

## CORRELATION BETWEEN HOMOCYSTEINE AND LIPID LEVELS IN PATIENTS WITH ISCHEMIC HEART DISEASE

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### Contribution

RM conceived the idea and designed study. MAK, MHM and MN did data collection and manuscript writing. MZL did review. All authors contributed equally to the submitted manuscript.

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### ABSTRACT

**Objective:** To determine the correlation between homocysteine and lipid profile in patients with ischemic heart disease.

**Methodology:** This cross-sectional study was conducted on patients of ischemic heart disease aged 25-60 years admitted in coronary care unit of Punjab Institute of Cardiology Lahore after ethical committee approval from 1st November 2014 to 31st October 2014. Fasting venous blood samples were obtained from the participants to measure the plasma homocysteine levels and lipid profile. The patients were also assessed for traditional risk factors such as age, sex, family history of CVD, hypertension, smoking, dyslipidemia and physical activity. The data was analyzed through SPSS version 22. Coefficient of correlation (r) was calculated to establish correlation between the variables.

**Results:** Total 105 patients were included. The mean age of the study population was  $44.7 \pm 8.59$  years. Among 105 participants 79 (75.2%) were males. The value of coefficient correlation (r) for total cholesterol and Homocysteine was 0.189 ( $p=0.006$ ), for triglycerides and homocysteine was 0.12 ( $p=0.082$ ), and for LDL-C and homocysteine was 0.295 ( $p=0.000$ ) showing weak positive correlation among the variables. On the other hand, the value of coefficient correlation for homocysteine and HDL-C represent a moderate negative correlation between these variables.

**Conclusion:** The study revealed that homocysteine has significant but weak correlation with Total C, Triglycerides, and LDL-C showing that in patients with high homocysteine level the level of these biomarkers is also found to be raised and vice versa. On the other hand, homocysteine has moderately weak correlation with HDL-C i.e., in patients with high level of homocysteine, the level HDL-C was found to be decreased.

**Key Words:** Homocysteine, Lipid profile, Ischemic heart disease, Cardiovascular diseases.

## INTRODUCTION

Cardiovascular diseases (CVDs) are considered as the primary cause of mortality and morbidity nationwide. According to an estimation these diseases accounts for about one third of all the deaths<sup>1</sup>. World Health Organization (WHO) declares that CVDs are responsible for about 30% of global deaths and this percentage is expected to encounter further increase in upcoming years<sup>2,3</sup>. It is worth mentioning that among the cardiovascular diseases, ischemic heart disease (IHD) is the most prevalent one, and is responsible for around 40-60% of all deaths. A lot of efforts are being put to control this devastating disease and the major focus have been shifted toward the preventive measures. Identification as well as the effective management of various risk factors of IHD has manifested significant milestones in this direction. Although the role of conventional risk factors for IHD like hypertension, diabetes mellitus and smoking have been widely established but there is a persistent search for other possible risk factors. Among the emerging risk factors, significant attention have been focused towards the role of homocysteine and lipid levels as the risk factors of CVDs<sup>5,6</sup>. Homocysteine (Hcy), a normal metabolite of the essential amino acid methionine, is thought to be involved in the vascular changes in patients with homocystinuria. Research has documented the significant association of the higher levels of Hcy with IHD. This evidence led to the hypothesis that even moderately elevated Hcy levels may be of importance in the progression of heart disease. Number of studies have already been conducted to reveal the relationship between homocysteine level and the risk of CVDs<sup>7</sup>. However, it is still uncertain that the increased level of homocysteine is a risk factor for the CVDs or is an independent indicator for some other causal risk factors<sup>8</sup>.

Dyslipidemia or abnormal lipid level has also been identified as major cause of IHD leading to global morbidities and mortalities<sup>9</sup>. Dyslipidemia are characterized by raised levels of total cholesterol, triglycerides (TGs), and low density lipoprotein (LDL) whereas decreased levels of HDL cholesterol.<sup>10</sup> Although mortality rate due to IHDs has reduced over the past few decades, further strategies for reducing IHD risk are still being discovered. The global impact of homocysteine and dyslipidemia on health has encouraging a lot of researches to minimize this public health issue<sup>11,12</sup>. This study is aimed to determine the correlation between homocysteine and lipid profile among patients with ischemic heart disease.

## METHODOLOGY

An analytical cross-sectional study was conducted from November 2014 to October 2015. The study subjects were newly admitted patients of ischemic heart disease at Punjab Institute of Cardiology, Lahore. Patients of both genders were included in the study. The study subjects were included after the diagnosis of IHD by coronary angiography. However, the patients who were taking lipid lowering treatment or with known history of diabetes, renal problems, hepatitis or thyroid disorders were excluded from the study. Pregnant females and those taking antiseptic drugs or any other drugs that affect the liver function, or any form of vitamin B complex used during the past 6 months were also excluded. The study was approved by the ethical committee of the Institute.

After the written informed consent from all the study subjects detailed personal, family and medical history including socio-economic status, dietary habits and physical activity was recorded on a pretested questionnaire. Height and weight were measured to calculate the body mass index (BMI). Fasting venous blood was taken and standard procedure for sample collection and storage was opted. The blood sample was centrifuged at 400rpm for 10 minutes to obtain serum. The serum levels of total cholesterol, triglycerides, high-density lipoprotein were determined using enzymatic colorimeter method (RANDOX, UK). Low density lipoprotein (LDL) cholesterol concentration was calculated using Friedwald formula. Plasmahomocysteine level was analyzed using Fluorescence Polarization Immunoassay (FPIA) method on automated immunoassay analyzer (Abott, IMX).

The collected data were entered in SPSS version 22 for analysis and interpretation. Mean  $\pm$  S.D were used for quantitative data like age, homocysteine level and lipid profiles. The relationship between homocysteine levels and lipid profile was found by the Pearson correlation.  $P \leq 0.05$  was considered significant

## RESULTS

Among the total 105 study participants, 79 (75.2%) were males and 26 (24.8%) were females. The age of the participants ranged between 25 to 60 years with a mean of  $44.7 \pm$  SD 8.59 years. The basic profiles of the study subjects including gender distribution, BMI and risk factors are presented in table 1.

Out of 105 participants of the study, 21% had normal level of homocysteine, 60% had moderate Hyperhomocysteinemia whereas 19% had intermediate hyper homocysteinemia. The classification was based on the following distribution, normal 5-15  $\mu\text{mol/L}$ , moderate >15-30  $\mu\text{mol/L}$  and intermediate Hyperhomocysteinemia >30-100  $\mu\text{mol/L}$ .<sup>13</sup> The average plasma Hcy level of study population was  $22.33 \pm 9.22 \mu\text{mol/L}$ . The analysis of Hcy level in different classes of hyper homocysteinemia showed that only 21% of had normal homocysteine level i.e.  $13.06 \pm 1.27 \mu\text{mol/L}$ . The percentage of patients with moderate and intermediate hyper homocysteinemia was 60.0% and 19.0% respectively. These findings are presented in table 2. The lipid profile of the study subjects is also illustrated in table 2. Significantly high proportion of patients was found to have raised serum cholesterol and low-density lipoprotein cholesterol (LDL-c) 39% and 26.7% respectively. High density lipoprotein levels were lower in 40% participants. The raised level of serum triglyceride was present in 29.5% of the participants.

The correlation between homocysteine and lipid profile has been shown in table 3. The value of coefficient correlation ( $r$ ) for total cholesterol and Homocysteine was 0.189 ( $p=0.006$ ), for triglycerides and homocysteine was 0.12 ( $p=0.082$ ), and for LDL-C and homocysteine was 0.295 ( $p=0.000$ ), showing were weak positive correlation among the variables. On the other hand, the value of coefficient correlation for homocysteine and HDL-C showed moderate negative correlation between these variables.

**Table 1: Base line Characteristics of the Study Population (n = 105)**

Variable		Frequency n (%)
Age (years)		44.7±8.59
Body mass index (kg/m <sup>2</sup> )		25.69±2.91
Gender	Male	79(75.2%)
	Female	26(24.8%)
Risk factor	Hypertension	41(39%)
	Family History of IHD	28(26.7%)
	Smoking	48(45.7%)
	Sedentary lifestyle	36(34.3%)

**Table 2: Lipid profile of study population (n = 105)**

Variables		Frequency n (%)	Mean ± SD	
Plasma Homocysteine Level	Normal (5-15 μmol/L)	22 (21%)	13.06±1.27	
	Moderate Hyper homocysteinemia (> 15-30 μmol/L)	63 (60%)	20.23±2.46	
	Intermediate Hyperhomocysteinemia (>30-100 μmol/L)	20 (19%)	39.14±5.70	
	Total Homocysteine	105 (100%)	22.33±9.22	
Lipid Profile	Triglycerides	Within Normal range (<150mg/dl)	74 (70.5%)	128.96±35.84
		Hyper triglyceridemia (>150mg/dl)	31(29.5%)	
	HDL Level	Within Normal range (>35mg/dl)	63 (60%)	36.30±5.48
		Below Normal (<35mg/dl)	42 (40%)	
	LDL Level	Within Normal range (<130mg/dl)	77 (73.3%)	110.11±27.48
		Above Normal (> 130mg/dl)	28 (26.7%)	
	Total Cholesterol	Within Normal range (<200mg/dl)	64 (61%)	184.74±42.16
		Hypercholesterolemia (>200mg/dl)	04 (39%)	

**Table 3 Correlation between Homocysteine and Lipid Profile**

Lipid Profile (mg/dl)	Homocysteine Level (μmol/l)	
	Pearson correlation (r)	P-value
Triglycerides	0.12	0.082
HDL Level	-0.341	0.000
LDL Level	0.295	0.000
Total Cholesterol	0.189	0.006

## DISCUSSION

Ischemic heart disease is one of the major causes of death worldwide. The control or avoidance of the known modifiable risk factors is a rational approach for prevention. Moreover, there is a dire need to search for the unidentified or less investigated risk factor to combat this major health issue. This study not only demonstrates the possible linear relationship among the variables but also the strength of this relationship<sup>14</sup>. There is a well-established association between the abnormalities of lipid profile and ischemic heart diseases. The deranged levels of lipid profile including increased total cholesterol, raised triglycerides, high HDL and low LDL enhances the risk of heart disease and stroke<sup>15</sup>. It is worth mentioning that high serum total and LDL cholesterol are important risk factors for IHD<sup>16,17</sup>. The raised LDL levels are linked with myocardial infarction and peripheral vascular disease, while HDL cholesterol protects against these disorders. The mean levels of serum lipid profile among the study participants who were patients of ischemic heart disease have been summarized in table 2. Interestingly, the mean levels of lipid profile were found in the normal range. In previous studies elevated levels of total Cholesterol, LDL, triglyceride and decreased level of HDL were reported to be major risk factors for IHD<sup>18</sup>. Specifically a 10% increase in serum Cholesterol is associated with a 20-30% increased risk of ischemic heart disease and elevation earlier in life may be associated with higher risk of IHD as reported by Ben Lacey<sup>19</sup>. A low serum level of HDL and raised triglyceride along with increased LDL levels can occur alone or in combination and multiply the risk of IHD.

In the present study when related to homocysteine levels, total cholesterol and LDL-C showed significant positive correlation ( $r=0.189$ ,  $p=0.006$  and  $r=0.295$ ,  $p=0.000$  respectively), whereas HDL-C showed moderatenegative correlation ( $r=-0.34$ ,  $p=0.000$ ) with homocysteine. These results coincide with the finding of a meta-analysis by Robert Clarke, in which this was concluded that at maximum elevated levels of homocysteine, it can be considered as a moderate risk factor for ischemic heart disease and stroke among healthy population. This meta-analysis was conducted on the articles published over a period of 33 years from 1966 to 1999.<sup>20</sup> Another relevant study concluded that homocysteine levels are a novel and independent risk factor for coronary heart disease in Indian and Asians living in UK, as compared to Europeans. The authors proposed that these levels are most probably elevated because of Vitamin B12 and folate deficiency and they suggested to improve by supplementing C vitamin.

A non-significant correlation was observed between homocysteine and triglyceride ( $r=0.120$ ,  $P=0.082$ ) as presented in table 3. These results suggest concomitant alteration in lipid profile along with homocysteine levels in CHD patients. Similar results were reported by Cut Aria Arina and Mohetaboer Momin al, who recorded strong positive correlation of homocysteine with total Cholesterol and LDL-C and an inverse association with HDL-C<sup>22,23</sup>.

## CONCLUSION

The study revealed that homocysteine has a positive correlation with total cholesterol triglycerides, and LDL showing that in patients with high homocysteine level the level of these biomarkers is also found to be raised and vice versa. However, homocysteine has a negative correlation with HDL i.e., in patients with high level of homocysteine, the level HDL was found to be decreased.

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