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Original Research Article

The Relationship between Plasma Homocysteine Levels and Diabetic Complications in Patients with Type 2 Diabetes Mellitus

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Abstract:

Background: Patients with Diabetes Mellitus have 2- to 6-fold increase in the prevalence of cardiovascular disease (CVD) as compared to non-DM subjects. Epidemiological data has shown that DM is synergic with other conventional risk factors. Total plasma homocysteine (tHcy) is an emerging CVD risk factor. We did a cross-sectional study to explore the relationship between tHcy and CVD in patients with DM.

Methods: The present study was conducted in department of medicine in collaboration with department of Physiology in IIMSR for a period of one year from June 2022 to May 2023.A total number of 316 diabetic patients between age group 25-65 years were enrolled from the diabetic clinic and those admitted in the Department of Medicine IIMSR who satisfied the selection criteria (n=316)..

Results: Out of 316 diabetic patients, 197 have duration of diabetes less than 5 years, out of these 116 (58.9%) had normal and 81 (41.12%) had raised plasma Homocysteine level. 108 diabetic patients had duration between 5 to 10 years, out of these 46 (42.59%) patients had normal and 62 (57.4%) patients had raised plasma Homocysteine level which was statistically significant (x^2=1.91, p=0.019). 11 patients had duration more than 10 year So, majority of diabetic patients who had raised plasma Homocysteine level had duration between 5 to 10 years. Out of 316 diabetic patients, 26 (8.2%) patients had stroke and 24 (7.5%) had coronary artery disease. These patients had significant elevation of plasma homocysteine level as compared to those patients who had no evidence of cerebrovascular or cardiovascular disease (p=<0.001). homocysteine level .

Conclusions: This study concludes plasma homocysteine level can be considered as an early marker, It can be concluded from our study that diabetic patients who had elevated homocysteine level have more complications in the form of nephropathy, neuropathy, retinopathy and higher incidence of cerebrovascular disease and ischemic heart disease as compared to those diabetic patients who had normal plasma homocysteine level. We also recommend for routine screening of plasma homocysteine level for purpose of treating elevated homocysteine concentrations in the wider adult populations.

Key words: Total plasma homocysteine, Coronary artery disease, Nephropathy, Ischemic Heart Disease.

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Introduction

Diabetes mellitus is a highly prevalent metabolic disease and is a major global health problem. Prevalence of diabetes has tripled since 1970. The number of cases of diabetes mellitus World Wide in 2000 among adult of >20 years of age is estimated to be 171 million. The prevalence of diabetes for all age group worldwide was 2.8% in 2000 and estimated to be 4.4% in 2030[1].

In India >40 million people have diabetes mellitus. The crude prevalence rate of diabetes is estimated to be around 9% in urban areas and 3% in rural areas. [2]. Homocysteine (Hcy) is the transmethylation product of the essential sulphur-containing amino acid methionine. Experiments have shown that high concentrations of homocysteine may cause vascular Epidemiological research suggests an association between elevated total homocysteine (tHcy) levels and cardiovascular disease (CVD), which is the most common cause of mortality in patients with type 2 diabetes mellitus [3]. The association between homocysteinemia and atherosclerotic vascular disease is especially strong in patients with type 2 diabetes, compared to nondiabetic subjects. Increased plasma tHcy levels are reported to be associated with hypertension, hyperlipidemia, smoking, hyperuricemia, and impaired adrenal function. Plasma tHcy concentration is strongly related to renal function. A study in rats identified the kidney as a major site for removal and metabolism of Hcy. Two mechanisms appear to be involved. The main source of Hcy is adenosylmethionine-dependent methylation of guanidoacetate to form creatine and its anhydride creatinine. Second, renal function plays a central role for clearance of both creatinine and Hcy[4]. Growing interest is being focused on the association of homocysteinemia with diabetes mellitus. However, consensus on how type 2 diabetes affects plasma homocysteine concentrations has not been achieved. Homocysteinemia has been established as a risk factor for cardiovascular disease and occurs with high prevalence in patients with type 2 diabetes: 31% of type 2 diabetic patients have homocysteine concentrations above >15 mmol/L**.** Only a few studies found no significant differences in fasting plasma tHcy levels between type 2 diabetic patients without microalbuminuria and healthy control subjects. A large amount of evidence supports increased plasma tHcy levels in type 2 diabetes [5].

Material and methods:

The present study was conducted in department of medicine in collaboration with department of Physiology in IIMSR for a period of one year from June 2022 to May 2023.A total number of 316 diabetic patients between age group 25-65 years were enrolled from the diabetic clinic and those admitted in the Department of Medicine IIMSR who satisfied the selection criteria (n=316). Diabetic patients who were enrolled were non-smokers, doesn't have vitamin B12 deficiency or hypothyroidism, non-hypertensive, not on antifolate drugs, and does not have established chronic kidney disease.

The information collected and observations made during the study are presented below.

Mean age of the diabetic patients (n=316) is 52.12 years. Mean age of the male patients were 53.76 years and of the female patients were 50.51 years. Male: Female ratio of the diabetic patients were 1.65:1.

Results

Demographic Profile Of The Study Group And Its Correlation With Plasma Homocysteine:

Table 1: Homocysteine level in selected diabetic patients according to age distribution

Age (years)	Normal Hcy.		Abnormal Hcy.		Total	'p' value
	No.	%	No.	%		
25-35	8	80	2	20	10	0.11
35-45	19	38.8	30	61.2	49	0.065
45-55	75	61.98	46	38.02	121	0.13
55-65	67	49.26	69	50.73	136	0.41

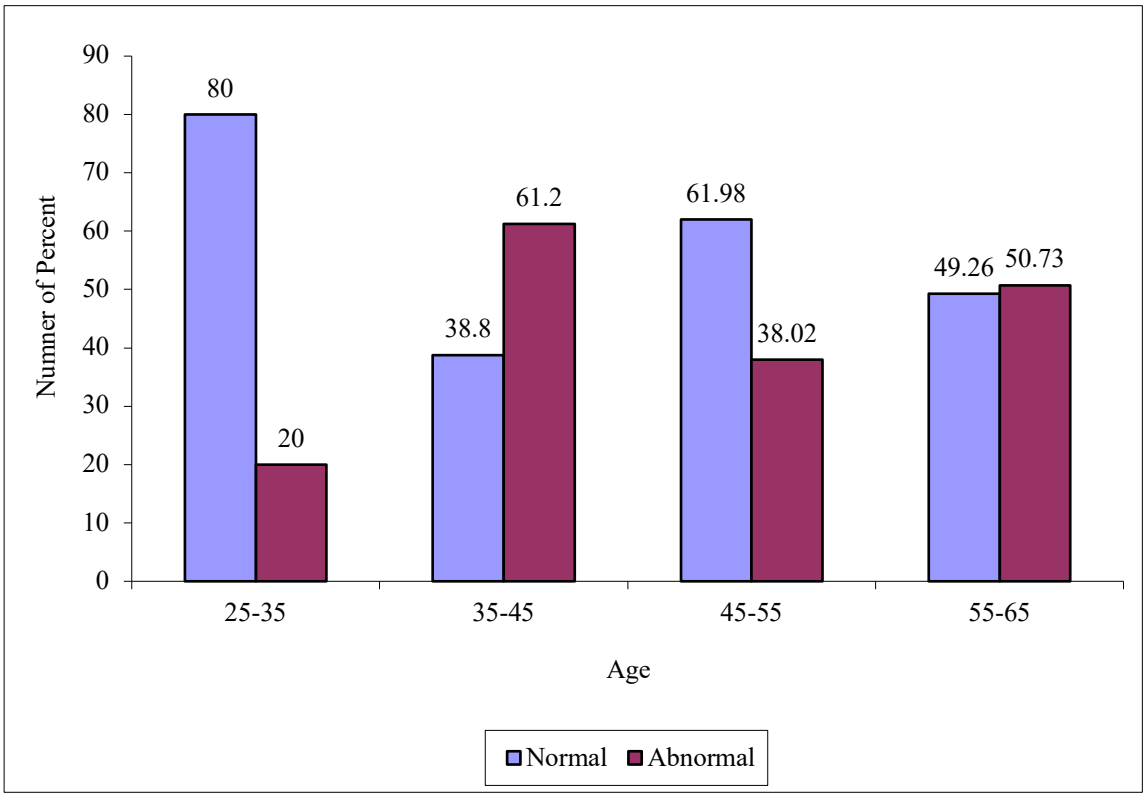

Figure 1:

Out of 316 diabetic patients in the study group, majority of patients are above the age of 45 years, 59 (18.6%) patients were below the age of 45 years whereas 257 (81.32%) patients were above 45 years. Patients between the age group between 35-45 years have significant elevation of plasma homocysteine level as compared to other age group. Out of 49 patients in this age, 30 (61.2%) have elevated plasma homocysteine level as compared to 19 (38.8%) who have normal homocysteine level, which was statistically significant (p=0.009, x2=11.5).

Table-2: Homocysteine level in selected diabetic patients according to duration of Diabetes

Duration (years)	Normal Hcy.		Abnormal Hcy.		Total	'p' value
	No.	%	No.	%		
<5	116	58.9	81	41.12	197	0.23
5-10	46	42.59	62	57.40	108	0.58
>10	7	63.63	4	36.36	11	0.55

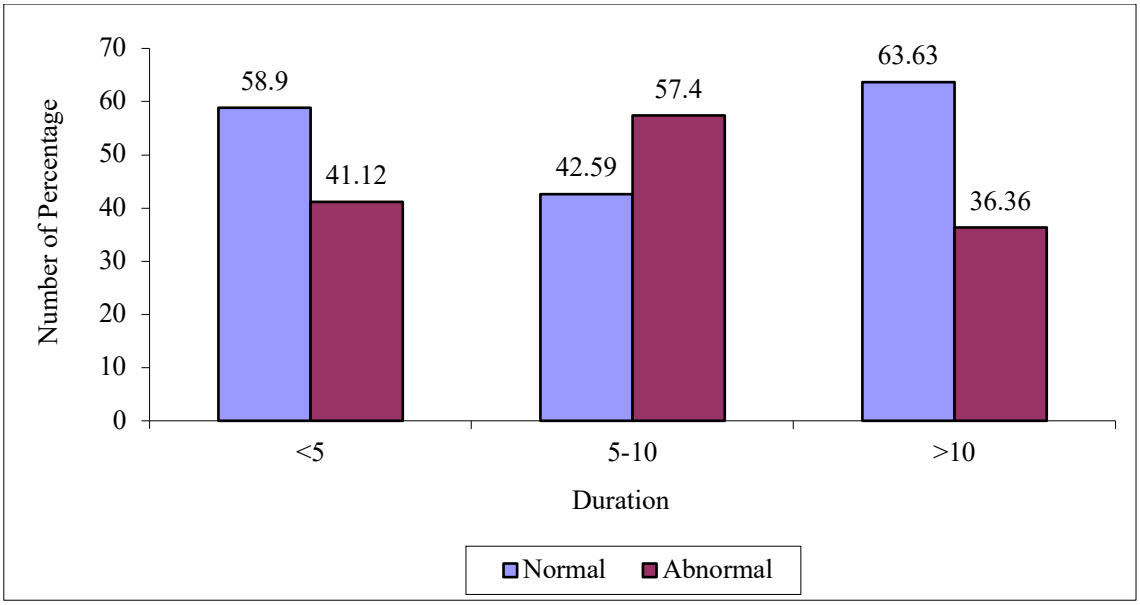

Figure 2:

Out of 316 diabetic patients, 197 have duration of diabetes less than 5 years, out of these 116 (58.9%) had normal and 81 (41.12%) had raised plasma Homocysteine level. 108 diabetic patients had duration between 5 to 10 years, out of these 46 (42.59%) patients had normal and 62 (57.4%) patients had raised plasma Homocysteine level which was statistically significant (x^2=1.91, p=0.019). 11 patients had duration more than 10 years. So, majority of diabetic patients who had raised plasma Homocysteine level had duration between 5 to 10 years.

Table 3: Homocysteine level in selected diabetic patients according to serum triglyceride level

Triglyceride (mg/dl)	Normal Hcy.		Abnormal Hcy.		Total	'p' value
	No.	%	No.	%		
<150	99	63.06	58	36.94	157	0.045
>150	70	45.74	89	54.26	129	0.052

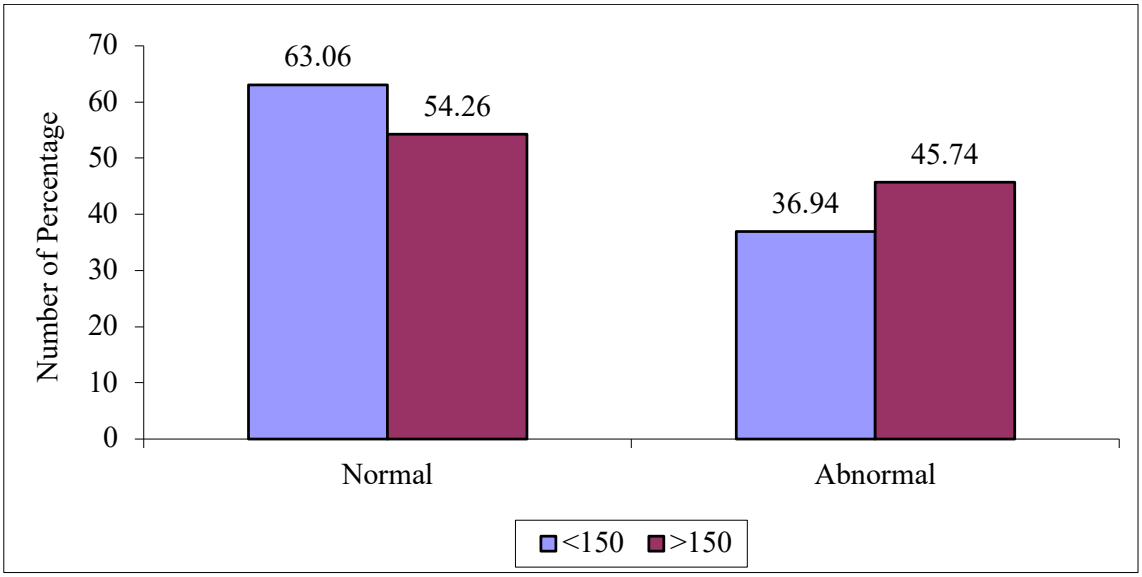

Figure 3

Out of 316 diabetic patients, 157 patients had normal triglyceride level (<150 mg/dl). Out of this 99 (63.06%) had normal and 58 (36.94%) had raised plasma Homocysteine level. 129 diabetic patients had raised triglyceride (>150 mg/dl) out of which 89 (54.26%) had raised and 70 (45.74%) had normal plasma Homocysteine level which was found to be statistically significant (x^2=11.50, p=0.001).

Table 4: Homocysteine level in selected diabetic patients according to HDL cholesterol level

HDL (mg/dl)	Normal Hcy.		Abnormal Hcy.		Total	'p' value
	No.	%	No.	%		
Normal	84	52.5	76	47.5	160	0.84
Abnormal	85	54.49	71	45.51	156	0.84

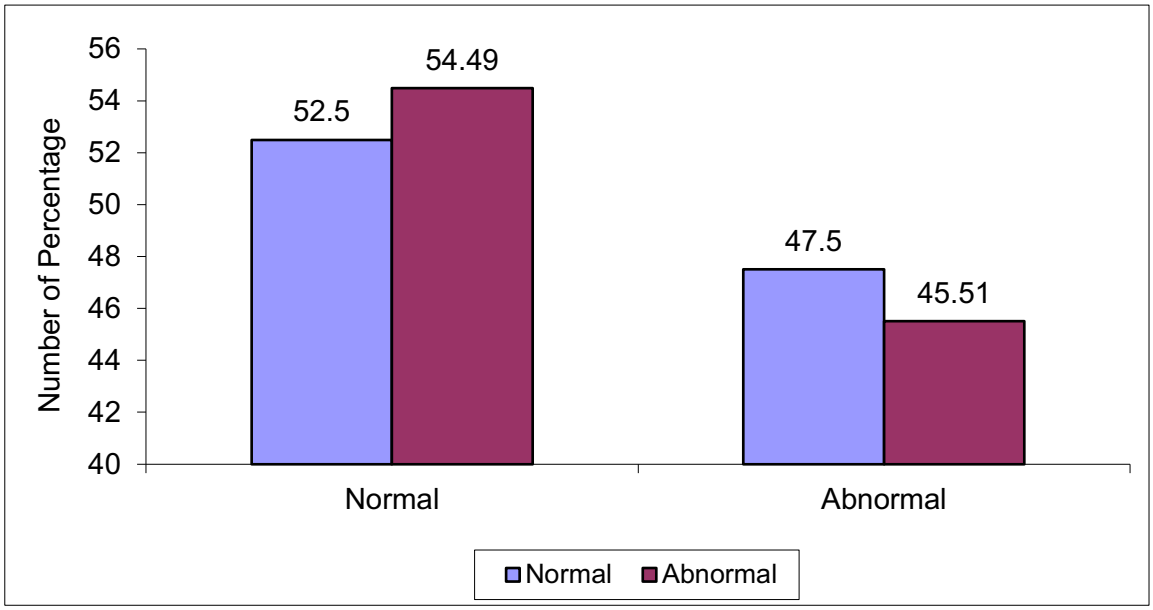

Figure 4:

Discussion

Out of 316 diabetic patients, 160 had normal HDL level out of which 84 (52.5%) had normal and 76 (47.5%) had raised plasma Homocysteine level. 156 diabetic patients had low HDL level out of which 85 (54.49%) had normal and 71 (45.51%) had raised plasma Homocysteine level. No correlation was found between plasma LDL and Homocysteine level (X2=013, p=0.72).

Out of 316 diabetic patients in the study group, majority of patients was above the age of 45 years. 59 (18.6%) patients were below the age of 45 years whereas 257 (81.32%) patients were above the age of 45 years. Patients between the age group between 35-45 years have significant elevation of plasma homocysteine level as compared to other age group. Out of 49 patients in the age group between 35-45, 30 (61.2%) patients had elevated plasma Homocysteine level as compared to 19 (38.8%) patients who had normal level which was statistically significant (x2=11.57, p=0.009). Although previous studies did not find any significant relationship between plasma homocysteine level and age of diabetic patients. In a study conducted by Jose Miguel Gonzalez Clemente et al in which they enrolled 93 diabetic patients with microalbuminuria in which they did not found any correlation between age of diabetic patients and plasma homocysteine level. Another study conducted by Lamia Borazines et al in 2008 in which they enrolled 168 diabetic patients with retinopathy and they also did not find

any significant correlation between plasma homocysteine level and age of diabetic patients. Though the sample size of the patients in our study in between the age group of 35-45 years was small (49 patients), homocysteine level was found to be elevated significantly. Further larger studies will be required in the near future to found some more definitive results.

In our study, out of 316 diabetic patients, majority of patients had duration of diabetes less than 5 years, however, significant correlation between plasma Homocysteine level and diabetic patients was found who had duration between 5-10 years. Out of 108 (34.17%) diabetic patients between this age group, 62 (57.40%) had raised plasma Homocysteine level as compared to 46 (42.59%) who had normal level which was found to be statistically significant (x2=7.91, p=0.019). A study conducted by Ilhan Tarkun et al in 2003 in which 38 diabetic patients were enrolled found no significant correlation between plasma Homocysteine level and duration of diabetes mellitus. Laima Brajionis et al conducted a study in which 168 patients were enrolled found no significant correlation between plasma Homocysteine level and duration of diabetes mellitus. In our study, a significant correlation was found between plasma Homocysteine level and elevated cholesterol and triglyceride level. Out of 316 diabetic patients, 44 (13.92%) patients had elevated cholesterol level (>200mg/dl). Out of these 44 patients, 28 (63.34%) patients had elevated plasma Homocysteine level while 16 (36.36%) patients had normal level which was found to be statistically significant (X2=6.02, p=0.014). 272 diabetic patients had normal cholesterol level. 129 (40.82%) diabetic patients out of 316 patients had elevated serum triglyceride level (>150mg/dl). Out of these 129 patients, 89 (54.26%) patients had raised plasma Homocysteine level as compared to 70 (45.74%) patients who had normal Homocysteine level which was found to statistically significant (x2=11.50, p=0.001). 157 patients had normal triglyceride level. Previous studies did not show any significant correlation between the plasma Homocysteine level and diabetic dyslipidemia. In the study conducted by Marie Jose J. Pouwels et al in 2008 found no significant correlation between elevated total cholesterol, triglyceride level and plasma Homocysteine level in diabetic patients. No significant correlation was found between plasma Homocysteine level and HDL, and LDL cholesterol level in our study

Conclusion

A significant correlation was found between plasma homocysteine and diabetic patients having duration between 5-10 years. 62 (57.40%) patients out of 108 patients had elevated plasma homocysteine level as compared to 46 (42.59%) patients who had normal homocysteine level (p=0).Those diabetic patients who had raised cholesterol and Triglyceride level had significant elevation of plasma homocysteine level (p=0.001) but no correlation was found with LDL and HDL cholesterol level.Out of 316 diabetic patients, 26 (8.2%) patients had stroke and 24 (7.5%) had coronary artery disease. These patients had significant elevation of plasma homocysteine level as compared to those patients who had no evidence of cerebrovascular or cardiovascular disease (p=<0.001).homocysteine level. Thus, plasma homocysteine level can be considered as an early marker It can be concluded from our study that diabetic patients who had elevated homocysteine level have more complications in the form of nephropathy, neuropathy, retinopathy and higher incidence of cerebrovascular disease and ischemic heart disease as compared to those diabetic patients who had normal plasma homocysteine level. Complications were also found in those diabetic patients who had normoalbuminuria but elevated plasma homocysteine level. Thus, plasma

homocysteine level can be considered as an early marker of progression of diabetes and its complications. We also recommend for routine screening of plasma homocysteine level for purpose of treating elevated homocysteine concentrations in the wider adult populations

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