pressure index (ABPI) via Doppler probe were assessed in all patients in test group. Carotid intima media thickness (CIMT) was measured on the far wall of the common carotid artery, around 1 cm below the carotid bifurcation using a high-resolution B-mode ultrasound. CIMT was assessed on both sides of the neck and the greater value was chosen for analysis. The biochemical parameters such as serum creatinine, lipid profile, and cardiac enzymes were also analyzed in all test group patients. The serum coagulation parameters like tissue plasminogen antigen (TPA), plasminogen activator inhibitor-I (PAI-I) and anti-thrombin-III (AT-III)were analyzed for patients in both the groups.

Statistical analysis

All data were analyzed using Statistical Package for the Social Sciences (SPSS version 20). The continuous variables were presented as mean ± SD and analyzed using Chi-square/ Fisher Exact test. The categorical variables were presented as frequency and percentage and analyzed using two-tailed independent student t-test. To find the degree of relationship between the study variables Pearson correlation test was used. A p-value of 0.05 was considered statistically significant.

RESULTS

The study population consisted of 46 young patients (age <45 years) and 46 elder patients (>60 years) with STEMI. In young group, majority of patients are in the age group 36-40 years (39.1%). The youngest patient included in the study was a 26-year-old male. Out of 46 young patients, 43 patients survived and 3 died during the hospital stay. The detailed demographic details, clinical characteristics, lipid profile and time of thrombolysis are outlined **in Table 1 and 2**.

Smoking (65.2%) was the commonest risk factor of CAD among young patients. Among young patients, 54.2% patients were in normal weight range i.e. BMI <23 kg/m^2.History of alcohol intake was noted in 39.1% of young patients. Seven patients out of 18 patients were abusers, and others were social drinkers. Two of eight female patients had significant alcoholic history. Out of three patients, two had more waist-hip ratio and both hypertension and diabetes. Later two patients of them have double vessel disease (DVD) on angiography.

One of the patient was taking Eltroxin for hypothyroidism and four patients were on anti-depressant drug for various reasons. Most of them were agricultural workers, and four patients were sedentary workers. None of them had any major stressor preceding to the episode, documented fever or any significant illness.

Out of 46 young patients, 42 (91.3%) hadchestpain which was predominantly left sided (36 patients) and rest of them had central retrosternal chest pain. Out of 46 patients majority i.e. 23 (50%) patients had onset of chest pain in between 6.01 am and 12 pm. At the time of admission, 11 patients had systolic blood pressure <90 mmHg. Five of them were fluid responsive, and other six patients were given inotropes during first 24 hours of hospital stay.

Cardiovascular examination revealed two patients were having S3 gallop rhythm and one patient presented with shock. Furthermore, respiratory examination revealed clear lung fields in almost all young patients. Seven patients were having crepitation involving half or less than half of the lung fields; three patients were having crepitationin almost all lung fields, and two patients presented with cardiogenic shock at presentation. All young patients had creatinine kinase-MB fraction positive (mean CK-MB fraction: 83.8ug/L) and 34 out of 46 patients had positive levels of cardiac troponin.

Subsequently, 2D ECHO examination revealed wall motion abnormality in 40 patients. The mean ABPI in the total study group was 0.96.Coronary angiography was performed in 41 patients as three patients died before and two had deranged renal function tests (serum creatinine: 1.7 and 3.7 mg/dl). Total 20 patients had single vessel disease (SVD), among which 15 patients had left anterior descending artery involvement, four patients had right coronary artery involvement and one patient had left circumflex artery involvement. The details of ECG, echocardiography and CIMT are mentioned in **Table 3**.

The levels of biomarkers were compared in young patients (<45 years) and in elderly patients (>60 years). The statistically significant difference was observed TPA levels between young and elderly patients (p= 0.02) however, no statistically significance was established for PAI and AT-III (p=0.08 and 0.59, respectively). The comparison of serum coagulants between both the groups are depicted in **Table 4**.
Pearson coefficient of correlation was also established which resulted a negative association between CIMT and TPA(r= -0.35); and a positive association was observed between BMI and serum LDL levels (r= 0.34) which were statistically significant (p= 0.020).**Table 5** displays the distribution of various risk factors in relation to coronary angiographic findings.

DISCUSSION

The present study was designed to identify various risk factors that are prevalent among the younger age group (<45 years) along with their clinical presentations, coagulation profile and angiographic findings. In the present study, the mean age of younger patients was 37.96±4.59 years. It is well-established fact that CAD is a predominant male disease, especially in the young population and in this study also men constituted 82.6% of patients. The low incidence of CAD among the females could be due to the protective action of the estrogen hormone at younger age. A study in Haryana, Siwach SB, Singh H et al.(10) in young myocardial infarction patients showed 20:1

male to female ratio, however in the present study, it was 4.8:1, but the trend remains the same.

Among the conventional risk factors, cigarette smoking was the commonest one as 65.2% patients were smokers in the present study. In a study in rural/semi-urban population of India, smoking was found to be the most common (85%) risk factor in young patients (below 40 years).(4) However, in numerous previous studies diabetes and hypertension were found to be less frequent in young adults (4, 5, 11)which was consistent with the results of the current study.

Previous epidemiologic data support the hypothesis of a genetic component conditioning the development of coronary heart disease. According to the results of the Lipid Research Clinics Trail, there is a direct association between the cholesterol levels, the plasma lipoprotein profile and the morbidity and mortality from coronary atherosclerosis. In this study, dyslipidemia was present in 60% of patients which is high compared to other studies. This discrepancy may be due to varying time of sample collection for lipid profile estimation. In our study, we collected within the 24 hours of hospital admission. In addition, three patients got expired in our study during the hospital stay before coronary angiography and all three had dyslipidemia.

In this study, the mean BMI was 23.45±2.8 kg/m2. As per the latest guidelines of BMI for Indians, the mean BMI of young patients is just above the normal range i.e. within the overweight range and the majority of patients had normal BMI (52.2%). Obesity is present in 17.4% of patients.

In our study, the mean CIMT of subjects with angiographic ally normal coronaries was 0.56 mm. An increase in mean CIMT was observed with increase in severity of CAD. The mean CIMT of patients with SVD, DVD and TVD were 0.60mm, 0.75mm and 0.90 mm, respectively. According to the study done by Hansa.G.et.al (12), the maximal values of CIMT in healthy Indian population and CAD population were 0.80 mm and 1.02 mm, respectively. The significant increase in CIMT in these young patients indicate that atherosclerosis could be responsible for most prematurely occurring acute myocardial infarction. It shows the main target in primary prevention should be atherosclerosis risk factors. A study showed that CIMT more than 0.822mm increases the risk of first myocardial infarction.(13)However, in our study, 38 patients had CIMT <0.8mm and eight patients had <0.8 mm which suggested that CIMT may not be a useful surrogate marker of atherosclerosis in the young population.

Previous studies have evaluated the utility of ABI in CAD(14, 15). In a study in African American population, ABI <0.9 showed specificity of 77% and sensitivity of 85% for predicting multi-vessel or left main diseases.(16)In our study, we got an average ABPI of 1.04 for normal coronary angiogram patients and 0.77 for TVD patients. Only three patients had ABPI of less than 0.9 reflecting ABPI is not a good marker of atherosclerosis in this age group.

Furthermore, the levels of serum thrombotic markers including TPA and PAI-1 were found to be high in the young group when compared to elderly group. We observed a significant rise in serum TPA levels (p= 0.006) in acute myocardial infarction patients compared to elderly patients. Literature state that TPA antigens at initial stage of presentation of acute myocardial infarction has strong association with higher short-term risk of death. Thus, TPA might be considered as a useful prognostic biomarker for the early risk stratification in young patients but more valid studies randomized are required to implement it in clinical practice. The rise in PAI-1 (p =0.08) levels were showing a trend towards significance but did not satisfy statistically.

The mean serum ant thrombin-III levels in young and elder group were 360.5µg/ml and 378µg/ml respectively, and they were almost the same with no significant difference.

Study limitations

The main limitations of the study were small sample size and unstructured design of the study. The study also done limited workup for thrombophilia evaluation and thus larger and well-designed studies on large number of patients are required to prove the same and to implement this in routine clinical practice for young patients with CAD

Table 1 Baseline demography of 46 young patients with coronary artery disease

Characteristics		n=46
Age, years (mean ± SD)		37.96 ± 4.59
Age distribution, n (%)		
• 20-29 years		2(4.3%)
• 30-35 years		13(28.3%)
• 36-40 years		18(39.1%)
• 41-45 years		13(28.3%)
Male, n (%)		38 (82.6%)
Smokers, n (%)		30 (65.2%)
• 2-5 years		5 (10.9%)
• >5 years		25 (54.3%)
Diabetes mellitus, n (%)		13 (28.2%)
Hypertension, n (%)		11 (24%)
Body mass index, n (%)		
• 18.5-22.99 kg/m^2		24(52.2%)
• 23-24.99 kg/m^2		14(30.4%)
• 25-29.99 kg/m^2		5(10.9%)
• 30-34.99 kg/m^2		3(6.5%)
Waist Hip Ratio, n (%)		
Male	<0.9	25 (65.8%)
	>0.9	13 (34.2%)
Female	<0.8	2 (25%)
	>0.8	6 (75%)
Clinical Presentation, n (%)		
• Chest pain		42 (91.3%)
<6 hours		16 (38%)
6-12 hours		19 (45.2%)
>12 hours		9 (21.4%)
• Diaphoresis		26 (56.5%)
• Shortness of breath		17 (39.9%)
• Palpitations		10 (21.7%)
• Giddiness		2 (4.3%)
• Sudden collapse		2 (4.3%)

Table 2 lipid profile, KILLIP classification and time to thrombolysis of 46 young patients with coronary artery disease

Characteristics		n=46
Lipid profile		
Total cholesterol (mg/dl)	<200	34 (73.9%)
	≥200	12 (26.1%)
HDL (mg/dl)	Women: <40	6 (75%)
	Men: <50	13 (34.2%)
TG (mg/dl)	<150	26 (56.5%)
	≥150	20 (43.5%)
Ratio of TC/HDL	<4.5	30 (65.2%)

LDL (mg/dl)	>4.5	16 (34.8%)
	<100	24 (52.2%)
	100-129	14 (30.4%)
	≥130	8 (17.4%)
KILLIP classification		
•	Class-I	34 (73.9%)
•	Class-II	7 (15.2%)
•	Class-III	3 (6.5%)
•	Class-IV	2 (4.3%)
Time to thrombolysis		
Mean thrombolysis time		41.5 minutes
Thrombolysis done		42 (91.3%)
•	<30 min	10 (21.7%)
•	30-60 min	26 (56.5%)
•	>60 min	1 (2.2%)
•	Thrombolysed outside	5 (10.9%)

HDL: high density lipoprotein; LDL: low density lipoprotein; TG: triglyceride; TC: total cholesterol

Table 3 Specific cardiological findings of 46 young patients presented with STEMI

Characteristics	N=46 young patients (<45 years)
ECG findings	
• Anterior septal wall MI	23 (50%)
• Extensive anterior wall MI	6 (13%)
• Lateral wall MI	1 (2.2%)
• Inferior wall MI	12 (26.1%)
• Inferior wall MI with posterior infarction	2 (4.3%)
• Inferior wall MI with right ventricular infarction	2 (4.3%)
2D Echocardiographic findings	
• Normal	6 (13.1%)
• Hypokinesia	40 (86.9%)
• Anterior	19 (41.3%)
• Inferior	15 (32.6%)
• Septal	3 (6.5%)
• Global	3 (6.5%)
Coronary angiography (41 patients)	
• Abnormal	38 (31.7%)
• Single vessel disease	20 (48.7%)
• Double vessel disease	6 (14.6%)
• Triple vessel disease	2 (4.8%)
Carotid intima-media thickness (CIMT), mm	
• Normal coronaries	0.56 ± 0.023
• Single vessel disease	0.60 ± 0.020
• Double vessel disease	0.75 ± 0.005
• Triple vessel disease	0.90 ± 0.000

STEMI: ST-elevation myocardial infarction; ECG: electrocardiogram; and MI: myocardial infarction

Table 4 Comparison of various biomarkers in younger and elderly patients with coronary artery disease

	Elderly patients (43 patients)	Younger patients (46 patients)	p-value
Serum tissue plasminogen activator, (ng/ml)			
Mean ± SD	1.21±0.66	2.08±2.33	0.020
<2.5	42(97.7%)	35(77.8%)	
2.5-5.5	1(2.3%)	4(8.9%)	0.006
>5.5	00	6(13.3%)	
Serum plasminogen activator inhibitor-1, (ng/ml)			
Mean ± SD	21.58±9.31	25.28±10.26	0.080
<20	20 (46.5%)	13 (28.9%)	
20-40	23 (53.5%)	29 (64.4%)	0.070
>40	00	3 (6.7%)	
Antithrombin-III, (µg/ml)			
Mean ± SD	378.09±167.48	360.58±135.59	0.590
<100	0(0%)	2(4.4%)	
101-200	4(9.3%)	3(6.7%)	0.276
201-300	12(27.9%)	7(15.6%)	
>300	27(62.8%)	33(73.3%)	

Table 5 Distribution of various risk factors in relation to coronary angiographic findings

	CIMT (mm)	PAI-1 (ng/dl)	TPA (ng/dl)	AT-III (µg/dl)	BMI (kg/m^2)	ABPI	LDL-C (mg/dl)
SVD	0.60	23.3	1.88	365.1	24.6	1.03	102.8
DVD	0.75	18.5	1.45	265.1	24.7	1.05	110.0
TVD	0.90	19.8	0.90	112.5	27.0	0.77	123.0
Normal	0.56	30.2	2.88	401.1	24.6	1.07	98.1

SVD: single vessel disease; DVD: double vessel disease; TVD: triple vessel disease; CIMT: carotid intima media thickness; PAI-I: plasminogen activator inhibitor-1; TPA: tissue plasminogen activator; AT-III: antithrombin-III; BMI: body mass index; ABPI: ankle-brachial pressure index; and LDL-C: low density lipoprotein cholesterol

Conflict of interest: None
Funding source: None
Acknowledgement: None

CONCLUSION

In young STEMI patients, smoking and dyslipidemia are major contributing factors of CAD; this could be due to change in lifestyle pattern. In young STEMI, CIMT and ABPI don't appear to be useful surrogate markers of atherosclerosis unlike in the elderly. Thrombophilia whether inherited or acquired seems to have a role to play in the young STEMI patients and would be worthwhile studying further in larger studies, especially TPA and PAI-1.

Reference

1. Choudhury L, Marsh JD. Myocardial infarction in young patients. *The American journal of medicine*. 1999;107(3):254-61.
2. Egred M, Viswanathan G, Davis G. Myocardial infarction in young adults. Postgraduate medical journal. 2005;81(962):741-5.
3. Liapis CD, Avgerinos ED, Kadoglou NP, Kakisis JD. What a vascular surgeon should know and do about atherosclerotic risk factors. *Journal of vascular surgery*. 2009;49(5):1348-54.
4. Kanitz MG, Giovannucci SJ, Jones JS, Mott M. Myocardial infarction in young adults: risk factors and clinical features. *The Journal of emergency medicine*. 1996;14(2):139-45.
5. Sricharan K, Rajesh S, Rashmi, Meghana H, Badiger S, Mathew S. Study of acute myocardial infarction in young adults: risk factors, presentation and angiographic findings. J*ournal of clinical and diagnostic research*. 2012;6(2):257-60.
6. Nigam P, Narain V, Hasan M. Serum lipid profile in patients with acute myocardial infarction. Indian journal of clinical biochemistry. 2004;19(1):67.
7. Nicolo D, Monestier M. Antiphospholipid antibodies and atherosclerosis. Clinical Immunology. 2004;112 (2):183-9.
8. Vaarala O, Puurunen M, Mänttäri M, Manninen V, Aho K, Palosuo T. Antibodies to prothrombin imply a risk of myocardial infarction in middle-aged men. Thrombosis and haemostasis. 1996;75(03):456-9.
9. Coller B, Owen J, Jesty J, Horowitz D, Reitman M, Spear J, *et al*. Deficiency of plasma protein S, protein C, or antithrombin III and arterial thrombosis. Arteriosclerosis: An Official *Journal of the American Heart Association*, Inc. 1987;7(5):456-62.
10. Siwach S, Singh H, Sharma D, Katyal V. Profile of young acute myocardial infarction in Harayana. *The*

Journal of the Association of Physicians of India. 1998;46 (5):424-6.
11. Ca R, Mithun C, Iypec M. The Clinical Profile and Prognostic factors of Acute Myocardial Infarction in the Young–YSSI Study. Kerala Medical Journal. 2013;6(1):4.
12. Hansa G, Bhargava K, Bansal M, Tandon S, Kasliwal RR. Carotid intima-media thickness and coronary artery disease: An Indian perspective. Asian Cardiovascular and Thoracic Annals. 2003;11 (3):217-21.
13. Aminbakhsh A, Mancini GJ. Carotid intima-media thickness measurements: what defines an abnormality? A systematic review. Clinical and investigative medicine. 1999;22 (4):149.
14. Ezhumalai B, Krishnasuri SD, Jayaraman B. Comparison of diagnostic utilities of ankle–brachial index and Carotid intima-media thickness as surrogate markers of significant coronary atherosclerosis in Indians. *Indian heart journal*. 2013;65(2):137-41.
15. Su HM, Voon WC, Lin TH, Lee KT, Chu CS, Lee MY, *et al*. Ankle-Brachial Pressure Index Measured Using an Automated Oscillometric Method as a Predictor of the Severity of Coronary Atherosclerosis in Patients with Coronary Artery Disease. *The Kaohsiung journal of medical sciences*. 2004;20 (6):268-72.
16. Otah KE, Madan A, Otah E, Badero O, Clark LT, Salifu MO. Usefulness of an abnormal ankle-brachial index to predict presence of coronary artery disease in African-Americans. *The American journal of cardiology*. 2004;93(4):481-3.

How to cite this article:

Rakesh Tumula, Jenny Madhuri Gudivada and Malladi Srinivasarao (2020) 'Evaluation of Thrombophilic and Atherosclerotic Markers in Young Patients (<45 Years) with St-Segment Elevated Myocardial Infarction', *International Journal of Current Advanced Research,* 09(04), pp. 22001-22005. DOI: http://dx.doi.org/10.24327/ijcar.2020.22005.4333

****