Original Article

To Determine the Frequency of Homocysteinemia in Patient with Acute Coronary Syndrome

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ABSTRACT

Objective: To determine the frequency and factors associated with the ACS patients with homocysteinemia.
Study Design: Cross-sectional study design
Place and Duration of Study: This study was conducted at the Department of Cardiology, Liaquat National Hospital & Medical College, Karachi from 1st August 2018 to 31st January 2019.
Methods: All patient of age < 45 years presenting with chest pain were enrolled in the study. The patients were classified on the basis of ACS i.e. unstable angina, STEMI and NSTEMI. After confirming the diagnosis of ACS, homocysteine levels were assessed to confirm the diagnosis of elevated level of homocysteine (> 15µmol/l). Statistical analysis was done in SPSS version 26.
Results: In this study, 107 patients with acute coronary syndrome were included for the analysis patient 40.11+2.59 years. The mean age of patient was 40.11+2.59 years. Male preponderance was observed in our study. The most common type of ACS was unstable angina 54 (50.5%) followed by NSTEMI and STEMI. However, the frequency of homocysteinemia among patient with acute coronary syndrome was 26.2%.
Conclusion: In conclusion frequency of homocysyteinemia was 26.2%, common in males of particularly 31-44 years age group.
Key Words: Acute coronary syndrome, myocardial infarction, homocysteine, STEMI, NSTEMI

INTRODUCTION

Acute coronary syndrome (ACS) is characterized by sudden blockage or reduction in the cardiac blood flow. This includes unstable angina (UA), non-ST elevated myocardial infarction (NSTEMI), and ST-elevated myocardial infarction (STEMI). Diagnosis and classification of ACS involve a comprehensive assessment of all the clinical features along with electrocardiogram (ECG), serology testing and echocardiography. ACS representing the acute form of ischemia and is a significant illness globally. The prevalence of ACS in Pakistan was found to be 36.9%.[1]. Traditional risk factors can only account for half of all causes of ACS.

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To understand the remaining causes, it is needed to explore novel and emerging risk factors. These include biological serological markers like elevated sensitive C-reactive protein, homocysteine, interleukin-6, serum uric acid levels.[2] Homocysteine is an amino acid resulting from the demethylation of methionine. Elevated homocysteine levels (above 15 mmol/L) have been linked to vascular diseases such as peripheral vascular disease, carotid artery stenosis, and coronary artery disease[3]. Homocystein is found to be directly toxic to the endothelial vascular cells and also in the stimulation of the smooth mucle cells of the vascular muscles, and it is also found to be associated with venous thromboembolism[4] A study by Mukherjee et al. reported the frequency of high homocysteine in 42.86% of patients with acute coronary syndrome. However, raised homocysteine (>40 years) as compared to the younger age group (54.55% vs. 23.08%).[7] However, raised homocysteine levels were found to be more prevalent in older age groups greater than 40 years (54.5%) as compared to the younger group (24.08% less than 40 years).

This study is aims to determine frequency of homocysteinemia acute syndrome (ACS) in age less than 45 years. Several studies have shown homocysteinemia in patients with ACS.[5,6] However, the evidence is still lacking in the Pakistani population. As we do not have our own local statistics, we should

know the true frequency, age at onset in our population, and common duration of ACS at the onset. So that early suspicion is made to avoid diagnostic delay and to do further research to identify risk factors so that they can be avoided in our population.

METHODS

This was a cross-sectional study design, and the data was collected from Liaquat National Hospital and Medical College (LNH & MC). All patients > 18 years of age presenting with ACS were included. Participants with a previous history of myocardial infarction or renal insufficiency were excluded from the study. Participation in the study was entirely voluntary, and every participant was clearly briefed about the informed consent that the collected data will only be used for research purposes and will be kept confidential. The sample size of our population was calculated using the WHO sampling calculator, using the anticipated frequency of homocysteinemia in patients with ACS 23.08[7], a margin of error of 8%, and a confidence level of 95%. The required sample size is 107.

Acute myocardial infarction (AMI) was diagnosed using the recently established definition set forth by the ACC/AHA/ESC/WHF task force [8]. Unstable angina is defined as unexpected chest pain and usually occurs while resting, having any one of the symptoms like onset at rest or minimum physical exertion lasting for more than 20 minutes if the nitroglycerine is not given, having a new onset within a month with more severity, and occurring with a crescendo pattern (brought on by minimal activity, more severe, more prolonged, or increased frequency than previously). STEMI is characterized by the features of MI symptoms (myocardial infraction), electrocardiographic changes like ST elevation, and elevated serum biomarkers of cardiac myocyte necrosis. positive troponin-I (>0.30 ng/dl) at the time of presentation and 6 hours later. NSTEMI is defined as unstable angina along with an abnormal cardiac enzyme, i.e., positive Troponin-I (> 3.0 ng/dl) and/or CKMB (>25ng/dl). Hypertension was defined as a known hypertensive person who has been on anti-hypertensive medication for more than 6 months, as assessed by history and clinically. Patients were diagnosed as diabetic of known diabetics (HbA1c > 6.5) who have been on anti-diabetics for more than 6 months, as assessed by history.

All statistical analysis was performed in SPSS version 26. All the descriptive statistics, including qualitative and quantitative, are presented in tabular form. Quantitative variables are reported as mean and standard deviation. While qualitative variables such as gender, comorbidity (diabetes and hypertension), type of acute coronary syndrome, and homocysteinemia were reported in frequency (n) and percentage (%), For inferential statistics, chi-square tests were applied among the variables to determine any association. All

P-values less than or equal to 0.05 will be considered statistically significant.

RESULTS

A total of 107 diagnosed patients with ACS were included in the study. The mean age of the patients is 40.11 + 2.59 years. Among the 107 patients, the majority were male, 87 (81.3%). The mean duration of the final diagnosis of ACS was 7.67 + 1.681 hours (Table 1).

Table No. 1: Represents the demographic data of the participants in frequency and percentages.

Demographic data		Frequency (%)
Age (mean ± SD)		40.11+2.59 years
Gender	Male	87 (81.3)
	Female	20 (18.69)
Diabetes	Yes	33 (30.8)
	No	74 (69.2)
Hypertension	Yes	49 (45.8)
	No	58 (54.2)
Unstable Angina		54 (50.5)
STEMI		18 (16.8)
NSTEMI		35 (32.7)

In our study, 49 (45.8%) patients were hypertensive, and 33 (30.8%) had diabetes. However, the most common type of ACS was unstable angina (50.5%), followed by NSTEMI (27.7%), and STEMI (20.0%) (shown in Table 1). Furthermore, homocysteinemia among patients with ACS was observed in 28 (26.2%) (Figure 1).

Table 2 shows the comparison of homocysteinemia with baseline characteristics such as comorbidity and ACS type. There is no significant association between homocysteinemia and baseline In comparison to the sociodemographic information (age, gender, p = 0.486), complications (diabetes, p = 0.862, hypertension, p = 0.421), time duration since diagnosis of ACS (p = 0.680), and type of ACS (p = 0.592), there was no statistically significant association found.
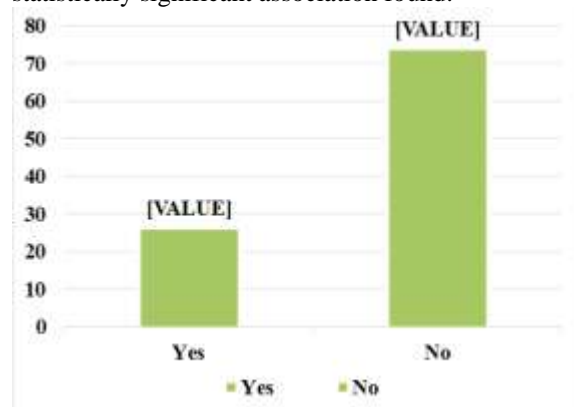

Figure No.1: Distribution of homocysteinemia among study population

Table No.2: Association of Homocysteinemia with demographic data of the patients

Independent Variables		Homocysteinemia		Total	P Value
		Yes	**No**		
Age (Years)	18-30	--	--	--	--
	31-44	28(26.16%)	79(73.83%)	107(100%)	
Gender	Male	24(27.5%)	63(72.41%)	87(100%)	0.486
	Female	4(20.0%)	16(80.0%)	20(100%)	
Duration of ACS diagnosis (hours)	9-June	23(27.05%)	62(72.94%)	85(100%)	0.68
	12-October	5(22.72%)	17(77.27%)	22(100%)	
Diabetes	Yes	9(27.27%)	24(72.72%)	33(100%)	0.862
	No	19(25.67%)	55(74.32%)	74(100%)	
Hypertension	Yes	11(22.44%)	38(77.55%)	49(100%)	0.421
	No	17(29.31%)	41(70.68%)	58(100%)	
Type of ACS	Unstable angina	16(36.36%)	38(86.36%)	44(100%)	0.592
	STEMI	5(27.77%)	13(72.22%)	18(100%)	
	NSTEMI	7(20.0%)	28(80.0%)	35(100%)	

DISCUSSION

Globally, CVD is one of the leading causes of morality, morbidity and in Pakistan aswell. At national level of Pakistan it lacks updated information reflecting the actual prevalence and incidence of acute coronary syndrome, despite having a high burden of CVS diseases. Recent research has reported the increase in aggressive conditions even in younger ages[9]. Homocysteine is a sulfur radical containing an amino acid, which is an intermediate metabolic byproduct of cysteine metabolism and is derived from methionine, an essential amino acid found in dietary proteins. In our study, the majority of patients were aged 31–44 years, as compared to the Mukherjee et al[7] study, in which the majority (64%) lies in the 35–45 age group, whereas in contrast to previous reported data, which shows the majority of cases reported after 50 years of age, the CREATE study[10].

In our study frequency of homocysteine was 26.2% as compare to Mukherjee et al[7] study which shows elevated homocysteine level 42.86%. It has been observed that elevated homocysteine levels are more prevalent in individuals aged over 40 (54.55%) compared to those under 40 (23.08%). This statistically significant data indicates that homocystein could serve as of the screening methord for individuals with ACS over the age of 40 years, regardless of gender[11]. The most suitable treatment for individuals falling in this age group including cobalamin (vitamin B-12) and Folic acid (vitamin B-9). Interestingly, males generally exhibit higher homocysteine levels than females, although this difference is not statistically significant. This lack of significance could be attributed to the overall higher number of males in the study. However, among females, groups tend to occurrences elevated levels. However in female which are not in there fertility period (peri and post-menopausal period) reported to have higher level of homocysteine level.

Such facts highlight the importance of homocysteine level in the development of CVSD. People with homocystinuria, an inherited disorder who are found to have high levels of homocystein in their blood were reported to have early atherosclerosis and thromboembolic complications[7,12]. It is believed that homocysteine is a possible contributor to the oxidation of LDL and the growth of smooth muscle cells located in the tunica media of the vessel wall. It is also an activator of coagulation factors, and platelets also cause endothelial dysfunction.

Some medical experts have recommended maintaining the homocystein level below 10 µmol/L, especially in high-risk CVSD patients, as a therapeutic goal[13]. Studies were done to compare homocystein levels in patients with and without coronary artery diseases and revealed that patients with CAD had statistically significant elevated plasma homocystein levels as compared to those with no CAD, with risk ratios ranging from 1.2 to 10.9 after adjusting for other risk factors[14,15]. Despite our study, we didn't identify any significant association between homocysteinemia and ACS. This warrants further research to relate pathophysiology to the underlying mechanisms. Additionally, the role of other possible factors, such as genetics and multimorbidity, should be studied with different study designs.

There are certain limitations to this study. Firstly, there was firstly, more studies should be done with a large sample size. Secondly, the involvement of different departments of medicine to study all possible effects of homocysteine in a more synchronized manner. Larger cohorts are needed to establish a causal relationship among the variables.

CONCLUSION

The frequency of homocysyteinemia was 26.2% among the patients with ACS, found to be most common in males between the ages of 31 and 44.

REFERENCES

1. Sher A, Bashir MA, Humerah S, Khan MR, Raja NS, Hussain I. Prevalence of acute coronary syndrome among patients presenting with chest pain. Pak J Med Health Sci 2022;16(10):932.

2. Kamath DY, Xavier D, Sigamani A, Pais P. High sensitivity C-reactive protein (hsCRP) & cardiovascular disease: An Indian perspective. Ind J Med Res 2015;142(3):261-8.

3. Ganguly P, Alam SF. Role of homocysteine in the development of cardiovascular disease. Nutr J 2015;14:6.

4. Pushpakumar S, Kundu S, Sen U. Endothelial dysfunction: the link between homocysteine and hydrogen sulfide. Current Medicinal Chem 2014;21(32):3662-72.

5. Yeh JK, Chen CC, Hsieh MJ, Tsai ML, Yang CH, Chen DY, et al. Impact of Homocysteine Level on Long-term Cardiovascular Outcomes in Patients after Coronary Artery Stenting. J Atherosclerosis Thrombosis 2017;24(7):696-705.

6. Kumar A, Palfrey HA, Pathak R, Kadowitz PJ, Gettys TW, Murthy SN. The metabolism and significance of homocysteine in nutrition and health. Nutr Metabolism 2017;14:78.

7. Mukherjee S, Manna K, Datta S, editors. Prevalence of novel risk factors in patients of acute coronary syndrome in eastern India: a detailed analysis. Int Cardiovascular Forum J 2015;4:4-18.

8. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. Third universal definition of myocardial infarction. Circulation 2012;126(16):2020-35.

9. Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63(25 Pt B):2889-934.

10. Xavier D, Pais P, Devereaux PJ, Xie C, Prabhakaran D, Reddy KS, et al. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. Lancet (London, England) 2008;371(9622): 1435-42.

11. Oudi ME, Aouni Z, Mazigh C, Khochkar R, Gazoueni E, Haouela H, et al. Homocysteine and markers of inflammation in acute coronary syndrome. Exp Clin Cardiol 2010;15(2):e25-8

12. Zaric BL, Obradovic M, Bajic V, Haidara MA, Jovanovic M, Isenovic ER. Homocysteine and hyperhomocysteinaemia. Current Medicinal Chem 2019;26(16):2948-61.

13. Ma Y, Peng D, Liu C, Huang C, Luo J. Serum high concentrations of homocysteine and low levels of folic acid and vitamin B12 are significantly correlated with the categories of coronary artery diseases. BMC Cardiovascular Disorders 2017;17(1):37.

14. Shenoy V, Mehendale V, Prabhu K, Shetty R, Rao P. Correlation of serum homocysteine levels with the severity of coronary artery disease. Ind J Clin Biochem : IJCB 2014;29(3):339-44.

15. Alawneh I, Saymeh A, Daraghmeh M, Jabri D, Yaseen L. Role of plasma homocysteine levels and other associated factors with coronary artery disease among Palestinian patients in North Palestine: a case control study. The Pan Afri Med J 2022;42:180.