Original Research Article **Biochemistry**

International Journal of Pharma and Bio Sciences

ISSN 0975-6299

A STUDY ON THE ESTIMATION OF SERUM LIPID PROFILE AND HOMOCYSTEINE IN CORONARY ARTERY DISEASE

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ABSTRACT

Coronary artery disease occurs due to inflammation and endothelial dysfunction of the blood vessels also known as atherosclerosis. The nonessential sulphur containing amino acid Homocysteine is considered to be a risk factor for myocardial infarction caused by damage to coronary arteries. The study was conducted on 60 individuals which included 30 cases of coronary artery disease diagnosed by angiography and 30 normal healthy individuals. Lipid profile and Homocysteine was estimated and compared among the two groups. There was a significant increase in Homocysteine in cases but no significant difference in lipid profile when compared to controls. Hence this study was done to indicate that Homocysteine can be considered as a risk factor for coronary artery diseases.

KEYWORDS: **Homocysteine, Lipoproteins, Coronary artery diseases**

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Received on: 09.02.2017
Revised and Accepted on: 05-04-2017
DOI: http://dx.doi.org/10.22376/ijpbs.2017.8.2.b662-665

INTRODUCTION

Coronary artery disease(CAD) is an important cause of mortality and morbidity in developed countries. As the age increases, coronary arteries that supply the heart with oxygen and nutrients develop atherosclerotic plaques in their walls. Myocardial infarction(MI) occurs when the blood flow to a portion of the heart decreases, leading to damage of heart muscle, thereby causing shortness of breath, angina and sometimes fatal heart attacks. Risk factors of MI include increasing age, high blood pressure, diabetes and family history of coronary artery diseases. Modifiable lifestyle changes like smoking, physical inactivity, eating fat rich diet are also risk factors. However, recent studies suggest a correlation between plasma Homocysteine and vascular disease.[1] Homocysteine is a nonessential sulphur containing amino acid that is obtained from metabolic demethylation of essential amino acid methionine. Homocysteine in plasma is present as reduced homocysteine (1%), in combination with albumin (70%), and remaining (29%) as low molecular disulphides mainly cysteine.[2] Homocysteine thiolactate a byproduct of oxidation of homocysteine combines with Low Density Lipoprotein (LDL) to form foam cells.The LDL rich foam cells become a fatty streak leading to atherosclerotic plaque which is important in the pathogenesis of vascular endothelial damage and coronary artery disease.[3] Homocysteine/folate metabolism is mainly regulated by methylene tetrahydrofolate reductase (MTHFR) enzyme which catalyses the reduction of 5,10 methylene tetrahydrofolate to 5 methyl tetrahydrofolate the major circulating form of folate. Polymorphism of MTHR677C → T reduces the enzyme activity which in turn increases homocysteine levels and reduces folate concentration.[4]Hyperhomocystinemia can occur due to genetic or nutritional deficiency of folate, vitamin B12 or vitamin B6.[5] Studies done in 1980's and 1990's linked elevated blood levels of Homocysteine to increased risk of premature coronary artery disease, stroke and venous blood clots, even among people with normal cholesterol levels. [6,7] A,S.Yadav in his 2006 study had reported elevated homocysteine and lipid profile in coronary artery disease.[8] Recent studies have reported similar findings. Hence the present study was undertaken to estimate the levels of plasma homocysteine and lipid profile in myocardial infarction due to coronary artery disease.[9]

MATERIALS AND METHODS

The study was conducted on 60 subjects who attended a tertiary heart hospital between the months of April and September 2016. Before commencement of the study, ethical clearance from the hospital was obtained. 30 subjects who were admitted with chest pain and diagnosed as coronary artery disease by ECG and coronary angiography included the cases.30 normal subjects who came for general health check up included the control group.The control group were symptomless on clinical examination with normal ECG. Subjects with a history of diabetes, hypertension, renal and thyroid disorders were excluded from the study. After obtaining written consent fasting blood samples of about 8ml were drawn; serum was separated and analysed for Total cholesterol (TC), Triglycerides (TGL)and Automated High density lipoprotein (A-HDL) cholesterol using the Siemens Dimension autoanalyser. Total cholesterol was estimated by using cholesterol esterase and oxidase method. Serum triglycerides estimated by Glycerol kinase and peroxidase method The A-HDL assay measures High density lipoprotein cholesterol (HDL-C) levels directly. The HDL-C is oxidized to hydrogen peroxide which forms a coloured dye whose intensity is proportional to serum HDL-C concentration.[10]Very low density lipoprotein cholesterol (VLDL-C) and Low density lipoprotein cholesterol (LDL-C) were calculated using the Friedwald equation, (LDL-C= TC – HDL-C – VLDL-C); VLDL-C=TGL/5[11.] Homocysteine was determined by using the chemiluminescent microparticle immunoassay(CMIA) technique on the ARCHITECT i system. The oxidized or bound homocysteine is reduced to free homocysteine, which is subsequently converted to S-adenosyl homocysteine (SAH). The SAH then competes with acridinium labeled S-adenosyl cysteine for particle bound monoclonal antibody. The resulting chemiluminescence measured as relative light units (RLUs) by the ARCHITECT i System optics indirectly indicates the amount of homocysteine in the sample.[12] The data were analysed ,descriptive statistics like mean,standard deviation were calculated for the biochemical parameters in cases and controls.The data between cases and controls were compared using Student's t test. p value < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS software.

RESULTS

Table 1
Demographic characteristics of the study subjects

	CASES		CONTROLS	
Gender	**Frequency**	**Percentage**	**Frequency**	**Percentage**
Males	26	87	24	80
Females	4	13	6	20
Age in years				
30-40	4	13.3	3	10
41-50	4	13.3	6	20
51-60	13	43.3	11	37
61-70	8	26.8	8	27
>70	1	3.3	2	6

Graph 1
Demographic characteristics of the study subjects

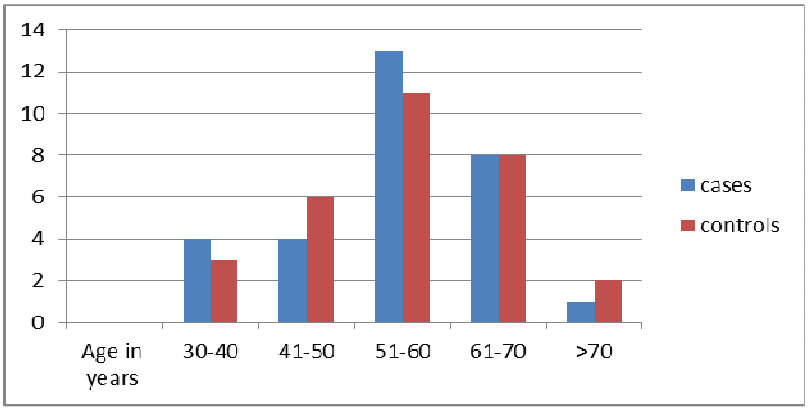
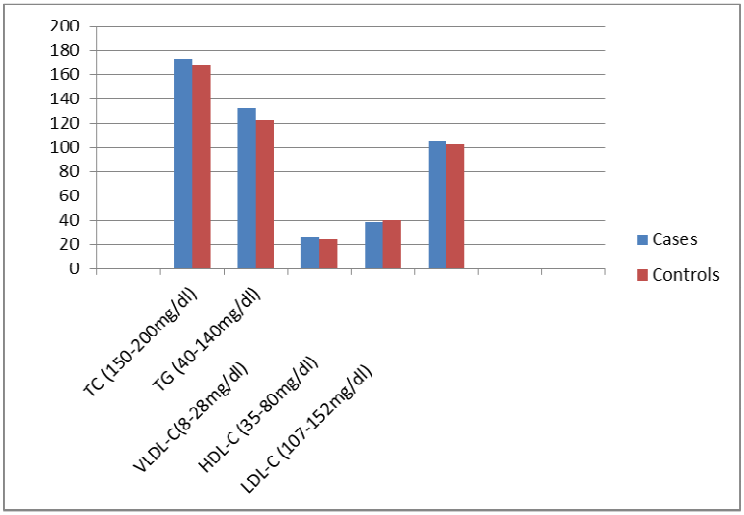


Table 2
Lipid profile in cases and controls

Lipid profile		Cases Mean±SD	Controls Mean±SD	p value	Significance
Total Cholesterol (TC)	(150-200mg/dl)	172.83±37.17	167.6± 30.34	0.55	NS
Triglycerides (TG)	(40-140mg/dl)	132.2±75.11	122.6±53.19	0.58	NS
VLDL-C	(8-28mg/dl)	26.5±15.59	24.5±10.67	0.56	NS
HDL-C	(35-80mg/dl)	38.96±8.22	40.37±8.39	0.51	NS
LDL-C	(107-152mg/dl)	105.36±27.27	102.7±24.61	0.69	NS

HS=Highly significant; NS= Not Significant; MS=Moderately Significant. ↑increase

Graph 2
Lipid profile in cases and controls

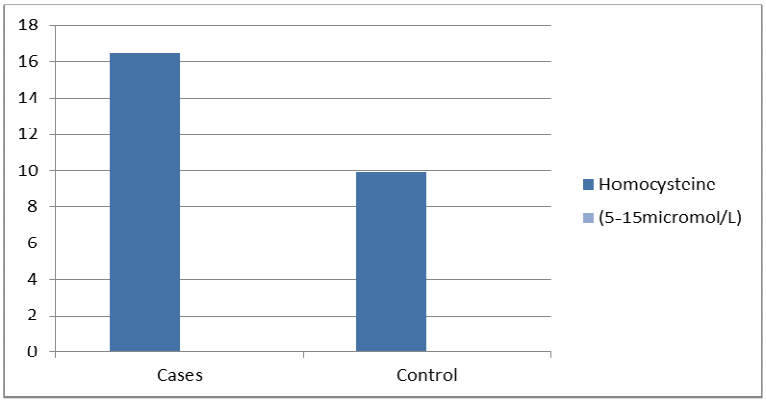


Note : There was no significant difference with p value ranging from 0.51 to 0.69 in all the lipid parameters between cases and controls as shown in the table and graph

Table 3
Homocysteine in cases and controls

Parameter	Cases Mean±SD	Controls Mean±SD	p value	Significance
Homocysteine (5-15micromol/L)	16.42±11.24	9.929±1.647	0.002	HS↑

Graph 3
Homocysteine in cases and controls



Note : There is a highly significant difference with p value of 0.002 in the Homocysteine level between cases and controls as shown in the table and graph

Table 4
Comparison of individual lipid parameters and Homocysteine in cases

Lipid parameters	Number of cases	**Homocysteine >15micromol/L**
TC<200-Normal	20	8
TC>200-Raised	10	2
TG<100-Normal	12	5
TG>100-Raised	18	5
LDL-C<100-Normal	16	4
LDL-C>100-Raised	14	6
HDL-C>40-Normal	10	3
HDL-C<40-Decreased	20	7

DISCUSSION

In this study Homocysteine and the serum lipid fractions were compared and analysed in normal controls and coronary artery disease cases. A number of studies have described an association between Homocysteine and cardiovascular events. According to Shenoy et al Homocysteine levels in coronary artery disease were significantly higher than in normal control .This was attributed to the severe endothelial dysfunction that occurred mainly due to the changes in vascular endothelial compliance and platelet coagulation. [13]In some studies Homocysteine was considered as an independent risk factor for atherosclerosis which is the most common pathological process that causes myocardial infarction, stroke and heart failure.[14] Other studies have observed an altered lipid profile like increased TC, increased TGL, increased LDL-C and a decrease in HDL-C along with elevated Homocysteine in coronary artery disease .Specifically a 10% increase in serum cholesterol is associated with a 20% to 30% increased risk of CAD and elevations earlier in life maybe associated with higher risk of CAD as given by Lorosa et al. [15] Liao et al in his study showed that homocysteine reduced the concentration of HDL cholesterol by inhibiting the synthesis of HDL apolipoprotein.[16] In this study Homocysteine levels in cases was significantly higher than in controls with a p value of 0.002.The TC,TGL,VLDL-C,LDL-C and HDL-C did not show any significant difference between cases and controls. However the correlation between Homocysteine and the individual lipid parameters in cases showed that a decreased HDL-C is associated with an increase in Homocysteine level .The study in Greece indicated that Homocysteine is not an independent risk factor for CAD but that the myocardial infarction patients showed an increased trend in Homocysteine levels.[17] The analyses by Veerana et al also established Homocysteine as a marker in predicting adverse cardiovascular disease events.[18] Most studies state that an elevated Homocysteine can increase the oxidative stress and inflammation of the vascular endothelial cells and thereby decrease the production of nitric oxide which is a strong relaxing factor .Homocysteine also increases HMG CoA reductase which increases cholesterol synthesis and hence atherosclerosis.[19] However ,in the present study there was no increase in cholesterol levels in cases when compared to controls. Yang et al has reported a negative co relation between Homocysteine and HDL-C along with Apo A-1. N homocysteinylation is the process where homocysteine thiolactone (HcyT) forms an isopeptide with the lysine residues of the proteins. N-homocysteinylation of Apo A-1 impairs its antioxidant ability. Hyperhomocysteinemia can therefore inhibit reverse cholesterol transport by reducing circulating HDL via the inhibition of Apo A-I protein synthesis, resulting in an increased risk of atherosclerosis.[20] In the present study also an association between a low HDL-C and increased Homocysteine was observed in the cases. However, a few studies have shown a negative correlation between Homocysteine and coronary artery disease.[21]Some clinical studies have shown that increasing dietary intake of vitamin B12 and folic acid has reduced the Homocysteine concentration and the risk of coronary artery disease. [22]From this study as there is a significant increase in Homocysteine levels in

cases when compared to controls, we can consider this biochemical parameter as a risk factor for coronary artery diseases. Even the association between a low HDL –C and increased Homocysteine observed in cases can be considered from this study.

CONCLUSION

Homocysteine was significantly elevated in coronary artery diseases when compared to controls in this study. However this investigation can only be an add on to the invasive coronary angiography. However an increase in the study group can further substantiate the study. Also estimation of Homocysteine before and after vitamin B12 and folic acid supplementation in the cases and controls over a longer period of study can further authenticate the study.

CONFLICT OF INTEREST

Conflict of Interest declared none.

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We sincerely thank the above reviewers for peer reviewing the manuscript