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Correlation of Plasma Homocysteine Level in Patients with Metabolic Syndrome

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Author`s Contribution

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ABSTRACT

Objective: To determine the correlation of homocysteine level with metabolic syndrome (MetS) among patients presented at LUMHS.

Methodology: This cross-sectional prospective study was conducted at Medicine department of Liaquat University of Medical and Health Sciences, from Dec 2020 to June 2021. Patients presented with metabolic syndrome, aged 18 to 60 years and of either gender were included. A 3ml blood sample was obtained from each patient to measure the homocysteine level. All the data will be recorded in self-made proforma and analysis was done using SPSS 20.0 version.

Results: Total 90 patients of metabolic syndrome were studied; with mean age was 46.62+14.82 years, mean HDL 34.93+8.14 mg/dL and mean triglyceride as 210.97+20.50 mg/dL. Mean albumin level was 25.76+8.48 mg/g and mean homocysteine level was 15.94+5.72 mcmol/L. Overall hyperhomocysteinemia was found in 72.2% patients, which was further statistically insignificant based on genders, hypertriglyceridemia and low HDL level p-values were quite insignificant (>0.05), while its was statistically significant based on microalbuminuria (p-0.001).

Conclusion: Hyperhomocysteinemia was observed to be highly frequent among patients with metabolic syndrome. Microalbuminuria was positively correlated with homocysteine levels.

Keywords: Metabolic syndrome, homocysteine, urine albumin

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Introduction

Metabolic syndrome has emerged as a significant global health concern, placing a substantial burden on medical resources.[1] MetS encompasses conditions such as elevated blood pressure, raised level blood glucose, abdominal fat accumulation and the abnormal cholesterol or the raised level of triglyceride, with rising prevalence, affecting approximately 25–35% of the adult population.[2]

As a result of this trend, the incidence of cardio-metabolic abnormalities and MetS is anticipated to increase among young individuals as well. Cardiovascular diseases remain the leading cause of death worldwide, making the early detection, treatment, and prevention of major risk factors a critical priority. Additionally, homocysteine is an emerging biomarker for cardiovascular disease and may play a key role in linking metabolic syndrome to cardiovascular conditions.[1] The MetS and high blood homocysteine (Hcy) concentrations have been identified as independent risk variables of CVD in this context. Hyperhomocysteinemia is linked to insulin resistance and increased oxidative stress, that promotes endothelial dysfunction, hypertension, and atherosclerosis by causing lesions in the vascular endothelium.[3] Total Hcy concentrations have been found to be a substantial predictor of death in individuals with angiographically diagnosed coronary artery disease (CAD) in studies.[4] There has been a link between increased serum Hcy and sudden unexpected mortality, particularly in diabetic individuals.[5] High Hcy was found to enhance the production of vascular cell adhesion molecule-1 (VCAM-1), monocyte chemoattractant protein-1 (MCP-1), and E-selectin in the lack of other

established risk factors. This increases monocyte adherence to endothelium of arterial wall, which may play a role in development of atherosclerosis through enabling macrophage/ monocyte infiltration into arterial wall.[6] Hcy destroys artery cells as well as tissues through causing the production of cyclins, cytokines, and other inflammatory and cell-division factors.[6] Furthermore, Hcy promotes oxidative stress through altering cellular respiration, resulting in the oxidation of LDL and other plaque ingredients. Hcy antagonises the vasodilatory effects of nitric oxide (NO) by generating S-nitrosohomocysteine, contributing to atherogenesis and endothelial dysfunction, according to Stamler and colleagues.[6] The MetS is thought to affect 20 to 25 percent of adult population as well as has been linked to a higher risk of CVD and death.[7,8] In Pakistan, it is estimated that between 18 and 49 percent of the urban population is affected.[9] Clinical and epidemiological evidence point to a strong relationship between hyperhomocysteinemia and MetS, with some research even suggesting that elevated blood concentrations with this amino acid are a component of MetS.[1,10]

Hyperhomocysteinemia is a sulfur-containing amino acid generated through the metabolism for methionine, and it is linked to the development of cerebrovascular and CVD. The nature of this association, however, is yet unknown.[1] Increased plasma tHcy and MetS are both linked to CVD, according to another previous research, however the link between tHcy and MetS is not fully understood.[11,12] Understanding the link between homocysteine and MetS could provide insights into novel biomarkers for early risk assessment and potential therapeutic targets. However this study aims to clarify the association between HHcy and MetS, addressing inconsistencies in previous findings and contributing to a more comprehensive understanding of the metabolic and cardiovascular risks associated with hyperhomocysteinemia.

Methodology

This cross-sectional prospective study was conducted in the Department of Medicine at Liaquat University of Medical and Health Sciences (LUMHS) after obtaining ethical approval. The study took place from December 2020 to June 2021. Participants were selected from the Department of Medicine at LUMHS, Hyderabad.

The sample size was calculated using the RaoSoft software for sample size determination, based on a prevalence of hyperhomocysteinemia of 18.4% in individuals with metabolic syndrome. With a margin of error of 8% and a confidence level of 95%, the required sample size for the study was determined to be 90 participants.

The study included patients diagnosed with metabolic syndrome, of both genders, aged 18 to 60 years. Individuals on medication for metabolic syndrome, pregnant women, smokers, and women using contraceptive medication were excluded. Written informed consent was obtained from all participants.

All participants underwent a complete physical examination and routine laboratory investigations. The assessment of metabolic syndrome included measurements of body mass index (BMI), blood pressure, fasting blood sugar, triglycerides, and high-density lipoprotein (HDL) cholesterol levels. Metabolic syndrome was defined as the presence of three or more of the following risk factors: central obesity, insulin resistance, hypertension, elevated triglycerides, low HDL cholesterol, and elevated fasting blood glucose.

A 3 mL blood sample was collected from each patient to measure homocysteine levels. Serum homocysteine was analyzed using the Fluorescence Polarization Immunoassay (FPIA) method with the IMX analyzer from Abbott Laboratories, Pakistan. Homocysteine levels were categorized as follows:

Normal: 5–12 micromoles per liter (µmol/L), Mildly elevated: 13–30 µmol/L, Moderately elevated: 31–100 µmol/L, Severely elevated: >100 µmol/L

All data was recorded using a self-designed proforma and analyzed using SPSS version 20.0.

Results

A total of 90 cases of metabolic syndrome were studied. The mean age of participants was 46.62 ± 14.82 years, ranging from 23 to 60 years. The average duration of the

Table I: Descriptive statistics of age, hypertension HDL, triglyceride, hypertension, diabetes and Homocysteine. (n=90)

Statistics	Age (years)	Systolic (mmHg)	Diastolic (mmHg)	FBS (mg/dl)	HDL (mg/dl)	TG (mg/dl)	Hcy (mcmol/L)
Mean	46.62	136.75	90.00	140.78	34.93	210.97	15.94
Std. Deviation	14.82	17.75	8.93	18.90	8.14	20.50	5.72
Minimum	23	120.00	70.00	125.00	21.00	102.00	2.42
Maximum	60	190.00	120.00	199.00	62.00	260.00	26.98

disease was 13.51 ± 4.54 years. The mean systolic blood pressure was 136.75 ± 17.5 mmHg, while the mean diastolic blood pressure was 90.0 ± 8.93 mmHg. The mean fasting blood sugar level was 115.78 ± 18.90 mg/dL. The mean HDL level was 34.93 ± 8.14 mg/dL, and the average triglyceride level was 210.97 ± 20.50 mg/dL. The mean homocysteine level in this study was 15.94 ± 5.72 µmol/1, as shown in table I.

In this study, hyperhomocysteinemia was observed in 72.2% of cases, while 27.8% had normal homocysteine levels. Figure 1

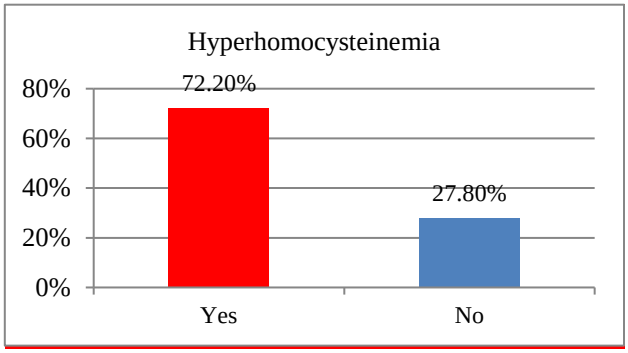

Figure 1. Frequency of hyperhomocysteinemia. (n=90)

The prevalence of hyperhomocysteinemia was not statistically significant concerning gender (p = 0.692). Table II

However, a significant positive correlation was found of homocysteine levels with HDL and triglyceride level (at the 0.05 level (2-tailed). Table III

Table III: Pearson correlation of HDL, triglyceride and microalbumin with homocysteine level. (n=90)

Variables	Homocysteine level	HDL	Triglyceride
Homocysteine level			
Pearson Correlation	1	.208*	.154
Sig. (2-tailed)		.049	.148
HDL			
Pearson Correlation	-.200	1	-.188
Sig. (2-tailed)	.069		.076
N	90	90	90
triglyceride			
Pearson Correlation	.154	-.188	1
Sig. (2-tailed)	.148	.076	
N	90	90	90

*. Correlation is significant at the 0.05 level (2-tailed).

Discussion

The MetS is linked to an increased risk of CVD. IR can produce or result in increased plasma homocysteine, which might signal vascular risk or play a role in atherogenesis. The prevalence of metabolic syndrome is depending on geographical location and age of the study population.[11] Elevated fasting plasma homocysteine levels have been reported in hypertensive patients of different age and ethnicity. In this study mean age of the patients was 46.62±14.82 years, average duration of disease was 13.51±4.54 years and males were in majority 56.7%. However, Gori F et al[11] found a higher mean age of 55 ± 14 years and reported an inconsistent finding regarding gender as females in majority at 75%. On the other hand, Esteghamati A et al[12] reported a mean age of 57.1 ± 11.5 years, with males comprising 58% of the study population. These some variations in findings may be attributed to differences in study populations, geographic locations, and sample sizes.

In this study, hyperhomocysteinemia was observed in 72.2% of cases, while 27.8% of participants had normal homocysteine levels. Consistently, Tarcau BM et al[13] reported a prevalence of hyperhomocysteinemia in 45.3% of individuals with cardiometabolic syndrome, reinforcing the association between elevated homocysteine levels and metabolic disorders. Similarly, Saeed A et al[14] found that 40% of metabolic syndrome (MS) patients exhibited raised plasma homocysteine levels. Additionally, a recent study reported hyperhomocysteinemia in 82% of individuals with schizophrenia and 74% of those with bipolar disorder, indicating a potential link between psychiatric conditions and metabolic syndrome.[15] However; inconsistencies exist in the reported prevalence rates. For instance, Yakub M et al[16] reported a significantly lower prevalence of hyperhomocysteinemia at 18.4%. This discrepancy may be attributed to the younger age of participants in their study, as the mean age was 7.48 ± 0.65 years, whereas hyperhomocysteinemia is more commonly observed in older populations. Age-related metabolic changes and variations in dietary intake likely contribute to these differences. In contrast, Fu S et al[8] reported an

Table II: Frequency of hyperhomocysteinemia according to gender. (n=90)

Variables			Hyperhomocysteinemia		Total	p-value
			Yes	No		
Gender	Male	Count	36	15	51	0.692
		% of Total	40.0%	16.7%	56.7%	
	Female	Count	29	10	39	
		% of Total	32.2%	11.1%	43.3%	

even higher prevalence, with 91.6% of individuals exhibiting both hyperuricemia and hyperhomocysteinemia, suggesting potential regional, genetic, or lifestyle-related influences on these metabolic markers. Serum Hcy levels are associated to MetS among general population and the aged population, according to research.[17,9] Furthermore, just a few research have looked into this link in China, let alone in Chinese centenarians.

In this study, a positive association was observed between triglyceride (TG) and homocysteine (Hcy) levels, while a negative correlation was found between high-density lipoprotein cholesterol (HDL-C) and Hcy levels. Consistent with these findings, Wu DF et al[20] reported that elevated homocysteine concentrations in the blood were directly correlated with increased levels of total cholesterol (TC), TG, and low-density lipoprotein cholesterol (LDL-C), as well as with advancing age. Similarly, Momin M et al[20] found that elevated Hcy levels were associated with hypertriglyceridemia and low HDL-C levels, suggesting that Hcy may play a role in TG metabolism and HDL-C regulation.

Additionally, Amena F et al[21] reported a significant negative correlation ($r = -0.32$) between serum Hcy and HDL-C, along with a positive association between serum Hcy and TG levels. Previous research has also suggested a potential link between hyperhomocysteinemia and atherosclerosis. Studies in both humans and various animal models of HHcy have documented an inverse relationship between lipoproteins and Hcy, particularly HDL-C.[22] Homocysteine has been implicated in the regulation of lipid metabolism by promoting cholesterol and triglyceride production. Its accumulation in endothelial cells may serve as a mechanistic link between elevated plasma homocysteine levels and the development of atherosclerosis.[23] Moreover, Hcy induces endoplasmic reticulum stress, which activates genes involved in the synthesis and absorption of triglycerides and cholesterol.[24] The present study also identified an association between MetS and hyperhomocysteinemia, suggesting that elevated Hcy levels may serve as a potential marker for MetS development.

This study possess certain limitations like limited sample size, lifestyle and dietary influences were not thoroughly assessed. Furthermore, key inflammatory and oxidative stress biomarkers were not included, restricting a comprehensive understanding of underlying mechanisms. Further large scale-studies are recommended using longitudinal designs, larger diverse populations, and detailed lifestyle assessments.

Conclusion

According to the study conclusion, the hyperhomocysteinemia was found to be highly prevalent among patients with metabolic syndrome and is also considered a potential marker for the condition. However, its association with gender, low HDL levels, and serum triglyceride levels was statistically insignificant. Further large-scale studies are needed to explore this subject in greater depth.

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