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RELATION BETWEEN DIABETIC CONTROL AND SERUM VITAMIN B12 LEVELS IN TYPE 2 DM PATIENTS IN A TERTIARY TEACHING CARE HOSPITAL

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ABSTRACT

Introduction: Vitamin B12 deficiency is most commonly associated with autoimmune disorders. However, at present there is increased incidence of B12 deficiency among diabetics particularly in type II diabetes mellitus patients. This may be influenced by the control of the disease based on Fasting and postprandial blood sugar levels and also glycosated Hb levels. If our study demonstrates the presence of low serum B12 levels association with these control parameters then a recommendation for regular screening and supplementation of vitamin B12 could be considered in these uncontrolled diabetic patients. **Aims and Objectives:** To evaluate the serum vitamin B12 levels in in type II diabetes also to evaluate the influence diabetic control on B 12 levels. **Materials and Methods:** This was a cross- sectional study. 50 diabetic patients were randomly selected based on inclusion/ exclusion criteria from the patients attending diabetic OP in GMKMC, Salem. Serum vitamin B12 level and parameters for diabetic controls were assessed using fully automated methods. All statistical analysis was carried out using SPSS version 21. **Results:** The study showed that 24% of the diabetics had low B12. There was no significant difference in B12 levels between males and females (mean difference = - 14.3: $P > 0.05$). The study did demonstrate positive significant correlation between vitamin B12 levels with diabetes control statistically but there was no significant effect of duration of disease. **Conclusion:** Results of our study shows the presence of low serum B12 levels in diabetics which very much low in poorly controlled diabetic patients. These findings merits further research on a larger population to investigate into the cause of deficiency and the benefit of B12 supplementation in these patients who have uncontrolled DM.

KEYWORDS: Vitamin B12 deficiency, Diabetes mellitus, diabetic control, HbA1c.

INTRODUCTION

Vitamin B12 is one of important and essential micronutrient which is primarily required for proper hemopoetic, neuro-cognitive and cardiovascular function of our body. Biochemical and clinical vitamin B12 deficiency has been revealed to be highly common among patients with type 1 and type 2 diabetes mellitus. It mostly presents to us with a range of clinical signs ranging from impaired memory, dementia, delirium, peripheral neuropathy, sub acute combined degeneration, megaloblastic anemia and pancytopenia. In addition, the dietary habits which vary from one population to another could also contribute to the deficiency. Association of vitamin B12 deficiency in type 1 diabetic patients has been demonstrated in previous studies.[1,2] Vitamin B12 deficiency is a potential comorbidity that is often ignored, despite the fact many diabetic patients are at risk for Vitamin B12 deficiency. For example, many diabetic patients are treated with metformin, a drug that decreases serum vitamin B12 levels[3,4] and ends up in vitamin B12 deficiency., In addition, almost half of all diabetic patients are older than 60, an age group in which the prevalence of B12 deficiency ranges from 12% to 23%.[5,6] Because of these risk factors, defining the prevalence in the diabetic patients may help in having an idea whether physicians should consider screening for B12 deficiency in diabetic patients. However, there is insufficient data regarding prevalence of vitamin B12 deficiency in the South Indian population. Hence this study was undertaken to evaluate serum B12 levels in type 1 diabetics in South Indian population attending a tertiary care hospital. If the study shows a considerable proportion of type 1 diabetics with low vitamin B12 levels in this population, then it would be worthwhile to consider regular screening and supplementation of vitamin B12.

MATERIALS AND METHODS

This is a cross sectional observational study done in patients who are having confirmed diabetes mellitus for longer term in GMKMC, Salem. All patients with Type 2 DM attending the diabetes outpatient clinics at Government Mohan Kumaramangalam medical college hospital, Salem in past three months has been taken up

for study after getting informed consent from them. Those on current B12 treatment for any condition were excluded.

Data collected included age, duration of disease and Fasting and Postprandial blood glucose, Glycosylated Hb, vitamin B12 concentration. Patients were grouped into 3 categories based on their of serum vitamin B12 concentration: Vitamin B12 deficiency (<150 pmol/L), borderline vitamin B12 (150–219 pmol/L) and normal vitamin B12 (≥220 pmol/L).

Statistical Analysis

Data were analysed using SPSS version 21.0. The primary outcome results are presented as arithmetic means. Assessment for significance between means was tested using ANOVA. All tests were two-sided and p values of <0.05 were considered to be statistically significant at 95% confidence interval. Ethics approval for the study was obtained from Institutional ethics committee.

Operational definitions

• Type 2 diabetes was diagnosed based on history, clinical evaluation and laboratory findings. The American Diabetes Association criteria were used for the diagnosis.[7]

• Vitamin B12 levels were evaluated based on the manufacturer's recommendations as follows:

- Vitamin B12 deficiency (<150 pmol/L)
- Borderline vitamin B12 (150–219 pmol/L)
- Normal vitamin B12 (≥220 pmol/L)

RESULTS

Table below shows the characteristics of the study population. A total of 50 patients were included in the study. There was nearly equal representation of males and females in the study (24:26). The average age of patients was 58.6 years, while the average duration of diabetes was 10.4 years. The mean fasting blood sugar (FBS) was 166.26 mg/dL, while the post-prandial blood sugar (PPBS) was 267.8 mg/dL and the glycated hemoglobin (HbA1c) was 9.35%. Serum B12 levels were analyzed and around 24% of patients had deficient B12 levels whereas 60% had borderline levels and rest had normal values.

MEAN VALUES OF PARAMETERS	
AGE	58.64 YRS
HbA1C	9.35%
DURATION OF DM	10.4 YRS
FBS	166.26
PPBS	267.8
VITAMIN B12	296.62

There was significant difference in B12 deficiency between males (mean B12 = 260.62 pg/mL) and females (mean = 329.84pg/mL) which shows that females have more common chance and getting deficiency. Next we analysed the effect of age, duration of diabetes and diabetic control over vitamin B12 levels. There was also no significant relation between B12 and age of patient with P value of 0.668.

VITAMIN B12 LEVELS	**AGE**	
	> 60 YRS	**< 60 YRS**
DEFICIENT	3	9
BORDERLINE	10	20
NORMAL	2	6
P VALUE	0.668	
SIGNIFICANT	NON SIGNIFICANT	

Similarly there was also not much significant impact of duration of diabetes over Vitamin deficiency, as among our patients there was equal distribution of deficiency which shows the disease has more impact than the duration of disease. The P value was also more than 0.05.

VITAMIN B 12 LEVELS	**MEAN DURATION OF DM**
DEFICIENT	11.17
BORDERLINE	10.4
NORMAL	9.25

Finally we analysed the impact of control of diabetes over vitamin B12 levels. First we compared the fasting and post prandial blood glucose levels and its impact on the B12 deficiency. There was also a steep rise in the blood sugar levels in comparison to the B12 levels. The glucose levels were much higher in patent who were

having borderline deficiency and deficiency and it was also statistically significant with P value less than 0.05. Similarly we also analysed HbA1c levels which also has an similar impact in vitamin B12 levels which was also statistically significant.

VITAMIN B 12 LEVELS	MEAN FBS	MEAN PPBS	MEAN HBA1C
DEFICIENT	172.68	273.67	11.52%
BORDERLINE	170.97	271.67	9.35%
NORMAL	139.98	244.5	7.8%

DISCUSSION

Type 2 diabetes is commonly treated by primary care physicians who must be able to manage both the disease and associated co- morbidities. Vitamin B12 deficiency is a potential co- morbidity that is often snubbed, regardless of the fact that many diabetic patients are at risk for this specific disorder. One important reason is many diabetic patients are treated with metformin, a drug that lowers serum vitamin B12 levels and is associated with vitamin B12 deficiency.[8,11] Also, symptoms of B12 deficiency occur late and it easily passed of due to this reason. B12 deficiency induced nerve damage may be confused with or may contribute to diabetic peripheral neuropathy. Hence recognising the correct aetiology of neuropathy is decisive because simple vitamin B12 replacement may reverse the neurologic symptoms which is sometimes incongruously attributed to hyperglycemia[12] Previous studies done in the western population have demonstrated the presence of vitamin B12 deficiency[7] in type 2 diabetes. There are limited studies on the B12 levels in type 2 diabetics in the South Indian population. Therefore by identifying such prevalence of low serum B12 levels in the diabetic population may help determine whether primary care physicians should consider screening for vitamin B12 levels in diabetic patients.

Our study showed around 24% prevalence of deficient serum B12 in type 2 diabetics. The difference in the prevalence of low B12 levels due to different cut- off values used has been reported in many studies in the past.[13] In addition, the lack of a gold standard tests complicates the diagnostic evaluations. Since serum B12 assays and other biomarkers such as MMA and holotranscobalamin lack adequate sensitivity and specificity when used alone, a blend of markers along with clinical evaluation is preferred to define the prevalence of cobalamin deficiency. Since these markers like MMA are expensive and not readily available in all laboratories serum B12 estimation continues to be used to assess the cobalamin status.[10] The mean B12 value obtained in our study was very low (296.62 pg/mL), however similar to other reports, the deficiency was similar in males and females.[12] Gender bias was ruled out since there was equal representation of males and females in the study.

Vitamin B12 deficiency is estimated to affect 10 -15% of people over the age of 60 and the laboratory diagnosis is usually based on low serum vitamin B12 levels or elevated serum MMA and homocysteine.[14] The average age of our patients was 58.64 years and therefore age cannot be considered as a risk factor in our study. Thus, it appears that factors other than age, duration of diabetes and diabetic control may play a role in B12 deficiency. Since some of our patients were on metformin, the observed B12 deficiency can also be attributed to the drugs.

The National health & Nutritional survey done from US 1999-2006 had documented Vitamin B12 deficiency in both diabetics with and without metformin therapy. But the biochemical B12 deficiency is higher in group with uncontrolled diabetes. It is correlated with our study where we found some relation with blood glucose, HbA1c levels and B12 deficiency. Matthew C Pflipsen et al[15], showed higher prevalence of vitamin B12 deficiency up to 22% of diabetics who are uncontrolled similar to our study. One another reason for the relation may as these patients are uncontrolled and they may require an increased dose for control which may also leads to an drug related deficiency, metformin in particular, hence all such factors end up in statistically significant effect of control of diabetes over Vitamin B12 levels.

Limitations of the study

Comparison with a control population was not carried out in our study and also we have not selected patients based on their drug intake which may also influence the final outcome. Secondly other markers such as MMA and holotranscobalamin were not evaluated. The assay results were not correlated with the signs and symptoms and so the clinical significance of low B12 levels in our patient group is unknown. So further study is warranted with stringent inclusion criteria. Also this was done as an cross sectional study with samples taken at a single visit so the effect of B12 supplementation cannot be analysed.

CONCLUSION

Our study demonstrated the presence of low serum B12 levels in type 2 diabetics which had an positive relation with the control of disease. Hence these results and outcome merit further research on a larger population using additional markers to investigate into the cause of deficiency, the factors involved and benefit of B12 supplementation in these patients.

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