



Original Article

Role of Vitamin B12 Deficiency in Patients with Type 2 Diabetes Mellitus

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Abstract

Diabetes Mellitus is now affecting many in the workforce: it has major and deleterious impact on both individual and national productivity. Vitamin B12 deficiency results in the disruption of methylation process and accumulation of intracellular and serum homocysteine which is toxic to the neurones and vascular endothelium. The main objective of the present research is to assess and compare levels of serum vitamin B12 in patients with type 2 Diabetes Mellitus with the controls.

A cross sectional study was conducted jointly by the Department of Biochemistry and Medicine, Govt. Medical College Jammu, involving 50 patients with diagnosed T2DM in the age group of 40-80 years of either gender attending the OPD of Medicine Department and 50 age and gender matched randomly selected healthy controls. Patients with T1DM, thyroid disorders, haemolytic anemia, hemoglobin variants, pregnancy, hepatic and infectious diseases were excluded from the study. Vitamin B12 was estimated in serum using Chemiluminiscent micro particle intrinsic factor technology, referred to as chemiflex. Glucose was measured by Hexokinase method.

The mean of vitamin B12 in controls was in normal value, but significantly low in cases. Vitamin B12 deficiency was significantly associated with increasing age, increased duration of diabetes. Even the difference in the mean values of FPG and HbA1C in controls and study cases were significant. Vitamin B12 deficiency may lead to clinically significant complications, highlighting the importance of regular screening of B12 levels for a better diagnostic procedure and treatment of T2DM.

Keywords: Type 2 Diabetes Mellitus , Vitamin B12, Glycated Hemoglobin.

Introduction

Diabetes mellitus is a disorder of carbohydrate metabolism in which there is hyperglycemia due to insulin resistance or defective insulin action or both. It is a common endocrine disorder and the complications arising from the disease are the leading cause of death worldwide. It is a condition

where the cells of the body cannot metabolize sugar effectively due to total or relative lack of insulin. The body then breaks down its own proteins, fats, glycogen resulting in high levels of blood glucose (hyperglycemia), because without insulin cellular uptake and utilization of glucose is limited.⁽¹⁾ The socio-economic consequences of

diabetes and its complications could have serious impact on the economies of developed and developing nations.⁽²⁾ Diabetes is rapidly gaining the status of potential epidemic in India with more than 62 millions diabetic individuals currently diagnosed with the disease. In the year 2000, India topped the world with the highest number of people with diabetes mellitus (31.7millions) followed by China (20.8million) with the United States (17.7million) in second and third respectively (WHO). It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India (WHO).⁽¹⁾ The most common complications of diabetes mellitus are diabetic neuropathy, nephropathy, retinopathy, coronary artery disease, cerebrovascular disease, etc. Among these, the peripheral neuropathy, is the commonest and earliest complication in diabetics.⁽³⁾ Vitamin B12 is water soluble vitamin. It exerts in physiological effects through mediating two principal enzymatic pathways, i.e. the methylation process of homocysteine to methionine and the conversion of methylmalonyl CoA to succinyl CoA. Vitamin B12 as a cofactor facilitates the methylation of homocysteine to methionine which is later activated into S-adenosyl-methionine that donates its methyl group to methyl acceptors such as myelin, neurotransmitters and membrane phospholipids. Metabolically significant vitamin B12 deficiency hence will result in disruption of the methylation process and the accumulation of intracellular and homocysteine. Hyperhomocystinemia has been shown to have potentially toxic effects on neurons and the vascular endothelium. This reaction is also in the conversion of dietary folate (methyl tetrahydrofolate) to its active metabolic form tetrahydrofolate. In another essential enzymatic pathway, Vitamin B12 as a cofactor mediates the conversion of methyl malonyl CoA to succinyl CoA; in the presence of vitamin B12 deficiency this conversion pathway is diminished and an increase in the serum methyl malonic acid ensues. Vitamin B12 is also essential in the synthesis of monoamines or neurotransmitters like serotonin

and dopamine. This synthesis is impaired with vitamin B12 deficiency.⁽⁴⁾ Therefore without early detection and treatment, Vitamin B12 deficiency can cause irreversible, clinically significant complications and increased morbidity among diabetics.

Materials and Methods

It was cross sectional study involving 50 patients with diagnosed type 2 diabetes mellitus in the age group of 40-80 years of either gender attending the out-patient department of medicine and 50 age and gender matched randomly selected healthy controls. The study was conducted as per the guidelines of institutional ethics committee and informed consent was obtained from all the participants.

50 cases of T2DM diagnosed as per standard criteria given by world health organization were included in this study; whereas patients with T1DM, thyroid disorders, haemolytic anemia, hemoglobin variants, pregnancy, hepatic diseases and infectious diseases were excluded from the study. 8- hours fasting sample was collected from the cases and controls. Vitamin B12, FBS and HbA1C were estimated in serum.

The ARCHITECT B12 assay is a two step assay with an automated sample pre-treatment, for predetermining the presence of B12 in human serum using CMIA (Chemiluminiscent microparticle intrinsic factor technology) with flexible assay protocols, referred to as chemiflex. Levels above 300 pg/ml were considered as normal.⁽⁵⁾

Glucose was measured by Hexokinase method. Hexokinase (HK) catalyses the phosphorylation of glucose in the presence of adenosine-5-triphosphate (ATP) and magnesium to form glucose-6-phosphate (G-6-P), which is then oxidized by glucose-6-phosphate dehydrogenase (G6-PDH) in the presence of nicotinamide adenine dinucleotide (NAD) to produce 6-Phosphogluconate and NADH. One mole of NAD is reduced to one mole of NADH for each mole of glucose present. The absorbance due to NADH

(and thus the glucose concentration) is determined using a bichromatic (340 and 383 nm) end point technique. Sample reagents delivery processing and printing of results were automatically performed by Siemens dimension clinical chemistry system. Expected normal values of Serum Glucose are 74-106mg/dl. HbA1C was analyzed using fully auto analyzer Architect c4000 and c8000 systems.⁽⁶⁾

Results

Two groups namely: controls and study cases were found to be in the respective age groups of: 53.1±8.2 and 55.0±6.8. Among them there were approximately 40% females and 60% males in the study cases, while in the control group there were approximately 33% females and 67% males.

The mean of vitamin B12 in controls and cases were 602 and 353 respectively and it was significantly low in cases (Table 2). It was found that, among the cases, prevalence of vitamin B12 deficiency was 8%, borderline deficiency was 20%.

Vitamin B12 Deficiency was significantly associated with increasing age, increased duration of diabetes (Table 4).

The mean of FPG in Controls and cases were 93.17 and 211.61 respectively and the difference was significant (Table 2).

The mean HbA1c was 5.21 in controls and 8.94 in cases and it was significantly high in cases (Table 2).

Table 1: Age and Gender distribution of controls and cases

| | Controls (Mean±SD) | Cases (Mean±SD) | p Value |
|----------------------|--------------------|-----------------|---------|
| Mean Age | 53.1±8.2 | 55.0±6.8 | 0.491 |
| Gender (Male/Female) | 29/21 | 33/17 | 0.775 |

Table 2: Showing comparisons of biochemical parameters of the control and case groups. Paired student t-test was used for comparison of means between the two groups.

| Parameters | Controls (Mean±SD) | Cases (Mean±SD) | p Value |
|---------------------|--------------------|-----------------|---------|
| FPG (mg/dl) | 93.17±9.63 | 211.61±68.23 | <0.0001 |
| HbA1C % (NGSP) | 5.21±0.31 | 8.94±1.87 | <0.0001 |
| Vitamin B12 (pg/ml) | 602 ± 201 | 353 ± 178 | <0.0001 |

Table 3: Prevalence of Vitamin B12 deficiency in study groups

| Parameters | Controls (Prevalence %) | Cases (Prevalence %) | p Value |
|--|-------------------------|----------------------|---------|
| Vitamin B12 < 200 pg/ml (Deficiency) | 0 (0%) | 4 (8%) | 0.111 |
| Vitamin B12 200-300 pg/ml (Borderline) | 5 (10%) | 10 (20%) | 0.331 |
| Vitamin B12 >300 pg/ml (Normal) | 45 (90%) | 36 (72%) | 0.045 |

Table 4: Association of Vitamin B12 levels and other continuous variables among cases

| Continuous Variables | Vitamin B12 | | | P value |
|----------------------------|-------------|-----------------------|---------------|---------|
| | Deficiency | Borderline Deficiency | No Deficiency | |
| Age (Mean±SD) | 64.23±4.85 | 59.41±5.25 | 50.77±6.50 | 0.065 |
| Gender | Male | 4 | 8 | 0.170 |
| | Female | 2 | 2 | |
| Disease duration (Mean±SD) | 11.68±2.92 | 9.09±3.44 | 5.75±3.48 | 0.0046 |

Discussion

While analysing the study cases, the mean of vitamin B12 was found to be significantly low in comparison to the controls, further, it was also found that, among the cases, prevalence of

vitamin B12 deficiency was 8% and borderline deficiency was 20%. This finding was similar with findings by Reinstalter Let al⁽⁷⁾ and Pflipsen M.C et al.⁽⁸⁾ The mean of FPG and HbA1C was significantly high in cases, while Vitamin B12

deficiency was significantly associated with increasing age and increased duration of diabetes. Choi BC et al⁽⁹⁾ and Becker J et al⁽¹⁰⁾ also found similar findings in their study. These findings in support of the previous observations extend the knowledge on the role of vitamin B12 and its risk factor on type 2 Diabetes patients. This highlights the importance of regular screening of B12 levels, but none of the guidelines as of today recommend measuring B12 levels regularly in type 2 diabetes, but physicians may do so for an upgraded diagnostic procedure.

Conclusion

Diabetes mellitus is a group of metabolic disorders of carbohydrate metabolism in which glucose is underused, leading to hyperglycemia. There is either insulin resistance or defective insulin action or both. Prevention and management of diabetes is a major health issue worldwide. Vitamin B12, a water soluble vitamin, whose deficiency leads to accumulation of serum homocysteine, which can cause irreversible, clinically significant complications and increased morbidity among diabetics. In the absence of guidelines, physicians may still recommend the measuring of B12 levels in T2DM for a better treatment and follow-up.

Sources of support: Nil

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