ASSOCIATION OF SERUM FOLIC ACID LEVELS AND CHOLESTEROL/HIGH DENSITY LIPOPROTEIN (HDL) RATIO WITH BASAL METABOLIC INDEX (BMI) IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Objective: Different lipid profile markers have been used recently in making the prognosis of acute myocardial Infarction Patients. Cholesterol-high density lipoprotein ratios and serum folic acid levels were compared with basal metabolic index (BMI) status in patients with acute myocardial infarction in this study.

Study Design: Cross-sectional study.

Place and Duration of Study: University of Health Sciences Lahore, from Oct 2017 to Oct 2018.

Methodology: Study approval from Advanced Studies and Research Board of University of Health Sciences Lahore. A validated questionnaire was filled by the patients after taking informed consent from them. Convenient sampling technique was used. Blood samples of the patients were also taken to calculate different parameters.

Results: The mean age of the patients included in the study was 52.31 years. Majority were males (85%). More than half were having no formal education (55%). Majority also belonged to middle class as per their socio-economic status (57.5%). About 50% were within normal weight category and 20% were in over weight category. Mean basal metabolic index of the study participants was found to be 25.32. We also calculated the association of serum folic acid levels with different groups of basal metabolic index. Among underweight study participants the mean folic acid levels were found to be very low (3.86ng/ml-normal is 6-17ng/ml). The result was also found to be statistically non-significant. When the association of basal metabolic index was assessed with cholesterol/HDL ratio, it was found to be highly statistically significant (p=0.047). The ratio was also seen to be decreased with increase in basal metabolic index status.

Conclusion: An association between increased C-HDL and basal metabolic index in serum of patients with AMI who had not yet made percutaneous coronary intervention.

Keywords: Acute myocardial infarction, Serum folic acid, Serum cholesterol/HDL ratio,.

INTRODUCTION

Dyslipidemia is characterized by an elevation of serum cholesterol and high-density lipoprotein (C-HDL) concentration[1] and is these are routinely assessed for the purpose of assessing cardiovascular risk. The prevalence of dyslipidemia varies geographically; although, it has been estimated that >50% of the adult population has dyslipidemia worldwide[2]. The prevalence of hypercholesterolemia, hypertriglyceridemia, high levels of C-HDL are reported to be 41.6, 46 and 43.9%, respectively in both sexes in the Iranian population[3].

Darroudi *et al* have recently reported the prevalence of dyslipidemia among a subsample of Iranian adults to be 83 and 87% in the total population and CVD patients, respectively[4]. CVD is a chronic non-communicable disease and one of the most important causes of death and disability. Basal metabolic index (BMI) has always been a major contributor in the prevalence of CVD events is increasing globally[5]. It is the leading cause of mortality in Iran, accounting for 50% of total mortality and 79% of deaths due to chronic diseases[6]. Atherosclerosis is the major underlying cause of CVD[7]; the World Health Organization (WHO) definition of CVD includes: coronary heart disease, cerebrovascular disease, rheumatic heart disease, myocardial infarction (MI), stable angina (SA), unstable angina (UA), and other conditions[7]. Public health organizations globally have focused on reducing modifiable CVD risk factors to control the rising prevalence of CVD and its risk factors; such as hypertension (HTN), unhealthy diet, obesity and dyslipidemia[8]. A high-fat and high-calorie diet can cause dyslipidemia and thereafter endothelial dysfunction[9]. Serum TG, TC, LDL-C, HDL-C, TC/HDL-C, and LDL-C/HDL-C ratios are independent predictors of CVD risk. Currently, the principal objective in the management of dyslipidemia is to reduce serum LDL-C levels[10]. Components of the circulating lipid profile, but particularly modified LDL-C, may be deposited within the tunica intima of

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the artery wall, and are involved in the subsequent atherogenic process[11]. The benefits of reducing plasma LDL-C concentrations on CVD risk are particularly evident in subjects with familial hypercholesterolemia[12]. Whilst it has been proposed that HDL-C is protective against CVD, partially related to its role in reverse cholesterol transport[13], some studies have reported that high or normal levels of HDL-C are not protective against CVD events[14]. A single serum HDL-C level reflects the HDL-C pool rather than its functionality[15]. Modified forms of the various protein components of HDL, perhaps generated by oxidative stress, may reduce the ability of HDL to take part in reverse transport[16].

Whilst several studies have demonstrated the association of serum Cholesterol and HDL ratios and serum Folic Acid Levels with the BMI of CVD in western population samples[17], there, are relatively few in Asian populations. We aimed to define the association between serum folic acid levels and cholesterol/HDL ratio of dyslipidemia with BMI in acute myocardial infarction events among a population sample of adults from Punjab, Pakistan.

METHODOLOGY

The cross-sectional study was conducted at University of Health Sciences Lahore, from October 2017 to October 2018 after approval from Advanced Studies and Research Board of University of Health Sciences Lahore. A validated questionnaire was filled by the patients after taking informed consent from them. Convenient sampling technique was used. Blood samples of the patients were also taken to calculate different parameters. Sample size was calculated according to following formula:

$$\text{Sample size} = \frac{Z_{1-\alpha/2}{}^2\, p(1-p)}{d^2}$$

$Z_{1-a/2}$= is standard normal variant (at 5% type 1 error (p<0.05) it is 1.96. As in majority of studies.

p-values are considered significant below 0.05 hence 1.96 is used in formula.

p=Expected proportion in population based on previous studies or pilot studies= 0.30[7].

d=Absolute error or precision= 0.15

Sample size (n)=40.

Diagnosed cases of Acute Myocardial Infarction presenting to Punjab Institute of Cardiology, Lahore, were included in the study.

Patients diagnosed with diseases other than Acute Myocardial Infarction were excluded from the study.

Convenient sampling technique was used. Blood samples of the study participants were taken and serum was separated by centrifugation. Different parameters were calculated.

The data was assessed by IBM-SPSS version 26. Frequency distributions of study participants were calculated. Significance of the associations was assessed by one way ANOVA test. p-value <0.05 was taken as statistically significant.

RESULTS

The mean age of the patients included in study was 52.31 years. Majority were males (85%). More than half were having no formal education (55%). Majority also belonged to middle class as per their socio-economic status (57.5%). About 50% were within normal weight category and 20% were in over weight category. mean basal metabolic index of the study participants was found to be 25.32 (table-I).

We also calculated the association of serum folic acid levels with different groups of BMI. Among underweight study participants the mean folic acid levels were found to be very low (3.86ng/ml- normal is 6-17 ng/ml). The result was also found to be statistically non-significant. When the association of BMI was assessed with cholesterol/HDL ratio, it was found to be highly statistically significant (p=0.047). The ratio was also seen to be decreased with increase in BMI status (table II).

Table-I: Frequency of demographic variables with percentages (n=40).

Variables	Groups	n (%)
Gender	Male	34 (85)
	Female	6 (15)
Education	Masters or Higher	1 (2.5)
	Bachelors	4 (10)
	Matric/F.Sc	11 (27.5)
	Primary	2 (5)
	Illiterate	22 (55)
Socioeconomic Group	Lower Class	16 (40)
	Middle Class	23 (57.5)
	Upper Class	1 (2.5)
Basal Metabolic Index	Under Weight	1 (2.5)
	Normal Weight	20 (50)
	Over Weight	12 (20)
	Obese	7 (17.5)

DISCUSSION

This research reveals a positive association between the serum cholesterol/HDL ratio and BMI in patients with recently diagnosed acute myocardial infarction. The increased level of C-HDL ratio in AMI

Table-II: Association of serum folic acid levels with basal metabolic index status in patients with acute myocardial infarction (n=40).

Variables	Basal Metabolic Index Status				*p*-value
	Under Weight (n=1)	Normal Weight (n=20)	Over Weight (n=12)	Obese (n=7)	
Serum Folic Acid Levels	3.80	6.46	6.32	6.10	0.253
Cholesterol/HDL Ratio	5.62	4.99	4.55	4.54	0.047

**Calculated by One Way Anova Test*

compared to a group of healthy subjects was observed in several studies[11,12], which is in accordance with our research results. However, studies related to association of serum folic acid levels and coronary arterial disease are contradictory, some of them indicating an association[13], while in other studies, such an association is not observed and is explained by high homocysteine level in healthy population[14]. Contradictory results are as well due to different criteria for inclusion and exclusion of patients in research, different numbers of patients, methods of analysis, genetic background and different eating habits[15]. Our research results are consistent with those of Cohen *et al*., who also found a positive association between cholesterol and HDL ratio and folic acid serum level[16]. Similar results have been obtained by other researchers as well[17]. The correlation between C-HDL ratio and AMI is explained by the fact that hydrolysis of HDL leads to cholesterol precursors[18], meaning that an increase of C-HDL concentration results in an increase in occurrence of atherosclerotic event. This correlation between these two parameters in AMI points out the need for a joint observation of these two variables in AMI patients.

Xanthine oxidase and oxidative stress, resulting with an increase of C-HDL levels. All these changes create a vicious circle in which the function of the heart is continuously deteriorating[22]. Inflammation plays a significant role in all stages of the atherosclerotic changes, starting from the beginning until the end result - The association analysis between folic acid (FA) and BMI status in patient with AMI was also found by Boras *et al*. This association was expressed in the group of patients with CRP concentration within the reference range. Taking these risk factors into consideration, it was of no surprise that correlations of C-HDL ratio and BMI were both expected and confirmed in the group of patients with AMI within the reference range. The distribution of patients in tertiles according to C-HDL ratios revealed elevated BMI values in all patients. Considering the fact that there are other factors which can cause elevation of C-HDL levels besides atherosclerosis or AMI, future research should take those factors into consideration. When patients were stratified on the basis of their mean levels of BMI on those below and above 25.32, significant difference in the concentration of C-HDL was observed between the two groups. However, significant difference in folic acid level between low and high BMI values was not observed, probably due to the weakness of the estrogenic protective effect in these patients. Although younger women have lower folic acid levels than men, this difference seems to disappear with aging[19]. A weak positive correlation was observed between the age and folic acid levels in different subgroups of patients in a past research [20] and is probably due to the changes in folic acid metabolism or renal function disorders. Recent studies associate decreased folic acid level with more rapid development of thrombotic states[21], which explains the level in patients with AMI, but clear mechanisms are still not fully clear. Decreased folic acid levels and Hyperhomocysteinemia is considered to cause the reduction of carotid intima media[22] and because of its prothrombotic effect is associated with platelet reactivity, explaining observed increased level in patients with AMI. Because of this, it might be the target of aspirin therapy[22]. Homocysteine increases arterial stiffness, reduces the possibility of methylation, leading to endothelial dysfunction and proliferation of smooth muscle cells in blood vessels, oxidative stress occurrence, NF-κB activation, inflammation, and inhibition of nitric oxide synthesis in the endothelium[22]. It has also been confirmed that the joint effect of decreased folic acid and hyperuricemia has a stronger effect on the aforementioned epithelial changes, which again points out synergistic effect of C-HDL and FA in CVD. The reported increased C-HDL concentration in patients with BMI in AMI is confirmed in this research. The High C-HDL level in the serum of male and female patients is greater than the reference range levels, which are usually associated with a positive antioxidative effect. Increased C-HDL level promotes emergence of free oxygen species and state of oxidative stress, inducing apoptosis of cardiomyocytes, thereby promoting myocardial remodelling. Furthermore, AMI cau-

ses tissue hypoxia and hypoperfusion leading to the activation of AMI.

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To our knowledge, this is one of the rare studies addressing the diagnostic value of C-HDL and folic acid, taken together in a clinical setting in the country with very high prevalence of CVD. Considering potential link between them, further research involving a greater number of patients and including the post treatment effects should be done.

Autor Contribution

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CONCLUSION

An association between increased C-HDL and body mass index in serum of patients with AMI who had not yet made PCI. Since both parameters are participants in the atherosclerotic process, our results seem to suggest that their serum levels should be analyzed and interpreted simultaneously.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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