



ORIGINAL RESEARCH PAPER

General Medicine

PLASMA HOMOCYSTEINE LEVELS AND ITS CORRELATION WITH DIABETIC RETINOPATHY

KEY WORDS: Diabetes Mellitus, Diabetic Retinopathy, Hyperhomocysteinemia

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ABSTRACT

BACKGROUND: Diabetic retinopathy (DR) is a microvascular complication that occurs in patients with diabetes mellitus (DM) and is the leading cause of new onset blindness. This study aimed to determine the possible association between plasma homocysteine (Hcy) levels and retinopathy.

METHODS: In this study, 100 subjects were divided into two groups, group 1 is diabetics without retinopathy and group 2 is diabetics with retinopathy.

RESULTS: Significant difference was seen in HbA1c, FBS, PPBS when compared between two groups. Hcy in group 1 was 9.74 ± 0.8 and group 2 was 14.598 ± 1.85 which was statistically significant ($p < 0.001$).

CONCLUSION: We found that there was a significant association between plasma Hcy level and DR in patients with type II DM.

INTRODUCTION

Diabetes mellitus (DM) is a major global health problem¹ In 2014 the global prevalence of DM was established to be 9% among adults aged 18 years². According to estimates of the World Health Organization, there were 346 million people suffering from diabetes worldwide in 2013³. WHO projects that diabetes will be 7th leading cause of death in 2030³. Type 2 DM accounts for 80% of all DM³. Diabetic retinopathy (DR) is microvascular complications of diabetes mellitus (DM), and the main cause of new onset blindness^{4,5}. The risk of blindness in diabetic patients is 25 times greater than non-diabetic population.¹ According to the literature the prevalence of DR varies from 6.7% to 35%.^{6,7}. It has been reported that over 60% of patients with type II DM develop retinopathy within one or two decades after diagnosis.⁸ DR results from microvascular decompensation beginning with basement membrane thickening, leading to vascular occlusion and eventual neovascularization. The duration of diabetes, poor glycaemic control, and hypertension (HTN) are documented risk factors in the development and progression of DR.⁹. Homocysteine(Hcy) is an emerging risk factor for cardiovascular and non-diabetic ocular vasooclusive diseases.⁶ Evidence has now accumulated showing that an elevated plasma Hcy concentration is a risk factor for vascular disease in both normal patients and those with renal disease. Elevated concentrations may induce endothelial dysfunction or abnormalities of coagulation factors and platelets.^{10,11} Hcy is a sulfur amino acid with a free thiol group, not present in dietary protein. This amino acid is a secondary by-product of methionine from cysteine metabolism. The mechanisms of Hcy pathogenesis in vascular damage are unclear. High Hcy levels can cause endothelial damage, with increased thrombosis and atherosclerosis. Hyperhomocysteinemia has been reported in both type 1 and type 2 DM patients. But limited research data is available regarding correlations of homocysteine levels and retinopathy in type 2 diabetes mellitus.

In this study we tried to evaluate the possible association between plasma Hcy level and DR in patients with type 2 DM.

MATERIAL AND METHODS

This study was conducted in diabetic patients with and without retinopathy above the age of 18 years, visiting medicine OPD of R L Jalappa Hospital, Tamaka, Kolar. Diabetic patient with Liver diseases, Thyroid disorders, on anti-epileptics, anticancer drugs, metformin, pregnant females and vasculitis were excluded. Detailed history regarding diabetes, family history and history of

drug intake was taken. Fundoscopy was done to look for retinopathy changes. At least two micro aneurysms and/or retinal hemorrhages and/or other signs of retinal damage were recognized as diabetic retinopathy. Serum homocysteine level was estimated by chemiluminescence immunoassay using Immulite 1000 immunoassay system (Siemens, Germany) Study population was divided into two groups: Diabetics without retinopathy and diabetics with retinopathy. Sample size of 50 patient in each group were included. Calculations were performed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Continuous data was represented as mean and standard deviation. p value < 0.05 was considered as statistically significant. The local ethic committee approved this study and all the subjects gave written informed consent.

RESULTS:

100 patients were included in the study and were divided into two groups: Group 1= DM without retinopathy. Group 2= DM with retinopathy. The mean ages in group 1 and 2 were 55.12 ± 11.755 and 56.08 ± 13.192 respectively. Males were predominant in the study population and 29 males out of 53 patients had retinopathy. Significant difference was seen in HbA1c, FBS, PPBS when compared between two groups. Hcy in group 1 was 9.74 ± 0.8 and group 2 was 14.598 ± 1.85 which was statistically significant ($p < 0.001$) (Table 2).

Duration of diabetes and Hcy values were significantly correlated, ie along with increase in duration of diabetes, homocysteine levels were also increased. Among different grades of NPDR, HbA1c, FBS, PPBS and Hcy showed significant correlation between mild, moderate and severe retinopathy (Table 3)

Table 1:- Distribution of subject according to sex among the group

SEX	DM		Total
	Without complication	With complication	
Female	26	21	47
	52.0%	42.0%	47.0%
Male	24	29	53
	48.0%	58.0%	53.0%
Total	50	50	100
	100.0%	100.0%	100.0%

P Value = 0.316, there was no statistically significant difference between sex and the group

Table 2:- comparison of mean age and clinical parameters among the group

	DM	Mean	Std. Deviation	P Value
AGE	Without complication	55.12	11.755	0.702 NS
	With complication	56.08	13.192	
HbA1C	Without complication	7.740000	.8882452	<0.001 S
	With complication	12.466000	1.5534832	
FBS	Without complication	138.98	8.707	<0.001 S
	With complication	214.20	28.559	
PPBS	Without complication	230.00	17.341	<0.001 S
	With complication	333.60	54.759	
Homocysteine	Without complication	9.740000	.8882452	<0.001 S
	With complication	14.598000	1.8546676	

Table 3:- comparison of clinical parameters among different type of Retinopathy

Retinopathy		HbA1C	FBS	PPBS	Homocysteine
Mild NPDR	Mean	11.965000	198.90	318.80	14.020000
	N	20	20	20	20
	Std. Deviation	1.3982226	12.818	59.185	1.9988418
Moderate NPDR	Mean	12.588889	229.44	324.61	14.577778
	N	18	18	18	18
	Std. Deviation	1.3559841	29.881	41.038	1.4735134
Severe NPDR	Mean	13.116667	216.83	371.75	15.591667
	N	12	12	12	12
	Std. Deviation	1.8944096	34.002	50.851	1.8387043
P value		<0.001 S	<0.001 S	<0.001 S	<0.001 S

DISCUSSION

The present study was aimed to evaluate the possible relationship between plasma total Hcy concentration and DR. Our finding indicated that there was significant association between the DR degree and plasma Hcy level. (p value <0.001). There was a positive association between the presence of retinopathy and the amount of HbA1c (p <0.001). Association between Hcy plasma level and DR data is controversy.¹³⁻¹⁴ Satyanarayana et al. conducted a cross sectional study and showed that mean plasma Hcy levels were found to be higher in the diabetic patients compared to normal subjects.¹⁶ In a study done by Lim et al. showed that Hcy concentration of blood plasma, vitreous and aqueous in the patients with DR was approximately 30% higher than observed in the control subjects¹⁷. Their findings have suggested that hyperhomocysteinemia might be associated with DR and partially explained the increased risk of microvascular angiopathy occurs in these patients.¹⁸ On the other hand, some studies indicated no significant differences were noted in plasma Hcy levels between diabetic and control groups.^{19,20} Another research has shown that Hcy levels in diabetic patients with pre-proliferative DR were not higher than the healthy normal group but were higher in the neovascular glaucoma group.

The main limitation of this study was the use of a cross-sectional design, which prevents determination of temporal direction and, therefore, of causal inference.

CONCLUSION

We found that there was a significant correlation between plasma Hcy level and DR. Nevertheless, it is necessary to perform more studies to clarify the possible association between Hcy and DR.

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