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ORIGINAL ARTICLE

IMPLICATION OF SERUM HOMOCYSTEINE LEVEL IN TYPE-2 DIABETES: A PILOT STUDY

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ABSTRACT: Increased level of Serum Homocysteine has been found to be responsible for macro and micro vascular complications in Type 2 Diabetes mellitus (T2DM). Homocysteine, a sulfur-containing amino acid, is emerging as an important risk factor for atherosclerosis in patients with end-stage renal disease. This study has been undertaken to observe the serum homocysteine status of the type 2 Diabetics and its co-relations between the glycogenic status and to find out the prevalence of hyperhomocysteinemia in T2DM. The serum homocysteine level of 80 consecutive previously known T2DM patients were measured along with other parameters and the obtained data was analyzed. Mean FPG was 130.30+6.13 mg/dl, mean PPPG was 191.76+10.99 mg/ mean HbA1c was 8.2+2.1 mg/ dl, mean BMl was 25.29+3.88 kg/m^2 and the mean serum homocysteine level was 15.12+6.68, while all 80 subjects were taken together. Considering the normal range for homocysteine as per laboratory standard (15 isu/i), the value could be considered as highest normal. Further, 34% of the patients showed high value i.e. hyperhomocysteinemia, 50% showed highest normal and only 16% showed low normal value. Morever, fasting and the post prandial plasma glucose (PPPG) showed inverse relationship level, which were elevated in 34% of T2DM patients, which indicates the scope for intervention. But the glycolic status was negatively related to the homocysteine level, though the relationship was not statistically significant, which might be due to the small sample size. However, larger population study is needed to validate, furthermore.

KEYWORDS: Homocysteine, Diabetes mellitus, Prevalence, Hyperhomocysteinemia

INTRODUCTION: Homocysteine is a homologue of the amino acid cytokine, differing by an additional ethylene (-CH2-) group. It is biosynthesized from methionine by the removal of its terminal methyl group and can be recycled into methionine or converted into cytosine with the help of B- vitamins. Methionine as such do not have any metabolic functions but homocysteine has been associated with extracellular matrix changes. Numerous studies have pointed towards an association of type 2 diabetes levels. [1]

Acute elevation in circulating homocysteine levels in coronary microcirculation in normal subjects. [2] More importantly, several studies have also reported increased levels of homocysteine in T2DM patients with microangiopathy, nephropathy and proliferative diabetic retinopathy.[3,4] However, it is yet to be conceived how hyper homocysteinemia increases the risk of death in type 2 diabetic patients. [5,6] Though, it can be stated that T2DM individuals with chronic elevated levels of homocysteine are at greater increased risk of multiple macro- vascular and micro vascular complications. [7]

Keeping the above information in mind, the objective of the present study was to investigate the serum homocysteine status of the type 2 diabetics and relationship between the glycolic status and serum homocysteine level, as well as to find out prevalence of hyperhomocysteinemia in type 2

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diabetics. Notably, various studies show that the prevalence of increased serum Homocysteine levels is high in patients with end-stage renal disease. In addition, diabetes mellitus is a recognized risk factor for atherosclerosis, and the morbidity of atherosclerosis in diabetic patients is two to three times higher than in the normal population. However, little is known about the significance of Homocysteine in diabetic patients and its outcomes. Therefore, purpose of the study was to elucidate the significance and effects of homocysteine in Type-2 Diabetes.

MATERIALS AND METHODS: This observational study was conducted in consecutive previously known Type 2 Diabetics patients. Diabetes was diagnosed according to ADA criteria. After screening, a total of 80 T2DM patients were included in the study. Patient with a genetic disorder associated with elevated homocysteine levels or on medications known to increase the serum level of homocysteine, like anticonvulsants, theophylline, levodopa, methotrexate etc; malignancy, disease of ovary and pancreas, severe psoriasis, choric heart disease or any major invalidating disease and deficiency disorders like anemia, hypothyroidism, systemic lupus erythematosus (SLE), anorexia nervosa, organ transplantation, severe skeletal muscle damage or trauma, the patients already on folic acid, pyridoxine and vitamin B12 therapy etc; were excluded from the study. All patients with diabetes mellitus were evaluated for plasma homocysteine level in association with the glycogenic parameters like fasting plasma glucose, post prandial plasma glucose (PPG) and glycosylated hemoglobin (HbA1c). The detailed history was taken and relevant clinical examination was performed.

RESULTS: Mean fasting plasma glucose (FPG) was 130.30+6 (SD), mean post prandial plasma glucose (PPPG) was 191.76+10.99 (SD), mean HbA1c was 8.2+2.(SD), mean body mass index (BMI) was 25.+25+3.88 (SD) and mean serum homocysteine level was found as 15.12+6.68 uGu/ml (SD), when all 80 subjects taken together. Considering the normal range for homocysteine as per laboratory standard (16 isu/l), the value could be considered as hashish normal. When the values are divided in three groups 34% of hyperhomocysteinemia, 50% showed highest normal and only 16% showed low normal value.

Table-1 Homocysteine level in 80 pateints

Higher Than Normal	Highest Normal	Low Normal
34% (27 patients)	50% (40 patients)	16% (14 patients)

Further, the fasting and post prandial glucose showed inverse relationship with the serum homocystein level though statistically insignificant (p>0.5). Which might be related to study design as homocysteine level were measured in a fairy controlled diabetic cohort.

DISCUSSION: Homocysteine is an intermediate form generated during the metabolism of methionine and is not present in food. The transformation of methionine to Hcy involves the demethylation pathway, which provides a methyl group with glycocyamine in the creation of creatinine. [8]

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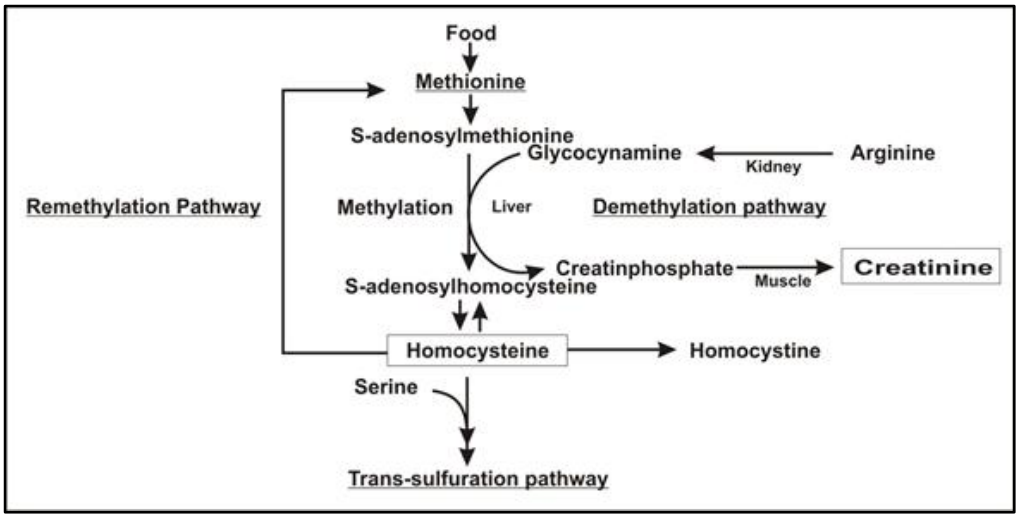

Fig. 1: Synthesis and metabolism of homocysteine

Synthesis and metabolism of Hcy involves three processes: demethylation, remethylation and trans-sulfuration. The demethylation pathway is associated with creatinine generation, i.e., S-adenosylmethionine provides a methyl group with glycocyamine on the generation of creatinine.[8] Plasma homocysteine were found to elevated in T2DM and also in pre- diabetes. In the present study, 31 of the patients showed hyperhomocysteinemia and 52% showed highest normal. The prevalence of hyperhomocysteinemia has been estimated to be 5 per cent in the general population, and 13-47 among patients with symptomatic atherosclerotic vascular disease.[9] Our study pointed out prevalence of hyperhomocysteinemia to be 31%, which is consistent with the previous findings. Our study, the mean plasma Homocysteine level found as 15.12+ 6.68 uGu/ml (SD), which is much higher than earlier studies which reported a mean Homocysteine level of 2.69 uGu/ml in diabetic patients.[1]

Subjects with elevated Homocysteine are at increased risk of atherothrombotic events. It has been proposed that Homocysteine induced endothelial injury exposes the sub- endothelial matrix leading to platelet activation by various mechanisms like impaired coagulant function, production of reactive oxygen species viz. superoxide and hydrogen peroxide resulting due to auto- oxidation of Homocysteine.[7] Homocysteine also found to enhance the coagulability by reducing protein C activation, inducing inhibition of anti- thrombin III, inhibiting the synthesis of anticoagulant heparin sulphate, suppressing thrombo- modulin.

Previous studies have reported elevated Homocysteine levels in diabetic patients associated with hypertension, albuminuria independent of other determinants and end-stage renal diseases.[10,11] Several studies have provided additional evidence that hyperhomocysteinemia is an important risk factor for developing vascular diseases including stroke, independent of long recognition, diabetic mellitus, and smoking[12,13] as well as re-stenosis after coronary angioplasty.[14,15]

Hoogeven and colleagues have reported on increased mortality due to CVD in the population of diabetic patients with high Hay levels in the prospective Home study.[16] Meigs et al. have also found that hyperhomocysteinemia is an independent risk factors of cardiovascular disease incidence in diabetic patients.[17] Hence, Homocysteine may be considered to act like an mediator through which various risk factors may exert their deleterious effect.

Therefore, the hyperhomocysteinemia could serve as another important marker of poor diabetic control and developing complications. Thus, diagnostic measures for Homocysteine for lowering raised level of homocysteine may be administered to those having hyperhomocysteinemia; conclusively.

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