

**PREVALENCE OF VITAMIN B12 DEFICIENCY IN TYPE 2 DIABETIC PATIENTS****BY DR. N.N.ANAND** AND DR. MUKKAMALA VINDHYA****SREE BALLAJI MEDICAL COLLEGE AND HOSPITAL, NO.7 WORK'S LANE, CHROMEPET,
CHENNAI-44, TAMIL NADU, INDIA.***ABSTRACT**

The prevalence of vitamin B12 deficiency has been found to be high in type 2 diabetic patients who may cause peripheral neuropathy. Hence the identification of vitamin B12 deficiency is important because simple vitamin B12 replacement can improve the neurological symptoms. The aim of the present study is to assess the prevalence of vitamin B12 deficiency in patients with type 2 diabetes, who are in treatment. To evaluate the association of B12 deficiency with diabetic neuropathy. Study subjects were selected from the type 2 diabetic patients being treated in our hospital who had had an assessment for diabetic neuropathy and serum vitamin B12 levels are tested. Vitamin B12 deficiency was seen in 11.5% of subjects, 70% of which were on vitamin supplementation. 62.4% had diabetic neuropathy. Among the patients receiving vitamin supplementation majority (65.4%) had mild to moderate neuropathy. The study concluded that 1. Prevalence of B12 deficiency is relatively low among type 2 diabetic patients undergoing treatment. 2. Mild and moderate form of neuropathy was more common probably due to vitamin supplementation that prevented further progression. 3. Therefore early detection of vitamin B12 deficiency in prediabetic stages would be useful for prevention of neurological disorders by vitamin supplementation.

KEY WORDS: Vitamin B12 deficiency, Type 2 diabetes, diabetic neuropathy. * Post graduate
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INTRODUCTION

Diabetes mellitus is a disorder, characterized by chronic hyperglycemia, resulting from defects in insulin secretion, insulin action or both [1]. Vitamin B12 (Cyanocobalamin) plays an important role in DNA synthesis and neurological function. Deficiency of Vitamin B12 can lead to a wide range of both hematologic and neurological disorders. However, the prevalence of Vitamin B12 deficiency has been found to be high in type 2 diabetic patients [2]. One complication that may be related to the deficiency is peripheral neuropathy. As a result, B12 deficiency-induced nerve damage may be mistaken for diabetic peripheral neuropathy [3]. Identification of Vitamin B12 deficiency in type 2 diabetic patients is important, because simple B12 replacement may improve the neurological symptom. Long-term treatment with metformin has also been found to be associated with Vitamin B12 deficiency [7-10]. Metformin is one of the drugs widely used in the treatment of type 2 DM. One of the most common causes of peripheral neuropathy is diabetes mellitus. Other metabolic causes include chronic renal failure, liver failure and hypothyroidism. Another common cause of peripheral neuropathy is vitamin deficiency states, including vitamin B12, vitamin A and vitamin B1 (thiamin).

MATERIALS AND METHODS

(i) Inclusion Criteria:

Study subjects were selected from the type 2 diabetic patients being treated in a tertiary diabetes care centre during the period April to December 2010. Patients who had an assessment of diabetic neuropathy were selected.

(ii) Exclusion Criteria

Patients having anaemia, chronic renal insufficiency with serum creatinine ≥ 2.5 mg/dl, history of severe gastro-intestinal disorders or ileal resection were excluded. A total of 695 subjects (Male:Female, 486:209) were available for the study.

Clinical assessment

Patient's demographic and anthropometric details were recorded which included Age, duration of diabetes, drug history, including use of multivitamin/B12 supplements, height and weight in cm and kg respectively. Blood pressure was recorded in mm Hg using a sphygmomanometer. Peripheral neuropathy was diagnosed using biothesiometry test. Vibration perception threshold of the patients was tested. The cutoff value taken were 15-24 Hz for mild neuropathy, 25-39 Hz for moderate neuropathy and >40 Hz for severe neuropathy.

LABORATORY METHODS

Blood samples were collected from an antecubital vein for estimations of haemoglobin, glycosylated haemoglobin (HbA1c), (EDTA sample) and vitamin B12 (serum). Haemoglobin was estimated by cyanmethaemoglobin method. HbA1c was estimated using an immunoturbidimetric assay using the Tinaquant reagent of Roche Diagnostics, Germany. Vitamin B12 was assayed within 2 hours of blood collection using the Elecsys vitamin B12 assay. The Elecsys vitamin B12 assay employs a competitive test principle using an intrinsic factor for vitamin B12. Vitamin B12 in the sample competes with the added vitamin B12 labeled with biotin for the binding sites on the ruthenium-labelled intrinsic factor complex. Cobas 411 automated system was used for HbA1c and B12 assays. Normal range for HbA1c is 4.5 – 6 %. Patients with levels less than 7% are considered to have good glycaemic control. Plasma levels of vitamin B12 more than 200pg/ml were considered to be normal.

RESULTS

The study details were available for 695 patients (Male:Female 486:209). More than 85% of patients were receiving metformin in combination with other oral antidiabetic agents.

Table-1
Severity of neuropathy among patients receiving Vitamin supplementation

Neuropathy			Vitamin Supplementation			
			Yes (n=483)		No (n=212)	
	n	%	n	%	n	%
Normal	261	37.5	171	35.4	90	42.5
Mild + Moderate	284	65.4	210	43.5	74	35.0**
Severe	150	34.6	102	21.1	48	22.6

** Mild + Moderate = $\chi^2 = 4.13$, $p = 0.042$

Serum vitamin B12 concentrations were similar in patients with or without supplementation Table-2 shows the distribution of vitamin B12 levels in patients with neuropathy in comparison with persons without neuropathy. It also shows the number of subjects who had vitamin B12 deficiency, 57.5% of subjects without neuropathy and 42.5% of subjects with neuropathy had vitamin B12 deficiency. The difference was statistically significant. Higher percentage patients with neuropathy had normal B12 levels.

Table-2
Serum Vitamin B12 levels in relation to presence of neuropathy

	Neuropathy	
	Negative	Positive
	n (%)	n (%)
Total (n=695)	261 (37.5)	434 (62.4)
Male (n=486)	169 (34.8)	317 (65.2)
Female (n=209)	92 (44.0)	117 (56.0)*
Vitamin B12 (pg/ml) (Median Values)		
Total	419	714#
Male	377	673#
Female	462	874#
Vitamin B12 (pg/ml)	n (%)	n (%)
<200 (n=80)	46 (57.5)	34 (42.5)
≥ 200 (n=615)	215 (35.0)	400 (65.0)**

Neuropathy * - Male Vs Female $\chi^2 = 4.9$, $p = 0.026$

Vitamin B12 ** - positive Vs negative neuropathy $\chi^2 = 14.4$, $p < 0.0001$

Mann-Whitney Test - # - Negative Vs Positive

Total - Z=-7.5, $p < 0.0001$, Male-Z=-6.3, $p < 0.0001$, Female= Z=-4.5, $p < 0.0001$

DISCUSSION

The study has shown that vitamin B12 deficiency is present in 11.5% of type 2 diabetic subjects who are being treated with various antidiabetic agents. In a study of 203 diabetic patients in an outpatient diabetic clinic, reported vitamin B12 deficiency in 22% of the subjects [2]. The relatively low percentage of vitamin B12 deficiency noted in our study could be due to multivitamin supplementation prescribed in 70% of the patients. It is worth noting that vitamin B12 deficiency was seen in 56 patients (8%) who had received vitamin supplements. This

constituted 70% of the subject. This was a hospital Diabetic Clinic based study. Therefore a high prevalence of neuropathy was noted. A clinic-based prevalence is likely to be higher than the prevalence among the diabetic population in an epidemiological survey. . Another study had noted that 51.4% of type 2 diabetic patients had peripheral neuropathy [4]. In a cross-sectional, population-based study in Chennai, the overall prevalence of diabetic neuropathy was 26.1% [3]. Most of the participants in the study, (nearly 90%) were

treated with metformin in combination with other anti-diabetic agents. Therefore the isolated effect of metformin on B12 levels could not be assessed.

CONCLUSION

1. Prevalence of B12 deficiency is relatively low among type 2 diabetic patients undergoing treatment.

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2. Mild and moderate form of neuropathy was more common probably due to vitamin supplementation that prevented further progression.

3. Therefore, early detection of vitamin B12 deficiency in pre-diabetic stages would be useful for prevention of neurological disorders by vitamin supplementation.