

THE ASSOCIATION OF PLASMA HOMOCYSTEINE LEVELS WITH DURATION AND HBA1c LEVELS IN TYPE 1 DIABETES MELLITUS

Dr. Prahlad Dhakar¹, Dr. Govind Sharan Sharma^{2*}, Dr. Sudhir Bhandari³,

1.2. Assistant Professor, Department of General Medicine, RUHS College of Medical Sciences Jaipur, 3. Professor, Department of General Medicine, SMS Medical College, Jaipur

*Email id of the corresponding author- drgss26@gmail.com

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ABSTRACT

Background: Type 1 diabetes (previously known as insulin-dependent, juvenile or childhood-onset) is characterized by deficient insulin production and requires daily administration of insulin. The cause of type 1 diabetes is not known and it is not preventable with current knowledge. **Material & Methods:** The present hospital based Case-Control study was conducted in our tertiary care hospital, in the department of general medicine. Total 62 diagnosed cases of type 1 diabetes mellitus were randomly selected as cases and controls based on complications for the study after obtaining ethical clearance and informed written consent from the study subjects. **Results:** In cases, mean plasma homocysteine levels were higher as compared to controls (14.27 ± 4.99 vs. 10.21 ± 3.07). This difference was statistically highly significant (P -value < 0.01). Cases had a positive correlation with duration of diabetes and plasma homocysteine levels (r -value $+ 0.447$, P -value < 0.05). There was also a positive correlation between plasma HbA_{1C} and plasma homocysteine in case group ($r + 0.604$, $P < 0.01$). **Conclusion:** Plasma homocysteine levels were higher in type 1 diabetes patients with vascular complications compared to patients without these complications. Plasma homocysteine level has a positive correlation with duration of disease and HbA_{1c} levels.

KEY WORDS: Plasma homocysteine, Type 1 diabetes, vascular complications.

INTRODUCTION

Type 1 diabetes (previously known as insulin-dependent, juvenile or childhood-onset) is characterized by deficient insulin production and requires daily administration of insulin. The cause of type 1 diabetes is not known and it is not preventable with current knowledge (1).

The number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014. The global prevalence of diabetes among

adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014. WHO projects that diabetes will be the seventh leading cause of death in 2030 (2). Diabetes prevalence has been rising more rapidly in middle- and low-income countries.

Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation. Almost half of all deaths attributable

to high blood glucose occur before the age of 70 years (3). Although all of the known complications of diabetes can be found in both types of the disease, some are more common in one type than in the other.

Renal failure due to severe microvascular nephropathy is the major cause of death in patients with type 1 diabetes (4). Elevated total homocysteine levels were associated with microvascular complications, it is reasonable to hypothesize that total homocysteine may also be involved in the genesis of these complications in type 1 diabetes (5).

The biological mechanism for the interaction between diabetes and elevated total Homocysteine on vascular complications is still not well understood, although proposals are included oxidative stress, endothelial damage and decreased nitric oxide bioavailability (6). We conducted the present case-control study to evaluate the association of total plasma homocysteine level with duration and severity of type 1 diabetic patients.

MATERIALS & METHODS

The present hospital based Case-Control study was conducted in our tertiary care hospital, in the department of general medicine. Diagnosed cases of type 1 diabetes mellitus and controls were randomly selected from medical OPD and wards of S. M. S. Hospital. Total 62 subjects were randomly included in the study after obtaining ethical clearance and informed written consent from the study subjects.

Patients of more than 50 years of age, seriously ill or on life-supporting measures were excluded from the study. A thorough History and physical examination were done of enrolled cases and controls and all information was collected on pre-designed Performa. Patients were

investigated further for chronic complications indicated clinically or by initial investigations.

The data were analyzed using MS Excel 2010, Epi Info v7 and SPSS v22.

RESULTS

In the present study all 62 subjects, 31 were diagnosed cases with type 1 diabetes and 31 were controls. There were 25 (80.64%) males in cases and 27 (87.10%) in controls. In cases mean age was 26.45 ± 5.19 and among controls mean age was 23.87 ± 5.39 . The difference of age and sex between cases and controls was not statistically significant.

Table No.-1: Mean \pm SD of Plasma Homocysteine of case & control patients

P.Homocysteine levels	Mean \pm SD		P-value
	Case	Control	
	14.27 ± 4.99	10.21 ± 3.07	< 0.01

Table no.1 shows mean plasma homocysteine levels in both groups. In cases mean plasma homocysteine levels were higher as compared to controls (14.27 ± 4.99 vs. 10.21 ± 3.07). This difference was statistically highly significant (P-value < 0.01).

Table No.-2: Correlation between duration of diabetes & P. Homocysteine

Correlation: Duration v/s P.Homocysteine	r-value	P-value
Cases	+ 0.447	< 0.05
Control	+ 0.127	> 0.05

There were 13(41.94%) patients of ≤ 5 years duration of diabetes in cases and 17(54.84%) in controls. while >5 years duration of diabetes present in 18(58.06%) of cases and in 14(45.16%) in controls. In case of group plasma homocysteine is higher in patients with duration > 5 years as compared to patients with duration ≤ 5 years. This was significant in cases not in controls. (Cases: 16.46 ± 4.47 vs. 11.25 ± 3.99 , $p < 0.01$, controls: 11.08 ± 3.10 , 9.51 ± 2.87 , $P > 0.05$).

Also, cases show a positive correlation between duration of diabetes and plasma homocysteine and this was statistically significant (r-value + 0.447, P-value < 0.05) [table 2 fig 1]. There was

also a positive correlation between plasma HbA_{1c} and plasma homocysteine in the case group. It was statistically significant (r +0.604, P < 0.01). [Table 3 fig 2]

Table No.-3: Correlation between HbA_{1c} & P. Homocysteine

Correlation: HbA _{1c} v/s P.Homocysteine	r-value	P-value
Cases	+0.604	< 0.01
Control	+ 0.687	< 0.01

Fig. No.-1: Correlation between duration of diabetes & P. Homocysteine in case group patients

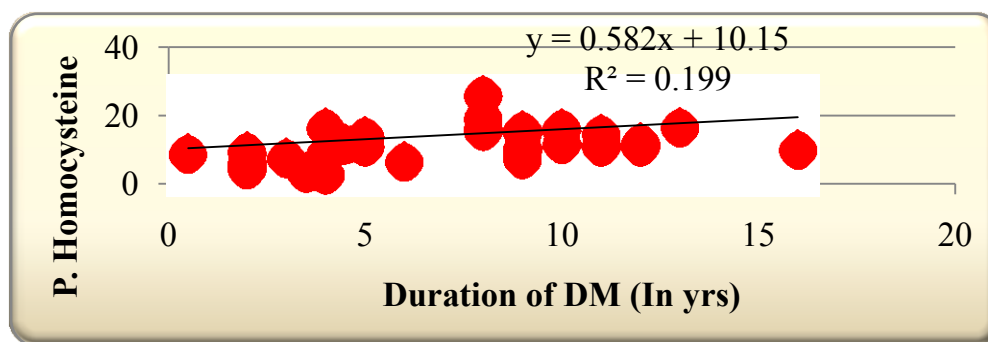
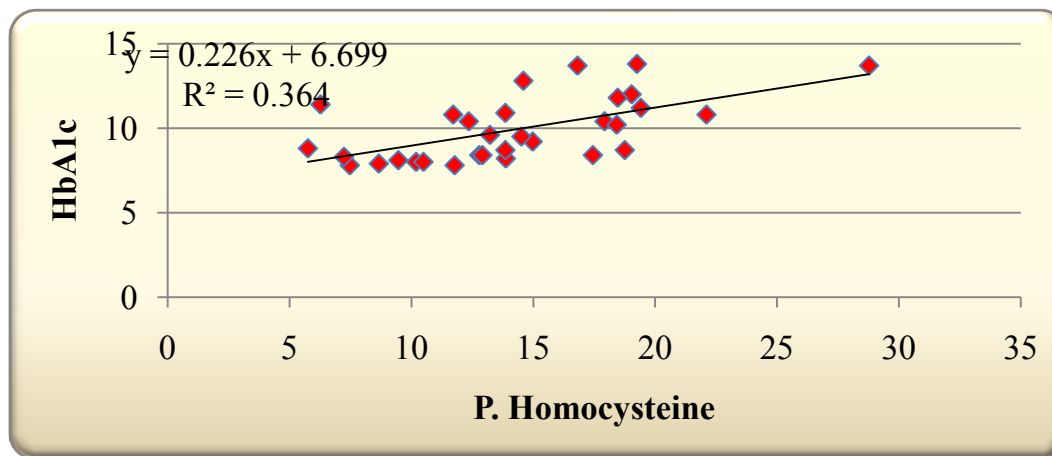


Fig. No.-2: Correlation between HbA_{1c} & P. Homocysteine in case group patients



DISCUSSION

In the present study, 62 diagnosed patients with type 1 Diabetes divide in case and control group based on the presence or absence of vascular (micro/macro) complications. Between case and control group difference in mean of age, duration of disease, HbA1c and vitamin status (vit.B12, folate) was statistically non-significant. In present study cases had higher plasma homocysteine as compared to controls, this difference was statistically significant (14.27 ± 4.99 vs. 10.21 ± 3.07 , $P < 0.01$).

A study conducted by Hofmann MA et al found that higher plasma homocysteine in diabetic patients compared to non-diabetic and Hyperhomocysteinemia in type 1 diabetic more common in those who had micro- and macrovascular disease (7). A study conducted by Vicar O. et al found that patients with microalbuminuria or proliferative retinopathy had significantly higher values than those without.

This difference was not attributable to confounders, such as age, sex, and smoking, nor to dissimilar plasma folate and vitamin B12 concentrations. They concluded that type 1 diabetes as such is not associated with increased plasma homocysteine levels, though patients with microalbuminuria and/or proliferative retinopathy display significantly higher values than those without this (8).

In the present study, we found in both case and control group plasma homocysteine is higher in patients who have a duration of Diabetes > 5 years as compared to < 5 years. This difference was also statistically significant in cases but not in controls. Plasma homocysteine has a positive correlation with duration of diabetes in both cases and this was statistically significant.

A study conducted by Mario cotellessa et al

found same results that plasma homocysteine levels increased with age (P , 0.001) and with diabetes duration (P , 0.05) in type 1 diabetic patients (9). Similar results were also found in a study done by Dinleyici E. C. et al. They found that the hyperhomocysteinemia group has longer disease duration and early onset of disease than non-hyperhomocysteinemia group (10).

In the present study, Plasma homocysteine positive correlation with HbA1c in both case and control groups and this was statistically highly significant. Most of the previous studies were also shown this fact. A study done by Omar S. et al tested the association between the levels of homocysteine and type 1 diabetes mellitus and it was found that in all subjects, homocysteine levels were significantly correlated to HbA1c and glucose level (11).

In contrast to this, another study conducted by Eun-Hee Cho et al found that study Baseline plasma homocysteine concentrations and mean HbA1C levels during follow-up were significantly higher in cases group than in control group (12). The biological mechanism for the interaction between diabetes and elevated homocysteine levels on vascular complications is still not well understood, although proposals include oxidative stress, endothelial damage and decreased nitric oxide bioavailability (13).

Hence, future studies are needed to establish hyperhomocysteinemia as a clinically significant modifiable risk factor in the pathogenesis of diabetic complications in type 1 diabetes.

In our study, we had few limitations. First was an association between plasma homocysteine levels and vascular complications cannot be studied because of very less number of patients with these complications.

The second was in our study, there were no

normal controls (non-diabetic persons) so we were unable to compare the plasma homocysteine levels in type 1 diabetic patient and normal persons. Since the sample size of our study was relatively small, therefore the generalizations of the study results are not possible.

CONCLUSION

Based on the results of the present study we concluded that Plasma homocysteine levels were higher in patients with vascular complications compared to patients without complications. Plasma homocysteine level has a positive correlation with duration of disease and HbA1c levels.

Diabetes can be treated and its consequences avoided or delayed with diet, physical activity, medication and regular screening and treatment for complications.

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