



ORIGINAL RESEARCH PAPER

General Medicine

ASSESSMENT OF SERUM VITAMIN B12 AMONG DIABETIC PATIENTS UNDER TREATMENT WITH METFORMIN IN A TERTIARY CARE CENTRE

KEY WORDS: Diabetes Mellitus, Glycosylated Hemoglobin, Metformin, Vitamin B12.

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ABSTRACT

Background: Type 2 diabetes mellitus (DM) is a widespread metabolic health disease. The oral hypoglycemic drug metformin is prescribed to type 2 diabetic patients worldwide as a first line treatment along with lifestyle changes. The risk of vitamin B12 deficiency and its medical repercussions in diabetic patients increases with ongoing metformin medication. **Aim:** To assess the vitamin B12 levels in type 2 diabetes mellitus patients on metformin and to determine the association with duration and dose metformin. **Materials and Method:** The present study was a Cross Sectional Observational Study conducted for a period of 6 months in department of General Medicine, Sree Mookambika Institute of Medical Sciences. There were 120 consecutive cases of Type 2 DM receiving metformin medication in the study group. Each patient's medical history was reviewed to identify the length of their metformin therapy and past dosages, and these dosages were vocally confirmed by the patients. Results were analyzed using SPSS 20.0 version and the association was tested using Chi square test. **Results:** The mean age group of patients included in the present study was 56.52 ± 11.3 years and the age group ranged from 32 to 76 years. The average duration of diabetes mellitus and metformin therapy were reported as 10.92±8.95 years and 8.66±7.24 years respectively. Vitamin B12 deficiency was seen in 49(40.83%) of the patients. When compared to other patients in the study population, patients with age greater than 50, duration of diabetes greater than 10 years, duration of metformin therapy greater than 5 years, and dose of metformin greater than 1000 mg/day had vitamin B12 deficiency. The association was found to be statistically significant (p0.05) with p values of 0.048, 0.012, 0.026, and 0.002, respectively. With diabetes for less than 10 years and more than 10 years, the mean serum levels of vitamin B12 were 183.518±94.75 and 152.384±36.26, respectively, and there was a significant correlation between the duration of diabetes exposure (p Value 0.004). **Conclusion:** Patients on metformin therapy frequently have vitamin B12 deficiency, especially those over the age of 50 years, with diabetes for longer than ten years, taking metformin for longer than five years, and receiving doses of more than 1000 mg/day. This strongly suggests routine screening for vitamin B12 in diabetic patients taking metformin. Before starting metformin, and afterwards on an annual basis, it is critical to screen for vitamin B12 insufficiency.

INTRODUCTION:

The term "Diabetes Mellitus"(DM) refers to a collection of metabolic disorders that share a hyperglycemic phenotype.¹ There are various clinically distinct types of DM due to a complex interaction between environmental and hereditary variables. Hyperglycemia is caused by a combination of causes including decreased insulin secretion, decreased glucose utilization, and increased glucose generation.²

Type 2 DM is in great epidemic proportion in India. The prevalence of overweight and obesity has increased as a result of rapid industrialization and urbanisation, which has also resulted in a drop in physical activity.³

Treatment for type 2 DM involves using an array of oral hypoglycemic drugs. Due to its low cost, great efficacy, and advantages for weight loss, metformin is the preferred oral hypoglycemic drug. It is also commonly used as a dietary modification.⁴ The majority of the current global clinical practice guidelines, such as those from the American Diabetes Association, the Korean Diabetes Association and the European Association for the Study of Diabetes, recommend starting metformin along with concurrent lifestyle changes at the time of initial diabetes diagnosis if there are no contraindications.⁵

Metformin primarily affects the liver by decreasing glucose release and then increasing glucose uptake in peripheral tissues, particularly muscles. By altering intestinal motility, fostering bacterial overgrowth, and altering the vitamin B12-IF complex, metformin prevents the absorption of vitamin B12. Age, metformin dosage, and length of treatment all have

an impact on how likely it is that a patient would experience vitamin B12 insufficiency brought on by metformin. The synthesis of DNA, hematopoiesis, and brain function are all significantly influenced by vitamin B12, often known as cobalamin.⁶

Vitamin B12 deficiency can cause a variety of problems including gastrointestinal, haematological, neurological, and psychological disorders as well as an increase in the severity of diabetic peripheral neuropathy. Anaemia, memory loss, low mood, and weariness are some of the additional mild symptoms associated with vitamin B12 insufficiency.^{7,8}

Vitamin B12 deficiency-related peripheral neuropathy may be mistaken for diabetic peripheral neuropathy or may exacerbate diabetic peripheral neuropathy. Early diagnosis and cobalamin treatment can halt the progression of vitamin B12 deficiency-related neurological damage.⁹

There are currently no reliable published recommendations supporting routine testing for vitamin B12 insufficiency among metformin-using patients. The primary objective of the current study was to determine how frequently metformin-treated Type 2 diabetes patients had Vitamin B12 deficiencies and also to evaluate the association with duration and dose metformin. Following the initiation of metformin medication, this would be beneficial in monitoring patients for vitamin B12 deficiency, which can considerably lower morbidity and enhance quality of life in these patients by commencing B12 supplements when necessary.

MATERIALS AND METHODS:

Present study was a Cross Sectional Observational Study conducted for a period of 6 months (Data collected from January 2023 to June 2023) in Department of general Medicine, Pathology, Sree Mookambika Institute of Medical Sciences, Kulasekharam. The study group included 120 consecutive cases of Type 2 Diabetes Mellitus on metformin therapy.

All patients with type 2 DM, regardless of metformin dosage or duration, between the ages of 18 and 80 years were included in the study. Patients who have given their agreement to take part in the study were enrolled. The current study excluded patients who were receiving irregular treatment, were pregnant, were younger than 18 but older than 80 years, were taking vitamin B12 supplements, did not give their consent, and were not receiving regular medical treatment.

All of the data was entered into a structured questionnaire. The information covered the age, gender, length of diabetes mellitus, and length of metformin treatment for the patient. Following the collection of the aforementioned information from patients as well as health care records, 5 ml of blood was drawn in a sample tube following an overnight fast and sent to the laboratory for measurement of blood sugar (fasting along with postprandial), HbA1C, and serum vitamin B12 levels. Biochemical deficiency was defined as serum vitamin B12 concentrations less than 180 pg/ml.

Statistical Analysis was carried out using SPSS 20.0 version. For quantitative data, mean and SD were determined, but for qualitative variables, frequencies and percentages were used. An Independent t-test was obtained to compare the mean of B12. ANOVA was done to compare the mean of B12 across the duration of treatment and treatment doses. Pearson correlation was obtained to study the relationship between the age and B12 level. A p value less than 0.05 was considered statistically significant.

OBSERVATION AND RESULTS:

A total of 120 patients were included in the study. The mean age group of patients included in the present study was 56.52 ± 11.3 years and the age group ranged from 32 to 76 years. The most common age group affected by type 2 DM was in age group of 50 to 60 years followed by 40 to 50 years seen in 45(3.5%) and 37(30.83%) respectively. Of the 120 patients 78(65%) were males and 42(35%) were females. The mean value of fasting plasma glucose was 116.25±18.71 and the mean value for postprandial plasma glucose was 160.64±25.21. The mean HbA1c was 7.14±2.84.

The average duration of diabetes mellitus and metformin therapy were reported as 10.92±8.95 years and 8.66±7.24 years respectively. Vitamin B12 deficiency was seen in 49(40.83%) of the patients.

Table 1: Comparison of vitamin B12 deficiency with age, gender, duration of diabetes and duration and dose of metformin therapy.

Parameters	Vitamin B12 deficiency		p value
	Present (n=49)	Absent (n=71)	
Age group			
≤40 years	6(12.24%)	9(12.68%)	0.048
41-50 years	16(32.65%)	21(29.58%)	
51-60 years	19(38.78%)	26(36.62%)	
>60 years	8(16.33%)	15(21.12%)	
Gender			
Male	33(67.35%)	45(63.38%)	0.34
Female	16(32.65%)	26(36.62%)	
Duration of diabetes			
< 10 years	18(36.74%)	42(59.15%)	0.012
>10 years	31(63.26%)	29(40.85%)	

Duration of metformin therapy			
≤ 5 years	11(24.45%)	48(67.61%)	0.026
>5 years	38(77.55%)	23(32.39%)	
Dose of metformin therapy			
≤1000 mg/day	15(30.61%)	45(63.38%)	0.002
>1000 mg/day	34(69.39%)	26(36.62%)	

Table 2: Comparison of mean vitamin B12 deficiency with duration of diabetes.

Duration of Diabetes	Vitamin B12 deficiency		v
	Mean	SD	
< 10 years	183.518	±94.75	0.004
>10 years	152.384	±36.26	

When compared with other patients in the study population, patients with diabetes for more than 10 years, metformin therapy for more than 5 years, and metformin doses greater than 1000 mg/day had vitamin B12 deficiency, and the association was found to be of statistical significance (p<0.05) with p values of 0.012, 0.026, and 0.002, respectively. (Table 1). When compared to individuals with diabetes lasting less than 10 years, people who had diabetes for over 10 years had lower mean vitamin B12 levels. Diabetes exposure time was shown to be significantly correlated (p = 0.004). (Table 2)

DISCUSSION:

Cobalamin, often known as vitamin B12, is crucial for the production of DNA, hematopoiesis, and neurological health. Insufficiency in vitamin B12 is linked to haematological and neuropsychological impairment.¹⁰ Numerous studies have demonstrated that long-term metformin therapy significantly affects the vitamin B12 levels in type 2 DM patients.

In the current study, out of the 120 diabetes patients, 49 (or 40.83%) had a vitamin B12 deficit. 33 of them (67.35%) were male, compared to 16 (32.65) who were female. In the study by Raqib TM et al.¹¹ including 100 diabetes patients, it was found that 48% of patients had low levels of serum vitamin B12; however, females had a higher proportion of low levels of serum vitamin B12 (70 cases) than males (30 cases).

The mean age of patients in the study population was 56.52 ± 11.3 years. The average duration of diabetes mellitus and metformin therapy were reported as 10.92±8.95 years and 8.66±7.24 years respectively. The average duration of Diabetes mellitus and metformin therapy in the study done by Kumar A et al.¹² were reported as 9.93±6.82 years and 9.60±6.15 years respectively and the average age was reported as 58.89±13.12 years.

Patients with duration of diabetes more than 10 years, duration of metformin therapy more than 5 years and dose of metformin more than 1000 mg/day had vitamin B12 deficiency when compared to other patients in the study population and the association was found to be statistically significant. The mean value of vitamin B12 was less with increased duration of diabetes.

Kumar A et al.¹², it was found that 29.3% of the 215 patients had vitamin B12 deficiencies. A statistically significant difference (p <0.05) was observed in the metformin treatment of about 55 patients with vitamin B12 deficiency over a period of more than 4 years.

Sekhri T et al.¹³ observed vitamin B12 insufficiency in 35.89% of those patients with type 2 diabetes who had been on metformin for more than 5 years. The most likely explanation is that none of the patients were taking vitamin B12 supplements and had all been using metformin for the previous five years. In the study conducted by Yakubu M et al.¹⁴ serum vitamin B12 insufficiency was identified in 5.8% of those with Type2 DM over 50 years of age who took metformin for a median of 5 years as opposed to 2.4% of Type 2 diabetes. patients who did not take the medication.

Mohammed AO et al.¹⁵ in their study found that the mean serum levels of vitamin B12 in the metformin-underused diabetes group and the control group were (252.6±101.3, 339.4±112.3, respectively). Patients receiving metformin treatment experienced significantly lower serum levels of vitamin B12 than patients who did not receive metformin treatment (p value = 0.000).

Similarly, Padma V et al.¹⁶ reported that the mean B12 levels in patients using metformin doses more than 1,000 mg were 349 pg/dl and 215 pg/dl, respectively. With a p value of 0.002, the difference among the two groups was statistically significant.

CONCLUSION:

The use of metformin medication in patients with type 2 diabetes has been found to be connected with low serum levels of vitamin B12, according to the findings in the present study. All patients who are older than 50 years, been diagnosed with diabetes for longer than 10 years, and are taking metformin at a higher dose and for a longer period of time should ideally be tested for vitamin B12 insufficiency and given supplements if necessary. Future studies should be conducted to determine whether preventive vitamin B 12 supplementation is beneficial for those with type 2 diabetes who are on metformin.

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Nil.

Conflicts Of Interest:

There are no conflicts of interest

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