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Clinical risk factors of acute myocardial infarction in young people: Anxiety in the lead?

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ABSTRACT

Background: Multiple risk factors are associated with acute myocardial infarction (AMI) but local data in young patients are limited. The present study explored risk factors of AMI in young patients. *Materials and Methods*: A cross-sectional study (n=224) was conducted on young adults with a recent first AMI and age-matched non-AMI controls. Demographic data, co-morbidities, lifestyle factors, family history, smoking history and anthropometric measures were recorded for each participant. Hamilton anxiety rating scale (HAM-A) was used to assess anxiety levels. Serum cardiac and liver enzymes were also measured. *Results*: AMI patients showed higher mean anxiety scores (25.16 vs. 13.27, p=0.000) and weekly cigarette consumption (4.32 vs. 0.21, p=0.000). 96.42% of AMI patients had moderate to severe anxiety. Other common risk factors included lack of regular exercise (82.14%), hypertension (HTN, 75%), unhealthy diet (66.08%), renal disease (60.71%), sedentary living (53.57%), diabetes mellitus (51.78%) and smoking (50%). Positive family histories of HTN, DM and AMI were observed in 96.42%, 94.64% and 57.14% of patients respectively. *Conclusion*: Anxiety is a major risk factor of AMI in young adults besides other conventional risk factors and controlling them may help lessen the burden of AMI.

Keywords: Acute Myocardial Infarction, Smoking, Anxiety, Hypertension, Diabetes Mellitus, Lifestyle

1. INTRODUCTION

Cardiovascular diseases (CVDs) result in almost one-third of global deaths but rates have declined by more than 10% in the last decade. However, the declining trend has not been uniform across age groups and geographical regions. The developing Asian regions have higher cardiovascular death toll as compared to the western world (Chan et al., 2016). Younger adults presenting with acute myocardial infarction (AMI) have also not shown decline similar to that observed in elderly populations and AMI in young persons is now reaching up to 10% of the total disease burden (Dreyer et al., 2017; Ge et al., 2017; Gulati et al., 2020). AMI is a leading cardiovascular cause of mortality and disability worldwide. Several potential modifiable risk factors for AMI in young patients have been identified including clinical,

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biochemical, pathological, anthropometric, dietary and lifestyle elements (Alboni et al., 2008; Ge et al., 2017; Gulati et al., 2020; Shah et al., 2021). Conventional non-modifiable risk factors such as family histories of hypertension (HTN) and diabetes mellitus (DM) are also linked to development of AMI at a young age.

Smoking, a strong modifiable risk factor of AMI in older patients, has particularly been highlighted as an independent risk factor for AMI in young adults (Hbejan, 2011). Co-morbidities including HTN, DM, obesity, renal disease and dyslipidemia have also been implicated as determinants of the risk of AMI in young patients (Yandrapalli et al., 2019). Psychological problems including anxiety and depression are associated with an increased risk of AMI in general population (Gustad et al., 2014). However, the role of anxiety in the development of AMI in young adults is not yet clear and no local data is available on this clinically relevant aspect. Moreover, the few studies that have presented data on other clinical risk factors of AMI in young patients from the local South Asian population are compromised by improper study designs, small sample sizes, lack of effective comparisons and statistical incongruities. As a result, local evidence about the risk factors of AMI in younger age group remains unconvincing. Keeping in view the existing void and the known predilection of CVDs for South Asian people (Volgman et al., 2018), the present study was undertaken to investigate anxiety and other clinical risk factors of AMI and compare them with age-matched healthy people from the local population without history of AMI.

2. MATERIALS AND METHODS

The cross-sectional case-control study was conducted for a duration of six months between May 2020 to November 2020. All study procedures were carried out in line with the ethical standards stipulated in the Helsinki Declaration. Recruitment of subjects (n=224) was done by non-random convenience sampling after obtaining written informed consent. Young hospitalized patients (n=112) with a recent first AMI ($\leq$3-days post-hospital admission) were enrolled for the study from the cardiology units of public sector tertiary care hospitals in Lahore, Pakistan. An age cutoff value of 45 years was used to define younger patients with AMI (Shah et al., 2016). Age-matched non-AMI healthy individuals (n=112) without any known history of CVDs were recruited from the general population as control subjects.

Each participant was asked to fill a paper questionnaire which recorded data including age, gender, weight and height as well as smoking history, lifestyle and dietary habits, co-morbid conditions and any family history of AMI, HTN and DM. Hamilton anxiety rating scale (HAM-A), a commonly used, validated and questionnaire-based psychometric tool, was used to determine the pre-AMI status of anxiety in the study participants (Sikandar et al., 2019). HAM-A and the research questionnaire were administered at the same time to the participants by a study investigator. Body mass index (BMI) was calculated using the standard formula of weight in kilograms divided by height in meters squared (Shah et al., 2019). For quantitative determination of cardiac profile and liver function, 10 ml of venous blood sample was collected from each subject and serum was separated by centrifugation for analysis. Serum levels of cardiac markers (creatine-Kinase MB, CK-MB; Cardiac troponin-I, cTnI; lactate dehydrogenase, LDH) and liver enzymes (alanine transaminase, ALT; aspartate transaminase, AST; alkaline phosphatase, ALP) were assessed using commercially available enzyme-linked immunosorbent assay (ELISA) kits.

Anonymized data were analyzed using SPSS version 23 after checking for errors in data entry. Normality was assessed using Shapiro-Wilk test. Mean $\pm$ SD of quantitative variables were calculated for both the groups. Qualitative variables were presented as absolute frequencies (n) and percentages (%). For quantitative variables, independent sample t test was applied to observe the mean differences between the two groups. P-values of < 0.05 were deemed to be statistically significant.

3. RESULTS

The age range of study participants (n=224) was 19 to 45 years. Mean age in group 1 (AMI patients) was 28.23 $\pm$ 4.89 while it was 30.23 $\pm$ 8.31 in group 2 (non-AMI healthy controls). Out of the 112 subjects in each group, 102 (91%) in group 1 and 76 (67.8%) in group 2 were less than 35 years old. Group 1 comprised of 86 males (76.78%) and 26 (23.2%) females while group 2 consisted of 98 males (87.5%) and 14 females (12.5%). Serum enzyme levels for CK-MB, LDH, cTnI and AST were significantly raised in group 1 (p=0.000, Table 1) as expected since AMI leads to release of these markers into blood as a result of myocardial injury (Wang et al., 2020). Anxiety levels and cigarette consumption were observed to be significantly higher in group 1 as compared to group 2 (p=0.000, Table 1, Figure 1). There was no difference seen in BMI values between the two groups (p=0.865, Table 1, Figure 1).

Subjects were segregated into those having mild anxiety (HAM-A score <17), moderate anxiety (HAM-A score 18-24) and severe anxiety (HAM-A score 25–30). Subjects were also categorized as underweight (BMI <18.5 kg/m2), normal weight (BMI 18.5 – 24.9 kg/m2), overweight (BMI 25 – 29.9 kg/m2), and obese (BMI ≥ 30kg/m2). Moreover, subjects were stratified into non-smokers, occasional smokers (up to 5 packs / week), moderate smokers (5-10 packs / week) and heavy smokers (more than 10 packs / week).

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Table 2 gives distribution of the study participants in both Group 1 and Group 2 in terms of their stratification based on anxiety rating, BMI and cigarette consumption.

Table 1 Differences between group means for anxiety, smoking, obesity, cardiac markers and liver enzymes

	Study Parameter	Group 1 (AMI) n =112	Group 2 (Control) n =112	p-value
Clinical Risk Factors	HAM-A score	25.16 ± 4.691	13.27 ± 9.48	0.000*
	Cigarette packs/week	4.32 + 4.814	0.21 + 0.9	0.000*
	BMI (kg/m^2)	24.79 ± 4.02	24.28 ± 4.47	0.865
Cardiac Markers	CK-2	49.25 ± 10.24	9.66 ± 6.27	0.000*
	LDH (U/L)	30.44 ± 1.96	19.26 ± 3.05	0.000*
	cTnI (ng/ml)	1.09 ± 0.27	0.200 ± 0.12	0.000*
Liver Enzymes	ALT (U/L)	36.01 ± 3.39	17.14 ± 5.93	0.000*
	ALP (U/L)	121.66 ± 19.85	76.48 ± 19.05	0.881
	AST (U/L)	44.00 ± 7.36	24.17 ± 4.23	0.000*

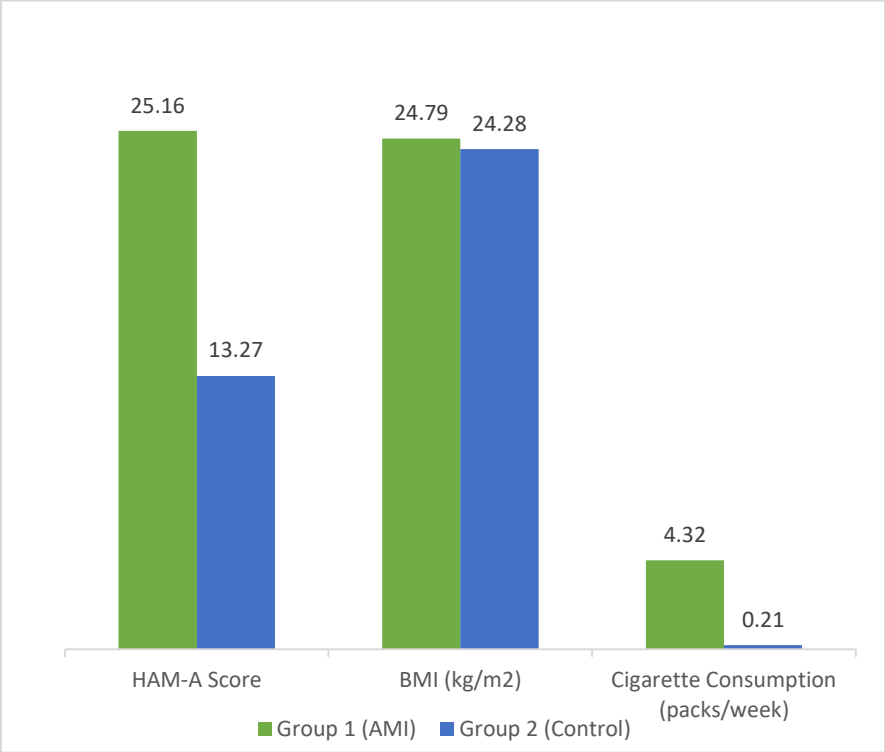

Figure 1 Group comparisons of means of HAM-A scores, BMI and cigarette consumption

Table 2 Distribution of subjects by grouping based on anxiety rating, body mass index and cigarette consumption

Parameter		Group 1 (MI) n (Percentage)	Group 2 (Control) n (Percentage)
Anxiety Rating	Mild	4 (3.57%)	72 (64.28%)
	Moderate	46 (41.08%)	16 (14.28%)
	Severe	62 (55.35%)	24 (21.44%)
BMI	Underweight	0 (0%)	8 (7.14%)
	Normal Weight	62 (55.35%)	62 (55.35%)
	Overweight	38 (33.92%)	34 (30.35%)
	Obese	12 (10.73%)	8 (7.16%)

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Cigarette Consumption	Non-Smokers	56 (50%)	104 (92.85%)
	Occasional Smokers	8 (7.15%)	8 (7.15%)
	Moderate Smokers	36 (32.14%)	0 (0%)
	Heavy Smokers	12 (10.71%)	0 (0%)

Table 3 provides distribution of the study participants in the two groups based on cardiac risk factors including co-morbid conditions, family history and lifestyle. Table 4 ranks all the studied risk factors based on their frequency in Group 1. Moderate to severe anxiety (96.42%), family histories of HTN (96.42%) and DM (94.64%), and lack of regular exercise (82.14%) were the most commonly observed risk factors in group 1 (Table 4).

Table 3 Distribution of subjects based on risk factors including co-morbidities, family history of diseases and lifestyle factors

Risk Factors		Group 1 (MI) n (percentage)	Group 2 (Control) n (percentage)
Known Co-morbidities	DM	58 (51.78%)	10 (8.9%)
	HTN	84 (75%)	24 (21.4%)
	Renal disease	68 (60.71%)	0 (0%)
Family History	HTN	108 (96.42%)	70 (62.5%)
	DM	106 (94.64%)	56 (50%)
	AMI	64 (57.14%)	70 (62.5%)
Lifestyle	Lack of regular exercise	92 (82.14%)	28 (25%)
	Smoking	56 (50%)	8 (7.1%)
	Unhealthy diet patterns	74 (66.08%)	0 (0%)
	Sedentary	60 (53.57%)	40 (35.7%)

Table 4 Ranking of clinical risk factors on the basis of frequency in patients of AMI

Rank	Clinical Risk Factor	n (percentage)
1	Moderate to severe anxiety	108 (96.42%)
2	Family history of HTN	108 (96.42%)
3	Family history of DM	106 (94.64%)
4	Lack of regular exercise	92 (82.14%)
5	HTN	84 (75%)
6	Unhealthy diet patterns	74 (66.08%)
7	Renal disease	68 (60.71%)
8	Family history of AMI	64 (57.14%)
9	Sedentary lifestyle	60 (53.57%)
10	DM	58 (51.78%)
11	Smoking	56 (50%)
12	Obesity	12 (10.73%)

4. DISCUSSION

The life-threatening condition of AMI, traditionally known to afflict the old, is now increasingly being seen to affect young adults. The present study was conducted to study the clinical risk factors including anxiety, smoking, co-morbid conditions, family history and lifestyle patterns which may contribute to this growing trend of AMI in younger age groups within local population. Our results highlighted anxiety as a key clinical risk factor for AMI. Anxiety ranked as the most prevalent clinically treatable and modifiable risk factor with more than 96% of the young patients suffering from moderate to severe anxiety prior to AMI. The present study, to the best of our knowledge, is the first one to assess and report anxiety as the foremost risk factor of AMI in young South Asian individuals. Anxiety scores in the AMI patients were found to be significantly higher as compared to non-AMI individuals. Competitive nature and socioeconomic pressures of the modern way of life are increasingly affecting the mental health of people right from a very young age. Psychosocial factors such as anxiety and depression, and type A personality are well known

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to heighten the risk for AMI in general population (Mal et al., 2019; Shah et al., 2020a; Shah et al., 2020b) and the present results suggest that young people are perhaps even more susceptible to their pervasive adverse effects. Anxiety is a clinical condition that creates a milieu of chronic stress which has been implicated in atherosclerotic progression and subsequent AMI through multiple pathways leading to lipid imbalances, endothelial injury, proinflammatory and prothrombotic changes as well as plaque rupture (Yao et al., 2019).

The current study also showed a high prevalence of co-morbidities including HTN, DM and renal disease in AMI patients. Nearly two-thirds of the AMI patients had unhealthy dietary habits, sedentary lifestyles and lacked regular exercise whereas most of the healthy individuals had active lifestyles, healthy diet patterns and engaged in regular exercise. Half of the patients of AMI were smokers while only 7% of the non-AMI subjects smoked cigarettes occasionally. Positive family histories of HTN, DM and AMI were revealed as common non-modifiable risk factors with more than 90% of AMI patients having first-degree relatives who had HTN and/or DM. Our findings are concordant with data reported in some recent studies conducted on South Asian populations. Smoking, hypertension and diabetes were demonstrated as key risk factors of AMI in young Pakistani patients (n=100) (Faisal et al., 2011). Smoking was identified as the most prevalent risk factor of AMI in a study of AMI patients (n=50) from eastern India younger than 35 years (mean age 33 years) (Bhandari et al., 2017). Another larger study (n=266) in Bangladeshi AMI patients less than 35 years of age (mean age 31 years) also reported smoking to be the most common risk factor of AMI (Malik et al., 2016). Smoking was also reported to be the dominant risk factor of AMI in a study of young patients (n=148, mean age 36 years) from South Asian and Arabian ethnicities. The study also showed a high prevalence of HTN, family history of CVDs, and DM in the study cohort (Jamil et al., 2013). Another recent study on young Pakistani AMI patients between 18-40 years old reported HTN, DM and smoking as key risk factors (Cheema et al., 2020). In a large retrospective study of 18-44 year old (mean age 39 years) American patients with first AMI (n=280,975), smoking and HTN were identified as two of the most common risk factors (Yandrapalli et al., 2019).

The current work has demonstrated considerably higher frequencies of multiple clinical risk factors in young AMI patients as compared to non-AMI individuals of the same age. The present data did not reflect any difference of obesity, an established traditional risk factor for CVDs (Cercato and Fonseca, 2019), between the young AMI patients and healthy controls, suggesting that detrimental effects of obesity on cardiac health are more likely to manifest in later life and risk factors other than obesity may have a greater role in the development of AMI in younger population. The current data also showed a high preponderance of AMI patients below the age of 35 years, thus depicting an alarmingly rising trend of AMI in younger population. The present findings are consistent with previous reports in many aspects but also add newer dimensions to the existing data, suggesting interplay of multiple risk factors in the development of AMI in young adults. It is quite plausible that various risk factors augment each other's negative effects by acting in concert and accelerating the pathological mechanisms leading to AMI.

Male gender has been identified as a predominant non-modifiable risk factor for AMI in young individuals in previous studies (Ge et al., 2017; Gulati et al., 2020; Shah et al., 2016), Men outweighed women in the present cohort of young AMI patients but non-random sampling for the study limits commenting definitively on any gender-based predisposition to AMI. The study employed subjective assessment of risk factors like most previous studies but increasing objectivity in future studies may allow for improved risk prediction. The present study did not determine serum lipid profile as it primarily focused on clinical and not metabolic risk factors. Nonetheless, dyslipidemia is an established conventional risk factor and familial predisposition to abnormalities in lipid profile has been suggested in young AMI patients, though its link with AMI in young patients is not as strong as in the elderly (Lei and Bin, 2019; Malik et al., 2016; Sharma et al., 2020). Anyhow, screening, preventive and therapeutic modalities aimed at normalizing lipid profile should form an integral part of evaluation and management of cardiac health in young individuals.

The present study has some limitations related to the relatively small sample size and the timing of sampling. The study included patients after their AMI when a considerable anxiousness can be expected. Suffering AMI at a young age is a traumatic experience and makes the patients worry about their life expectancy, family and work. This factor may have exaggerated the present findings of higher anxiety levels in AMI patients. The study instrument could not differentiate between pre-existing anxiety and anxiety induced by AMI. Furthermore, the anxiety questionnaire used in the study does not inform about how long into the past it can yield correct measures of anxiety.

5. CONCLUSIONS

The present study has demonstrated anxiety as a potentially leading risk factor of AMI in young people, necessitating the need for better management of psychosocial health in young age for mitigating the risk of AMI. Lack of regular exercise, HTN, unhealthy dietary patterns, renal disease, sedentary lifestyle, DM and smoking have also been highlighted as common modifiable risk factors

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of AMI in young adults. Randomized controlled trials of holistic preventive measures that incorporate psychosocial wellbeing, healthy lifestyle, smoking cessation, and control of HTN and DM are required to inform clinical guidelines. Preventive interventions are more likely to yield beneficial outcomes in young people and future work on such preventive strategies may enable formulation of global policies and community campaigns to reduce the health-economic burden of AMI in young adults and improve outcomes of health and quality of life.

Authors' contribution

SIAS, MZS, UYQ and IH were involved in the concept, design, definition of intellectual content, literature search, data acquisition, statistical analysis, manuscript preparation, manuscript editing and manuscript review.

Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

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Informed Consent

Written and oral informed consent was obtained from each study participant individually. No identifying information of any participant was included in this manuscript.

Ethical Approval

The study was approved by the Research Committee of the College of Pharmacy, University of Hafr Al-Batin, Saudi Arabia (RCCP/2020/02/CardiacHealth).

Data and materials availability

All data associated with this study are present in the paper.

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