

TERRITORIAL IMPACT ON CLINICAL OUTCOMES IN YOUNG POPULATION WITH ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

Kamran Ahmed Khan¹, Mahesh Kumar Batra¹, Dileep Kumar¹, Sajjad Ali², Vinesh Kumar¹, Rajesh Kumar¹, Danish Qayyum¹, Tahir Saghir¹, Abdul Samad Achakzai¹, Jawaid Akbar Sial¹, Musa Karim¹

1 National Institute of Cardiovascular Diseases, Karachi, Pakistan

2 Ziauddin Medical University, Karachi, Pakistan

Address for Correspondence:

Kamran Ahmed Khan

Assistant Professor of Cardiology,
National Institute of Cardiovascular
Diseases, Karachi, Pakistan

Emails: kamran00480@yahoo.com

Contribution

KAK conceived the idea and designed the study. Data collection and manuscript writing was done by KAK, MKB, DK, SA, VK, DQ, ST, ASA, JAS, and MK. All the authors contributed equally to the submitted manuscript.

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ABSTRACT

Objective: ST-segment elevation myocardial infarction (STEMI) at younger age though infrequent but very crucial entity, but there is dearth of available data, however, a rising trend has noticed recently in Asian countries. The aim was to see the territorial and clinical profile influence on overall outcomes of young individuals (≤ 35 years) with STEMI.

Methodology: Patients with STEMI having age of ≤ 35 years during August 2020 to December 2020 were recruited and divided into left anterior descending artery (LAD)-culprit and non-LAD-culprit STEMI groups in this prospective observational study. Territorial angiographic and clinical characteristics were compared.

Results: 1435 STEMI patients underwent coronary angiogram, 5.3% (94) were ≤ 35 years of age. LAD was culprit in 74.4% of STEMI mainly as a single vessel disease (SVD) involving the proximal segment as major territorial angiographic finding while 25.5% were non-LAD-culprit STEMI. Obesity, smoking, smokeless tobacco use especially gutka, were frequent in LAD-culprit group. In-hospital and at 3 months mortality was 2.1% (2) and 7.1% (5) respectively, all related to LAD territory. Rate of safe discharges and back to routine was 97.2% vs.100% and 70% vs.79.1% (72), respectively were comparable in both groups.

Conclusion: LAD predominantly its proximal segment is the commonest culprit territory in patients with STEMI in youth with significant association to obesity, smoking and smokeless tobacco use especially gutka. LAD-culprit STEMI is the major territorial determinant for mortality and heart failure, however, overall clinical outcomes were reasonably good and comparable with non-LAD-culprit STEMI considering alive discharges and back to routine life.

Keywords: STEMI, premature CAD, angiographic territory, outcomes, young

INTRODUCTION

An acute ST-segment elevation myocardial infarction (STEMI) is defined by transmural ischemia of myocardium results in cardiac muscle injury or necrosis, as a result of abrupt cessation of blood supply through the epicardial coronaries.¹ New ST-segment elevation is defined by elevation at the level of J-point in 2 contiguous leads with the cut-off of ≥ 1 mm in all leads other than leads V2 –V3 where the cut-point is ≥ 2 mm in men and ≥ 2.5 mm in men or new or presumably new onset left bundle branch block (LBBB) considered as STEMI equivalent as per European Society of Cardiology (ESC)/American College of Cardiology Foundation (ACCF).² The complete clinical definition of myocardial infarction (MI) also needs the confirmation of the cardiac muscle ischemic injury with abnormal rise or fall of cardiac biomarkers.³ Worldwide, STEMI is a major cause of morbidity and mortality among acute myocardial infarction (AMI), and its burden can be exponential if it affects younger individuals as they are commonly the most productive economical group and usually breadwinners of their family. Multifarious studies have focused that subset of individuals and depicted its incidence somewhere between 2 to 10 % in varying age of up to 45 years.⁴

The overall lifestyle of younger population, distinguished by their high job stress, rapid pace, overexertion, smoking and overeating, which are likely the predisposing factors for causing disturbances in internal milieu, in the form of atherosclerosis that enhances the incidence of AMI.⁵ In a study by Cases et al.⁶ reported that of 6892 STEMI patients who required percutaneous coronary intervention (PCI), smoking history was found in 46.4% vs. 20.5% of general population. There are Studies from China and other regions showed rate of smoking as high as 70-90% in young victims of AMI.⁷ Although the rate of acute coronary syndrome (ACS) has reduced in older populations, however younger individuals have not had similar pattern of decline (especially men) in cardiovascular events.⁸ Urbanization, obesity, overweight and drug abuse are other principal factors that impose a greater risk for younger individuals for CAD.

Moreover, ACS in younger population is distinct from the older subset as a result of their more thrombogenic internal milieu, which might be more

susceptible to aggressive pharmacological measures.⁹ Fibrinogen and HbA1c are also correlated with STEMI in patients ≤ 44 years of age without preceding angina pectoris.¹⁰ Dyslipidemia is also recognized as a major and modifiable contributor to cardiovascular diseases (CVDs) worldwide. Mainly the accumulated load of low density lipoprotein cholesterol (LDL-C) exposure over the lifetime highlighting the value of early identification and interventions to achieve optimal cholesterol levels during young adulthood.¹¹

In a study by Ricci, B et al. reported STEMI as the most common clinical presentation of ACS up to 68% in the younger age and found a higher incidence of non-obstructive CAD of up to 11.4%.¹² Even a significantly higher incidence of STEMI presentation has been observed in the recent years in South Asian population at younger age and a continuously rising trend of ACS patients has been witnessed in the last decade. The current study was proposed to see the overall burden of STEMI cases among ACS patients at a younger age of ≤ 35 years and to insight the impact of territorial involvement and risk factors profile on overall clinical outcomes in this substrate.

METHODOLOGY

The present study was designed as a prospective observational one for patients managed at a tertiary care hospital in the southern region of Pakistan mainly comprise urban population. Out of all STEMI patients (n=1435) who underwent coronary angiogram from August 2020 to December 2020, 5.3 % (n=94) were younger up to the age of ≤ 35 years, were recruited and analysed. Subsequently these patients were split-up into two main groups based on their angiographically territorial culprit artery as left anterior descending artery (LAD)-culprit group and non-LAD-culprit group. The non-LAD group comprised left circumflex artery (LCx) and right coronary artery (RCA) as angiographically territorial culprit vessel for STEMI.

The criteria for inclusion was to enroll all patients satisfying the criteria for diagnosis of STEMI as defined by ESC/ ACCF as new ST- segment elevation at the level of J-point in 2 contiguous leads

with the cut-off of ≥ 1 mm in all leads other than leads V2–V3 where the cut-off is ≥ 2 mm in men and ≥ 2.5 mm in women or new or presumably new onset left bundle branch block (LBBB) in electrocardiography (ECG). Patients with early repolarization ECG changes, initially taken as STEMI were excluded after documentation of angiographically normal coronaries and negative biomarkers, so as all patients with cardiomyopathies, perimyocarditis, congenital heart disease and atypical chest pain were also excluded.

Since there noticed to be a wide discrepancy in the size of sample of young individuals and the older age group in a study conducted by Batra MK et al.¹³, therefore sample size was calculated through systematic sampling. Data pertaining to age, gender, body mass index (BMI), smoking, history of smokeless chewable tobacco like plain tobacco, gutka (a kind of flavored tobacco mixed with crushed areca nut, catechu and paraffin wax) or paan (tobacco combined with areca nut and betel leaf) or naswar (moist powdered tobacco), drug abuse, alcohol use, family history of early onset CAD, hypertension, dyslipidemia, diabetes, and history of prior CAD was noted at the time of presentation through self-report after written and informed consent. The BMI was defined as per classification by World Health Organization (WHO), being 25-29.9 were classified as overweight and > 30 as obese. Dyslipidemia was labelled as having total serum cholesterol of ≥ 200 mg/dl, triglyceride (TG) > 150 mg/dl, high density lipoprotein < 40 mg/dl in men or < 50 mg/dl in women and low density lipoprotein (LDL) > 130 mg/dl. All patients were subjected for complete baseline biochemical and hematological investigations. Left ventricular ejection fraction (LVEF) was documented by echocardiography.

All patients underwent coronary angiogram via femoral or radial route after performing Allen's test using standard technique. Angiographic severity of coronary disease was evaluated by at least 2 experienced Cardiologist in at least two orthogonal views visually. Lesions with narrowing $\geq 70\%$ in epicardial coronaries including LCx, RCA, LAD or their major branches and $\geq 50\%$ in left main coronary artery (LMCA) were defined as obstructive. Rest of the lesions were grouped as non-obstructive. Lesion lengths were categorized as Type A (≤ 10 mm), Type B (10-20mm) and Type C (> 20 mm) and localized as proximal, mid or distal based on American College of Cardiology/American heart Association (ACC/AHA) classification. CAD was further characterized as single vessel disease (SVD), two vessel disease (2VD) or three vessel

disease (3VD).¹⁴ Method of definitive management was described as conservative medical management alone, early invasive or primary PCI and coronary artery bypass grafting (CABG).

Overall clinical outcomes were manifested as major adverse cardiovascular events (MACE) and were reported as all-cause mortality, cerebrovascular accident (CVA), heart failure (HF), arrhythmias, re-infarction and repeat revascularization in-hospital and at 3 months in post discharge follow up. Moreover, patients were evaluated for medication compliance and back to their routine or job at 3 months follow up.

Collected data were entered in to IBM SPSS (version 21), after quality assessment of data the analysis were conducted. Study variables were summarized with the help of appropriate descriptive statistics such as frequency and percentages and mean \pm standard deviation (SD). Data were stratified into two groups based on angiographic involvement of culprit territory as LAD-culprit and non-LAD-culprit groups. Study results in LAD-culprit were compared with non-LAD-culprit by applying Student's t-test or Mann-Whitney U test for continuous variables and Chi-square test or fisher exact test for categorical variables. A two-tailed p-value ≤ 0.05 was considered as significant.

RESULTS

Out of 1435 STEMI patients who underwent coronary angiogram during the study period, 5.3% (94) found to be younger with 20-35 years of age recruited according to study protocol and analyzed. Out of these 2.0% (29) were between 20 to 30 years and 4.5% (72) were between 30 to 35 years. The youngest patient was a male with age of 23 years with AWM. Of 94 younger patients with STEMI, LAD was found as territorial culprit in 74.5% (n=70) and characterized as LAD-culprit group while in only 25.5% (n=24) RCA and LCx were diagnosed as angiographically culprit and together grouped as non-LAD-culprit group. Male sex was predominant in both groups 90% (n=63) vs. 79.2% (n=19), a bit higher in LAD-culprit group. Overweight 62.8% (n=59) and obesity 19.1% (n=18) was a prominent risk factor overall in this patients' subset, however, obese were found to be more in LAD-culprit group 22.9% (n=16) vs. 8.3% (n=2). Smoking was found in 44.7% (n=42) overall, out of which predominant proportion was detected to be again in LAD-culprit group, 50% (n=35) vs. 29.2% (n=7). Use of smokeless tobacco as a whole was 13.9% (n=13) of

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which majority were consuming gutka 61.5% (n=8), which was too more common in LAD-culprit group. No significant difference in occurrence of conventional risk factors like family history of premature CAD 12.9% vs.12.5%, diabetes 11.4% vs.16.7%, hypertension 22.9% vs. 29.2%, dyslipidemia 7.1% vs. 8.3% and chronic kidney disease (CKD) 1.4% vs.0 %, were noted between the two groups (Table 1). Interestingly LAD was not the cause of all AWMIs as usually expected, but only in 92.9% vs.7.1% ($p \leq 0.001$), its involvement results in IAWMI as per ECG finding due to the wrap around supply of inferior wall. Similarly in 4.2% RCA involvement resulted in AWMIs electrocardiographically due to the predominant supply of anterior territory by the super dominant RCA and short type I LAD (Figure 1).

Table 1: Baseline demographic and clinical characteristics of young patients stratified by territorial involvement

	Total	Territorial Involvement		P-value
		LAD-culprit	Non-LAD-culprit	
Total (N)	94	70 (74.5%)	24 (25.5%)	-
Gender				
Male	87.2% (82)	90% (63)	79.2% (19)	0.170
Female	12.8% (12)	10% (7)	20.8% (5)	
Age (years)	32.17 ± 3.49	32.04 ± 3.59	32.54 ± 3.23	0.548
20-30 years	30.9% (29)	32.9% (23)	25% (6)	0.472
31-35 years	69.1% (65)	67.1% (47)	75% (18)	
Body mass index (kg/m ²)	27.2 ± 3.28	27.39 ± 3.48	26.65 ± 2.61	0.344
Under weight	1.1% (1)	0% (0)	4.2% (1)	0.086
Normal weight	17% (16)	18.6% (13)	12.5% (3)	0.495
Over weight	62.8% (59)	58.6% (41)	75% (18)	0.151
Obese	19.1% (18)	22.9% (16)	8.3% (2)	0.119
Heart Rate (bpm)	84.84 ± 13.99	85.09 ± 14.35	84.13 ± 13.13	0.773
Systolic	130.72	130.06	132.67 ±	0.536

blood pressure (mmHg)	± 17.71	± 18.43	15.62	
Diastolic blood pressure (mmHg)	84.97 ± 13.44	84.81 ± 13.45	85.42 ± 13.7	0.851
Smoking	44.7% (42)	50% (35)	29.2% (7)	0.076
Current smokers	85.7% (36)	85.7% (30)	85.7% (6)	>0.99
Ex-smokers	14.3% (6)	14.3% (5)	14.3% (1)	
Smokeless tobacco use	13.8% (13)	14.3% (10)	12.5% (3)	0.827
Paan	15.4% (2)	10% (1)	33.3% (1)	0.326
Gutka	61.5% (8)	70% (7)	33.3% (1)	0.252
Naswar	23.1% (3)	20% (2)	33.3% (1)	0.631
Chewable tobacco	23.1% (3)	30% (3)	0% (0)	0.279
Alcohol consumption	1.1% (1)	0% (0)	4.2% (1)	0.086
Diabetes Mellitus	12.8% (12)	11.4% (8)	16.7% (4)	0.507
IDDM	83.3% (10)	87.5% (7)	75% (3)	
NIDDM	16.7% (2)	12.5% (1)	25% (1)	0.584
Hypertension	24.5% (23)	22.9% (16)	29.2% (7)	0.535
Positive Family History	12.8% (12)	12.9% (9)	12.5% (3)	0.964
Dyslipidemia	7.4% (7)	7.1% (5)	8.3% (2)	0.848
Chronic kidney disease	1.1% (1)	1.4% (1)	0% (0)	0.556

LAD= left anterior descending artery, IDDM = insulin dependent diabetes, NIDDM = non-insulin dependent diabetes

In the spectrum of angiographic profile, though majority of the patients were found to have SVD 68.1% (n=64) overall, but among two studied group, SVD and non-obstructive or re-canalized vessels were predominant in LAD-culprit group than non-LAD-culprit group, 71.4% vs. 58.3% and 11.4% vs. 4.2% respectively, while 3VD was significantly more frequent in non-LAD culprits group, 16.7% vs. 2.9%

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($p=0.017$). Of note in the context of segmental involvement, proximal location was significantly higher in the LAD-culprit STEMI than non-LAD-culprit STEMI 78.6% vs. 20.8%, $p\leq 0.001$, while mid and distal locations were significantly more pronounced in RCA or LCx (non-LAD-culprit group), 50% vs. 18.6% ($p=0.003$) and 29.2% vs. 2.9% ($p\leq 0.001$) respectively. There was no significant difference noted in the length of lesion characteristics as described by ACC/AHA, all Type A, B or C lesions were comparable between the two groups, however overall Type B lesion was found to be more dominant in combined groups 43.6% ($n=41$). LVEF between 30-40% by echocardiography was found to be significantly more pronounced in LAD-culprit group than non-LAD-culprit group 62.9% vs. 8.3% ($p\leq 0.001$), while LVEF $>40\%$ was significantly predominant in non-LAD-culprit group 91.7% vs. 27.1% ($p\leq 0.001$). Furthermore, only 7.4% ($n=7$) overall were demonstrated to have LVEF $<30\%$ and all of them were belonged to LAD-culprit group. The predominant strategy of definitive management was primary PCI and it was comparable in both groups 82.9% vs. 91.7%, as majority of the patients were presented within the given time limit of reperfusion, however, considerable number of patients though statistically not significant 14.3% vs. 8.3% ($p=0.45$) were managed with medical treatment alone due to presence of re-canalized non-obstructive disease in LAD-culprit group.

Table 2: Angiographic characteristics and management of young patients stratified by territorial involvement

	Total	Territorial Involvement		P-value
		LAD-culprit	Non-LAD-culprit	
Total (N)	94	70	24	-
Type of ST-segment elevation myocardial infarction (STEMI)				
AWMI	70.2% (66)	92.9% (65)	4.2% (1)	<0.001 *
IWMI	29.8% (28)	7.1% (5)	95.8% (23)	
Number of vessels				
Single vessel disease	68.1% (64)	71.4% (50)	58.3% (14)	0.235
Two vessel disease	16% (15)	14.3% (10)	20.8% (5)	0.450
Three vessel	6.4% (6)	2.9% (2)	16.7% (4)	0.017*

disease	(6)	(2)	(4)	
NOCAD	9.6% (9)	11.4% (8)	4.2% (1)	0.297
Involved vessel				
Left main	2.1% (2)	2.9% (2)	0% (0)	0.403
Re-canalized vessels	9.6% (9)	11.4% (8)	4.2% (1)	0.297
Lesion Location				
Proximal	63.8% (60)	78.6% (55)	20.8% (5)	<0.001 *
Mid	26.6% (25)	18.6% (13)	50% (12)	0.003*
Distal	9.6% (9)	2.9% (2)	29.2% (7)	<0.001 *
Lesion Length				
Type A (discrete $<10\text{mm}$)	27.7% (26)	27.1% (19)	29.2% (7)	0.848
Type B (10 to 20mm)	43.6% (41)	44.3% (31)	41.7% (10)	0.823
Type C (diffuse $>20\text{mm}$)	28.7% (27)	28.6% (20)	29.2% (7)	0.956
Left ventricular ejection fraction (%) – echocardiography				
$<30\%$	7.4% (7)	10% (7)	0% (0)	0.107
30 to 40%	48.9% (46)	62.9% (44)	8.3% (2)	<0.001 *
$>40\%$	43.6% (41)	27.1% (19)	91.7% (22)	<0.001 *
Management strategy				
Primary PCI	85.1% (80)	82.9% (58)	91.7% (22)	0.296
Early Invasive PCI	1.1% (1)	1.4% (1)	0% (0)	0.556
Medical Treatment Only	12.8% (12)	14.3% (10)	8.3% (2)	0.451
CABG	1.1% (1)	1.4% (1)	0% (0)	0.556

LAD= left anterior descending artery, AWMI= anterior wall myocardial infarction, IWMI= inferior wall myocardial infarction, PCI = percutaneous coronary intervention, CABG =coronary artery bypass grafting, NOCAD = non obstructive coronary artery disease

With regard to in-hospital outcomes, overall MACE was predominantly higher in LAD-culprit group mainly due to HF 20% vs. 0% ($p=0.018$) and all-cause mortality 2.9% vs. 0% ($p=0.403$), however majority of patients were discharged safely and alive in both groups. At 3 months 6 patients were lost to

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follow up, all belonging to LAD-culprit group and 91.5% (86) patients were closely followed up after discharge. After 3 months, all-cause mortality was increased by 4.8 % (n=3) and reached a cumulative all-cause mortality of up to 7.1% (n=5), interestingly all mortality were belonging to LAD-culprit group, indicating the prognostic significance of proximal LAD as highlighted in the study results. However, no significant difference noted between the two groups in medication compliance and going back to usual routine or work at 3 months 95.2% vs.95.8% and 75.8% vs.75 % respectively.

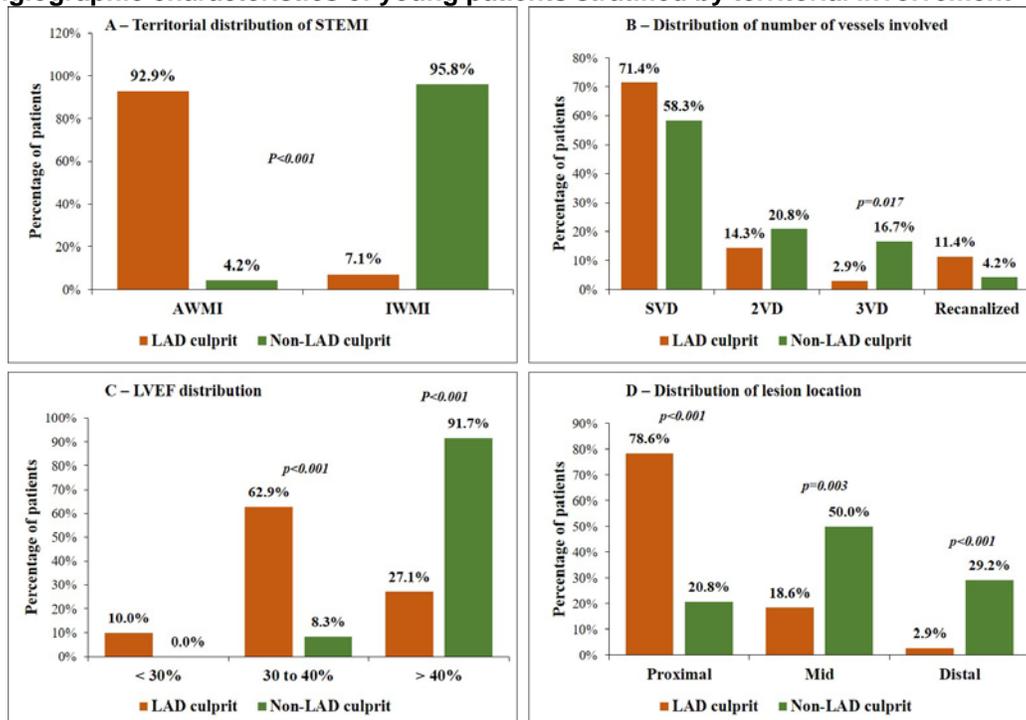
Table 3: Post procedure in-hospital and three months outcome of young patients stratified by territorial involvement

	Total	Territorial Involvement		P-value
		LAD-culprit	Non-LAD-culprit	
Total (N)	94	70	24	-
In-hospital outcomes				
Re-infarction	1.1% (1)	1.4% (1)	0% (0)	0.556
Repeat revascularization	1.1% (1)	1.4% (1)	0% (0)	0.556
Heart failure	14.9%	20%	0% (0)	0.018

(HF)	(14)	(14)		*
Arrhythmias	6.4% (6)	7.1% (5)	4.2% (1)	0.607
Expired	2.1% (2)	2.9% (2)	0% (0)	0.403
Successful 3-month follow-up	91.5% (86)	88.6% (62)	100% (24)	0.083
Follow-up outcomes				
Expired	3.5% (3)	4.8% (3)	0% (0)	0.303
Re-infarction	2.3% (2)	3.2% (2)	0% (0)	0.403
Repeat revascularization	1.2% (1)	1.6% (1)	0% (0)	0.556
Cerebrovascular accident	2.3% (2)	3.2% (2)	0% (0)	0.403
Hospitalization due to HF	2.3% (2)	3.2% (2)	0% (0)	0.403
Medication compliance	95.3% (82)	95.2% (59)	95.8% (23)	0.114
Back to routine/work	75.6% (65)	75.8% (47)	75% (18)	0.108
Cumulative mortality	5.3% (5)	7.1% (5)	0% (0)	0.178

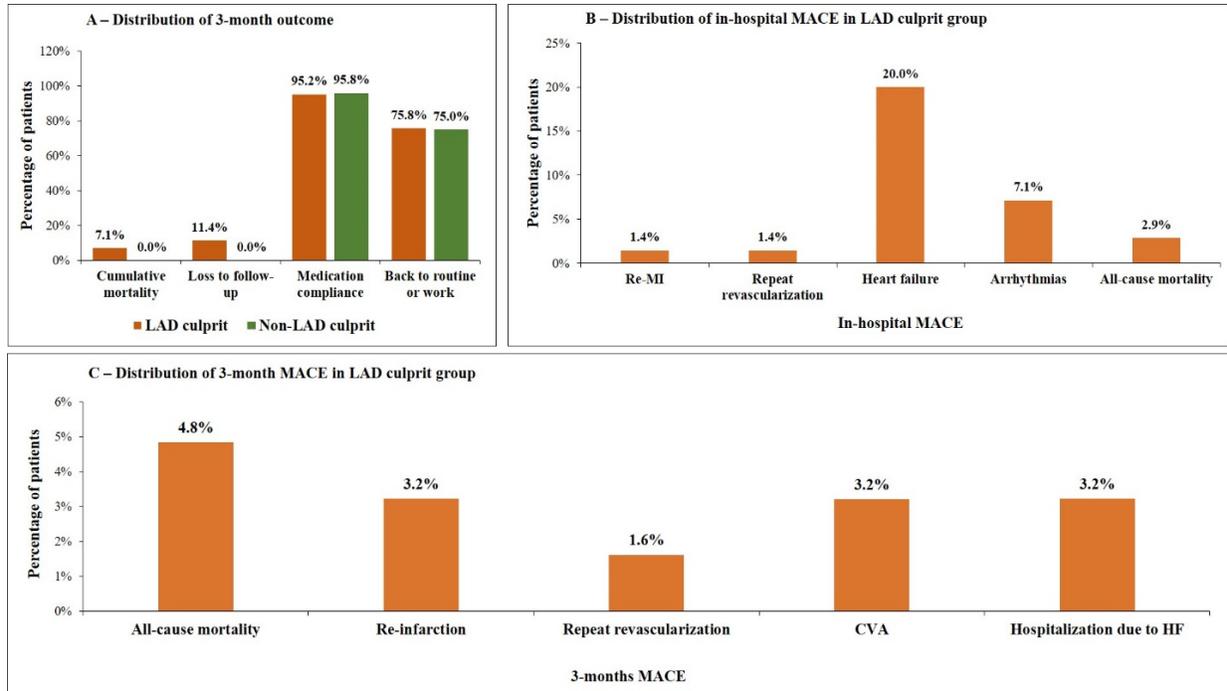
LAD= left anterior descending artery

Figure 1: Angiographic characteristics of young patients stratified by territorial involvement



STEMI=ST-segment elevation myocardial infarction, LAD= left anterior descending artery, AAMI= anterior wall myocardial infarction, IAMI= inferior wall myocardial infarction, SVD=single vessel disease, 2VD=two vessel disease, 3VD=three vessel disease, LVEF=left ventricular ejection fraction

Figure 2: Management, post procedure in-hospital and three months MACE of young patients with culprit LAD



LAD= left anterior descending artery, MACE=major adverse cardiovascular events, MI= myocardial infarction, CVA= cerebrovascular accident, HF=heart failure

DISCUSSION

The present study is one of the biggest prospective observational study with a central focus on youth having age range from 20 to 35 years with STEMI and underwent coronary angiogram, conducted at a high volume center in Pakistan, with their short follow up at 3 months. STEMI in earlier age has been the subject of curiosity and various studies has probed into this matter in several aspect, but major part of literature addressed the age substrate of 35–45 years.^{15,16} The present study focused only on those 94 (5.3%) younger STEMI patients who were ≤ 35 years of age and were extracted from a big sample size of 1435 STEMI patients who presented during the study period to that center. The selected patients were further split-up into two groups based on territorial involvement as LAD culprit or non-LAD culprit to highlight the demographic, angiographic and prognostic importance of territorial distribution of STEMI. Out of all younger STEMI, 29 (2.0%) were in the age range between 20 to 30 years and were

almost comparable in the two studied group 32.9% vs. 25%, however it is actually a really higher frequency compared with earlier studies, where its frequency was found to be <1%.^{17,18} Male gender has been extensively reported as a risk factor for development of CAD, mainly as a result of negative effect of androgens on development of CAD resulting in deviated sex distribution in this age group as this was also the case in the current study with 87.2% (n=82) patients were being male overall and there were no significant disparity in the LAD-culprit and non-LAD culprit group 90% vs. 79.2%, (p=0.17).¹⁹ Shielding influence of estrogen against atherosclerotic process in female gender and higher frequency of smoking in male sex have been ascribed for male propensity.²⁰ Smoking has always been considered as pivotal but modifiable risk predisposing factor in young patients for development of ACS due to nicotine vulnerability for creation of hypercoagulable milieu or spasm,²¹ however, in this study, smoking frequency was found to be predominant in LAD-culprit group, 50% vs. 29.2% and similar results were also observed in

the use of smokeless tobacco specially gutka (which is a kind of flavored tobacco grind with crushed areca nut, catechu and paraffin wax as explained earlier) suggesting smokers and smokeless tobacco user are more prone to develop STEMI due to LAD involvement.

High BMI in the range of overweight or obesity was of critical importance in the risk factor profile of younger population overall, apparently associated with unhealthy living style or dining out frequently junk food and poses a significant threat for early development of CAD, however more overweight patients 75% vs.58.6% were detected in non-LAD-culprit group, while high frequency of obese 22.9% vs.8.3% were found in LAD-culprit group. In their study, Twig et al. found a correlation between BMI and subsequent CVD mortality, in the age range of 17.3 ± 0.4 years more predominantly in midlife. It showed a hazard ratio of 3.0 for BMI in overweight (85th to 94th percentiles) and 4.89 for BMI \geq 95th percentile in obese for mortality from CHD.²² Diabetes mellitus, dyslipidemia and family history of premature CAD were less frequent in the population of consideration, while hypertension was found in a bit higher number, however, the frequency of these traditional risk factors were comparable in the studied groups (Table 1). In earlier studies too the frequency of hypertension has been reported up to 10 to 44 % consistent with the present study results.¹⁸ As it can be depicted from Table 1, that the most frequent mode of presentation was AWTMI 70.2 % (n=66) vs. 29.8% (n=28) of IWMI cases but surprisingly LAD was not the cause of all AWTMI as usually expected, but only in 92.9% vs.7.1% ($p \leq 0.001$) of patients with IWMI, as per ECG finding mainly due to the wrap around supply of inferior wall territory. Similarly in 4.2% RCA involvement resulted in AWTMI electrocardiographically due to the predominant supply of anterior territory by the super dominant RCA and short type I LAD (Figure1). Another interesting point was the frequent finding of SVD and re-canalized vessel in LAD culprit group 71.4% vs. 58.3% and 11.4% vs. 4.2% respectively, while significantly higher frequency of 3VD 16.7% vs. 2.9% was noted in the non-LAD culprit group, suggesting more abrupt clinical manifestation of CAD in LAD-culprit group in contrast to more gradual onset of symptoms in the non-LAD-culprit group.²³ Moreover, LAD-culprit group was characterized by significantly higher localization of disease or plaque rupture in the proximal segment 78.6% vs. 20.8%, ($p \leq 0.001$), while non-LAD-culprit group was distinguished by significantly predominant disease localization in the mid and distal segment 50% vs. 18.6 % ($p = 0.003$) and 29.2% vs. 2.9% ($p \leq 0.001$)

respectively (Figure 1), indicating the more extensive nature of STEMI in LAD-culprit group consequently more predisposition for development of serious consequences. However, the lesion length characteristics in the two groups were comparable as no significant difference was observed in the occurrence of type A, B or C lesions, defined as per AAC-AHA classification, manifesting the nature of lesion had no influence on the clinical presentation between the two groups, however, from interventional aspect it matters a lot, as patients with short lesions with large vessel diameter have reduced rates of MACE at 2 years after stent placement.²⁴ Another astonishing thing in the current study is the prevailing frequency of patients with re-canalized vessels in the LAD-culprit group 11.4% vs. 4.2%, suggesting a distinct mechanism of pathogenesis in this substrate leading to thrombogenic milieu, with significant clot burden, causing occlusion temporarily, resulting in ischemia or infarction. However, cumulative frequency of re-canalized vessels in both groups were in line with the results of contemporary studies like 15.8%, as reported by Iragavarapu T et al. and 16.9% as shown by Maroszyńska-Dmoch et al.^{17,25} Therefore, this young substrate of patients might be better managed with aggressive pharmacological therapy including anticoagulation/fibrinolysis and other guideline directed medical treatment. Higher cumulative frequency of type B or type A lesion $>80\%$ in total, (Table 2), also favoring this school of thought. As majority of patients were presented within the time frame of reperfusion, primary PCI was the predominant definitive management step in both groups with no significant variation 82.9% vs. 91.7%, however a large number of patients 14.3% vs. 8.3%, though statistically not significant were treated with medical management alone due to the presence of frequent re-canalized vessels in LAD-culprit group (Figure 2). Left ventricular ejection fraction (LVEF) as documented by echocardiography, showed significantly higher percentage of patients with LVEF of $< 40\%$ in the LAD-culprit group 62.9% vs. 8.3% ($p \leq 0.001$) while significantly more number of patients were found to have LVEF of $>40\%$ in the non-LAD-culprit group 91.7% vs. 27.1% ($p \leq 0.001$) (Figure 2). Furthermore all patients with LVEF of $< 30\%$ were belonged to LAD-culprit group again depicting the prognostic importance of this group of STEMI.¹⁷ In-hospital outcomes were found to be excellent in both studied group as majority of patients were safely discharged 97.2% vs.100% in LAD-culprit and non-LAD-culprit group respectively. However, in-hospital major adverse cardiovascular events (MACE), heart failure (HF) 20% vs. 0%, $p = 0.018$ was significantly more

frequent and all-cause mortality 2.1% vs. 0% was predominant in LAD-culprit group. Likewise other MACE indicator including re-infarction, repeat revascularization, arrhythmias were predominantly found in LAD-culprit group. At 3 months, cumulative all-cause mortality was extended 7.1 % (n=5) in LAD-culprit group verses no mortality noted in non-LAD-culprit group and similarly rest of other parameters of MACE were only observed in LAD-culprit group. (Figure 2). Interesting but not of surprise all mortality patients were found to have involvement of proximal segment of LAD as culprit their LVEF were <30%, endorsing the prognostic importance of proximal LAD disease (Table 3). Moreover the lesion characteristics were not of diffuse type as usually found in older substrate, but relatively simple and focal lesions were found in this group of younger patients. Moreover no significant difference was observed in terms of medications compliance and back to usual routine or work in the two groups (Figure 2).

This should highlight the point to take the maximum corrective measures for modifiable risk factors that should begin as earlier as possible from childhood one hand and be agile in taking care of all STEMI in young population specially those who presented with AWTMI so as to protect these young economically productive lives. In general, all health care workers are also required to identify STEMI as early as possible and play their part in the management vigorously as time is muscle.

To the extent of our best erudition, this is the biggest prospective observational study conducted at one of the largest cardiac care center of Pakistan focusing on territorial impact and influence of clinical profile or comorbidities on overall outcomes in younger subset with STEMI. One of the major strength of this study is the close follow up of both the studied groups, though short term. Despite that, this study has certain shortcomings like single center coverage and recruitment of mostly urban population. Secondly, due to exclusion of patients who refused for consent for invasive procedure and for participation in the study may have induced certain selection bias. Hence, larger multicenter studies are warranted with more geographical as well as demographical coverage to evaluate and understand the gravity of problem in general population.

CONCLUSION

LAD is the commonest territorial culprit for STEMI in younger population mainly as SVD with predominant

involvement of its proximal location and significant association to obesity, smoking and smokeless tobacco use especially gutka. LAD-culprit STEMI is the major territorial determinant for the MACE both in-hospital and at 3 months mainly in terms of heart failure and mortality, however, overall clinical outcomes were reasonably good and comparable with non-LAD-culprit STEMI considering alive discharges and back to routine life or work.

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