

Prevalence of Vitamin B12 Deficiency in Patient with Type-II Diabetes Mellitus on Metformin Therapy

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Abstract: Long-term metformin use in type 2 diabetes mellitus (T2DM) patients often leads to vitamin B12 deficiency, a commonly overlooked condition that can cause serious health issues. This study estimated the prevalence vitamin B12 deficiency in patients with T2DM on metformin therapy. In a cross-sectional study of 85 patients at a tertiary hospital, vitamin b12 levels were assessed, revealing that deficiency was more common in those with higher dosages and longer treatment durations. The findings highlight the need for routine screening and timely intervention for vitamin B12 deficiency in long-term metformin users.

Keywords: Type-2 diabetes mellitus (T2DM), Metformin, vitamin b12 deficiency, Anemia, peripheral neuropathy

1. Introduction

Diabetes Mellitus (DM) is one of the leading causes of mortality and morbidity globally. American Diabetes Association (ADA) has declared DM as sixth leading cause of death worldwide. According to World Health Organization (WHO), in 2019, DM caused an estimated 2 million deaths and there was a 3% increase in diabetes mortality rates by age. In 2019, diabetes directly caused 1.5 million deaths, with 48% occurring before age 70. It also contributed to 460,000 kidney disease deaths and about 20% of cardiovascular deaths. The prevalence of DM and impaired glucose tolerance in India is estimated at 9.3% and 24.5%, respectively, based on a national survey of adults aged 18-69. This highlights the growing diabetes burden in the country. Metformin is the primary oral medication for managing hyperglycemia in type 2 diabetes and is recommended as a first-line treatment by both European and American diabetes associations. Clinical trials confirm that metformin enhances cardiovascular outcomes in type 2 diabetes and is widely used for its effectiveness, safety, and compatibility with other medications, with over 150 million global users.^{11,12} The ADA and EASD have reported that metformin enhances peripheral insulin sensitivity, supports weight loss, and provides vascular protection. Chronic intake of metformin is seen to be associated with some side effects. Most side effects are mild, but evidence shows that metformin reduces vitamin B12 and folic acid absorption. About 30% of long-term metformin users experience vitamin B12 malabsorption, reducing serum levels by 14% to 30%. Vitamin B12 deficiency in T2DM patients can lead to serious complications and increased homocysteine levels, a risk factor for cardiovascular disease. Vitamin B12 deficiency can lead to megaloblastic anemia, cognitive decline, and Alzheimer's disease, as well as microangiopathic hemolysis. B12 is crucial for DNA synthesis, cellular repair, and red blood cell production. Neurological issues such as spinal cord degeneration, delirium, dementia, and axonal demyelination in metformin users may be mistaken for diabetic neuropathy. The ADA

recommends routine vitamin B12 screening for these patients due to this association. Furthermore, there are no guidelines to address how often T2DM patients on metformin should be screened for the risk of vitamin B12 deficiency in our tertiary center which would inform appropriate prescription of vitamin B12 supplements probably due to limited studies on the subject matter. This study highlights the growing need for regular monitoring of vitamin B12 levels in metformin treated diabetes patients, providing evidence for improved guidelines and intervention strategies to prevent severe health complications.

2. Methods

This study is observational, cross-sectional study and it was conducted at DR. Bhimrao Ambedkar Memorial Hospital Raipur C.G. from December 2022 to December 2023, to Estimate prevalence of vitamin B12 deficiency in patients with type 2 diabetes mellitus on metformin. This study included 85 patients with sample size calculated based on vitamin B12 deficiency prevalence. Participants were adults aged 18-65 years on metformin treatment over six months with Stable metformin dosage in past 3 months. Exclusion criteria included patient taking any vitamin B12 containing multivitamin by oral or parental route, Patients with major systemic disease like pernicious anemia, or inflammatory bowel disease, chronic kidney disease, Patients who underwent gastrectomy, colectomy in the past, strict vegetarian, smokers, alcoholic and other specified conditions like pregnancy. Demographic and clinical data were securely collected, and blood samples were analyzed for vitamin B12 levels. The data were analyzed using SPSS software.

3. Results

This hospital-based cross-sectional study at a tertiary care Centre included 85 type2 diabetes patients on metformin.

Table 1: Age distribution

Age group	frequency	percentage
30-40	5	5.9%
41-50	23	27.1%
51-60	33	38.8%
>60	24	28.2%

The average age was 54.14 ± 8.89 years. Most patients were aged 51-60 (38.8%), followed by those over 60 (28.2%) and 41-50 (27.1%), with the least in the 30-40 age group (5.9%). The majority were male 54(63.5%) and female were 31(36.5%).

Table 2: Distribution of patients according to Duration of Metformin in year

Duration of metformin use	Normal B12 level	B12 deficient
<5yrs	14 (7.2%)	0
6-10yrs	39(45.88%)	0
11-15yrs	1 (1.18%)	16(18.82%)
16-20yrs	0	12(17.64%)
>20yrs	0	3(3.5%)
total	54	31

36.5% of patients exhibited vitamin B12 deficiency, while 63.5% had normal levels. None of the 14 patients who utilized metformin for duration of up to 5 years exhibited vitamin B12 deficiency. All 39 patients who utilized metformin for duration of 6-10 years none exhibited vitamin B12 deficiency. Out of 17 Patients using metformin for duration of 11-15 years, 16 were B12 deficient only one had normal levels of vitamin B12. Out of 12 Patients using metformin for duration of 16-20 years all were B12 deficient. All 3 Individuals who utilized metformin for 20 years or more all were deficient for vitamin B12.

Table 3: Distribution of patients according to Metformin dose in mg per day

Metformin Dose in mg	Frequency	Percent
500	3	3.5%
1000	65	76.5%
1500	12	14.1%
2000	5	5.9%

Majority of patients had 1000mg/day dose that is 76.5% followed with 14.1% who had 1500mg/day dose, 5.9% had 2000mg/day dose and only 3.5% patients had 500mg/day dose.

4. Conclusions

It can be concluded from this study that, in type II diabetes mellitus higher dose and longer duration of metformin usage increases the risk of vitamin B12 deficiency, hence we recommend routine screening and periodic assessment of vitamin b12 levels in long term metformin users. For early detection and early management of vitamin B12 deficiency.

5. Limitations

The cross-sectional design limits causality, potential confounders may affect vitamin B12 status, and limited sample size.

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