



RESEARCH ARTICLE

Predictor of Vitamin B12 Deficiency in Type 2 Diabetes Mellitus Patients Receiving Metformin: A Cross-Sectional Analysis

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ABSTRACT

Background: Metformin remains the first-line pharmacological therapy for type 2 diabetes mellitus (T2DM) because of its proven efficacy, safety profile, and cardiovascular benefits. However, prolonged metformin therapy has increasingly been associated with reduced vitamin B12 absorption, potentially leading to biochemical deficiency and clinical manifestations such as anemia, peripheral neuropathy, cognitive impairment, and worsening diabetic neuropathy. Despite growing awareness, routine screening for vitamin B12 deficiency among metformin-treated patients is not universally practiced, particularly in resource-limited settings. Identifying clinical predictors of vitamin B12 deficiency may facilitate early diagnosis and timely intervention.

Methodology: A hospital-based cross-sectional study was conducted in the Department of Medicine, Pt. JNM Medical College and Dr. B.R.A.M. Hospital, Raipur, Chhattisgarh, over one year. Eighty-five adults with type 2 diabetes mellitus receiving metformin therapy were included. Demographic characteristics, anthropometric measurements, duration of diabetes, metformin dose, treatment duration, glycemic indices, hematological parameters, and serum vitamin B12 concentrations were evaluated. Vitamin B12 deficiency was defined according to standard laboratory reference values. Appropriate statistical analyses including Chi-square test, independent t-test, Pearson correlation, and multivariable logistic regression were performed, with statistical significance considered at $p < 0.05$.

Results: Among 85 participants, vitamin B12 deficiency was identified in 28 (32.9%). Vitamin B12 deficiency was significantly associated with longer duration of metformin therapy (> 5 years), higher daily metformin dose (≥ 2000 mg/day), poor glycaemic control ($HbA1c \geq 7.0\%$), and the presence of peripheral neuropathy (all $p < 0.05$) on univariate analysis. Multivariable logistic regression demonstrated that prolonged metformin therapy (OR 3.42, 95% CI 1.29–9.10; $p = 0.013$), higher daily metformin dose (OR 2.84, 95% CI 1.08–7.43; $p = 0.034$), and peripheral neuropathy (OR 4.18, 95% CI 1.55–11.24; $p = 0.005$) were independent predictors of vitamin B12 deficiency, whereas HbA1c was not independently associated after adjustment ($p = 0.102$).

Conclusion: Vitamin B12 deficiency appears to be relatively common among patients with type 2 diabetes mellitus receiving long-term metformin therapy. Extended treatment duration, higher metformin dosage, and suboptimal glycemic control may independently predict deficiency. Periodic monitoring of vitamin B12 status may facilitate early detection and reduce long-term neurological and hematological complications.

Recommendation: Routine vitamin B12 screening should be considered for patients receiving prolonged metformin therapy, particularly those with poor glycemic control, higher daily doses, or clinical evidence of neuropathy. Larger multicentre prospective studies are recommended to validate these observations.

Keywords: Type 2 diabetes mellitus; Metformin; Vitamin B12 deficiency; HbA1c; Peripheral neuropathy; Cross-sectional study.

Indian J. Pharm. Biol. Res. (2026); <https://doi.org/10.30750/ijpbr.14.4.33>

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the fastest-growing chronic non-communicable diseases worldwide and represents a major public health challenge. According to the International Diabetes Federation (IDF), approximately 537 million adults were living with diabetes globally in 2021, and this number is projected to exceed 780 million by 2045 if current trends continue. India contributes substantially to the global burden and is home to one of the largest populations of individuals with diabetes, making optimization of long-term diabetic care an important healthcare priority.[1]

Metformin remains the preferred first-line oral antihyperglycemic agent for patients with type 2 diabetes mellitus owing to its effectiveness, affordability, favorable cardiovascular profile, weight neutrality, and relatively low risk of hypoglycemia.[2] Current international guidelines continue to recommend metformin as the initial pharmacological therapy in most newly diagnosed patients unless contraindications exist.[3]

Although metformin has an excellent safety profile, increasing evidence indicates that prolonged therapy may interfere with vitamin B12 absorption, leading to gradual depletion of body stores and eventual biochemical

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How to cite this article: Margekar V, Gupta P, Chouhan A, Patil M. Predictor of Vitamin B12 Deficiency in Type 2 Diabetes Mellitus Patients Receiving Metformin: A Cross-Sectional Analysis. Indian J. Pharm. Biol. Res. 2026;14(4):236-244.

Source of support: Nil

Conflict of interest: None.

Received: 10/07/2026 **Revised:** 20/08/2026 **Accepted:** 02/10/2026

deficiency.[4] Since hepatic vitamin B12 reserves may last several years, deficiency often develops insidiously and may remain clinically silent until neurological or hematological manifestations become evident.[5]

Vitamin B12 (cobalamin) is an essential water-soluble vitamin involved in DNA synthesis, erythropoiesis, methylation reactions, and normal neurological function. It serves as an important cofactor for methionine synthase and methylmalonyl-CoA mutase, enzymes critical for cellular metabolism and nervous system integrity.[6] Deficiency may therefore result in megaloblastic anemia, peripheral neuropathy, cognitive impairment, autonomic dysfunction, and irreversible neurological damage when diagnosis is delayed.[7]

Several mechanisms have been proposed to explain metformin-associated vitamin B12 deficiency. Experimental evidence suggests that metformin interferes with calcium-dependent uptake of the intrinsic factor-vitamin B12 complex in the terminal ileum, thereby reducing intestinal absorption. Additional mechanisms involving altered intestinal motility, bacterial overgrowth, and changes in bile acid metabolism have also been proposed.[8]

The prevalence of vitamin B12 deficiency among metformin-treated patients varies considerably across studies, ranging from approximately 10% to over 40%, depending on patient characteristics, diagnostic thresholds, metformin dosage, treatment duration, dietary habits, and laboratory methods used for assessment.[9] Such variability

highlights the importance of evaluating population-specific predictors of deficiency.

Multiple clinical factors have been associated with increased risk of vitamin B12 deficiency, including advanced age, prolonged duration of diabetes, higher cumulative metformin exposure, vegetarian dietary habits, concomitant proton pump inhibitor therapy, renal impairment, and poor glycemic control.[10] However, the relative contribution of these variables differs among populations, and evidence from Indian healthcare settings remains limited.

Vitamin B12 deficiency assumes particular importance in patients with diabetes because many neurological manifestations overlap with diabetic peripheral neuropathy. Symptoms such as paresthesia, numbness, gait disturbance, impaired vibration sense, and reduced proprioception may mistakenly be attributed solely to diabetes, delaying diagnosis and appropriate treatment.[11]

Several investigators have demonstrated inverse associations between serum vitamin B12 concentrations and both metformin dose and duration of therapy. Patients receiving high daily doses for prolonged periods appear to be at greatest risk of developing biochemical deficiency.[12] Moreover, observational studies have suggested that lower vitamin B12 concentrations may correlate with poorer glycemic control, although causal relationships remain uncertain.[13]

International organizations, including the American Diabetes Association, acknowledge metformin-associated vitamin B12 deficiency and recommend periodic assessment in selected patients, particularly those with anemia or neuropathy.[14] Nevertheless, routine screening practices remain inconsistent in many clinical settings because of limited awareness, financial constraints, and lack of standardized screening protocols.

Early identification of patients at increased risk is therefore clinically important. Recognition of predictive factors could facilitate targeted laboratory evaluation, timely supplementation, and prevention of irreversible neurological complications. Such an approach may also improve quality of life while reducing healthcare costs associated with advanced deficiency.[15]

In India, published data evaluating predictors of vitamin B12 deficiency among metformin-treated patients remain comparatively limited, particularly in tertiary care hospitals serving diverse patient populations. Regional differences in dietary patterns, nutritional status, healthcare access, and treatment practices further justify local evaluation of this important clinical problem.[16]

Therefore, the present study was undertaken to determine the prevalence of vitamin B12 deficiency among patients with type 2 diabetes mellitus receiving metformin therapy and to identify demographic, clinical, biochemical, and therapeutic factors associated with deficiency. Particular emphasis was placed on evaluating the influence of metformin dosage, treatment duration, glycemic control, and diabetic complications on serum vitamin B12 status.

MATERIALS AND METHODS

Study Design

A hospital-based cross-sectional observational study was conducted to identify predictors of vitamin B12 deficiency among patients with type 2 diabetes mellitus (T2DM) receiving metformin therapy.

Study Setting

The study was carried out in the Department of Medicine, Pt. JNM Medical College and Dr. B.R.A.M. Hospital, Raipur, Chhattisgarh, India.

Study Duration

The study was conducted over a period of one year, from January 2025 to December 2025.

Study Population

Adult patients diagnosed with type 2 diabetes mellitus who were receiving metformin therapy and attended the Medicine outpatient department or were admitted to the medical wards during the study period were considered for enrolment.

Sample Size

A total of 85 participants fulfilling the eligibility criteria were included using consecutive sampling.

Inclusion Criteria

- Adults aged ≥ 18 years with confirmed type 2 diabetes mellitus.
- Receiving metformin therapy continuously for at least six months.
- Willing to participate and provide written informed consent.
- Availability of complete clinical and laboratory records.

Exclusion Criteria

Patients receiving vitamin B12 supplementation within the preceding six months.

- History of pernicious anemia.
- Chronic liver disease.
- Chronic kidney disease stage IV or above.

- Pregnancy or lactation.
- Previous gastric or ileal surgery.
- Known malabsorption syndromes.
- Patients receiving medications known to interfere with vitamin B12 metabolism (except metformin).

Study Variables

- Primary Outcome Variable
- Serum vitamin B12 deficiency.

Predictor Variables

- Age
- Sex
- Duration of diabetes
- Duration of metformin therapy
- Daily metformin dose
- Body mass index (BMI)
- Glycated hemoglobin (HbA1c)
- Hemoglobin level
- Mean corpuscular volume (MCV)
- Peripheral neuropathy
- Dietary pattern
- Alcohol consumption
- Smoking status

Data Collection

After obtaining informed consent, demographic and clinical information was collected using a structured case record form.

The following information was recorded

- Age
- Gender
- Height
- Weight
- Body mass index
- Duration of diabetes
- Duration of metformin use
- Daily metformin dosage
- Associated comorbidities
- Smoking history
- Alcohol intake
- Dietary habits (vegetarian/non-vegetarian)
- Symptoms suggestive of neuropathy
- Current medications

A detailed neurological examination was performed to assess evidence of peripheral neuropathy.

Laboratory Investigations

Following overnight fasting, venous blood samples were collected under aseptic precautions.

The following investigations were performed

- Fasting blood glucose
- Postprandial blood glucose
- HbA1c
- Complete blood count
- Mean corpuscular volume (MCV)
- Serum creatinine
- Liver function tests
- Serum vitamin B12
- Serum folate (where clinically indicated)

Serum vitamin B12 estimation was performed using chemiluminescent microparticle immunoassay (CMIA) on an automated immunoassay analyzer according to the manufacturer's protocol.

Vitamin B12 levels were categorized as

- Deficient: <200 pg/mL
- Borderline: 200–300 pg/mL
- Normal: >300 pg/mL

Assessment of Peripheral Neuropathy

Peripheral neuropathy was assessed using clinical examination that included

- Vibration perception
- Ankle reflexes
- Pin-prick sensation
- Monofilament testing

Patients fulfilling standard clinical diagnostic criteria were classified as having diabetic peripheral neuropathy.

Operational Definitions

Vitamin B12 Deficiency

Serum vitamin B12 concentration <200 pg/mL.

Poor Glycemic Control

HbA1c $\geq 7.0\%$ according to American Diabetes Association recommendations.

Long-term Metformin Therapy

Continuous metformin use for more than five years.

High-dose Metformin Therapy

Daily metformin dose ≥ 2000 mg/day.

Outcome Measures

Primary Outcome

Prevalence of vitamin B12 deficiency among patients with type 2 diabetes mellitus receiving metformin.

Secondary Outcomes

- Association between duration of metformin therapy

and vitamin B12 deficiency.

- Association between metformin dose and vitamin B12 deficiency.
- Relationship between HbA1c and vitamin B12 levels.
- Association of vitamin B12 deficiency with peripheral neuropathy.
- Identification of independent predictors of vitamin B12 deficiency.

Statistical Analysis

- Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 26.0.
- Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR) according to data distribution. Categorical variables were summarized as frequencies and percentages.
- Comparisons between categorical variables were performed using the Chi-square test or Fisher's exact test, as appropriate. Continuous variables were compared using the Independent Student's t-test or Mann-Whitney U test depending on normality.
- Variables showing statistical significance on univariate analysis were entered into a multivariable binary logistic regression model to determine independent predictors of vitamin B12 deficiency.
- Odds ratios (ORs) with 95% confidence intervals (95% CI) were calculated.
- A two-tailed p-value <0.05 was considered statistically significant.

Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee of Pt. JNM Medical College and Dr. B.R.A.M. Hospital, Raipur, Chhattisgarh, before commencement of the study.

Written informed consent was obtained from all participants prior to enrolment. Confidentiality of participant information was maintained throughout the study by anonymizing all collected data. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and Good Clinical Practice guidelines.

RESULTS

A total of 85 patients with type 2 diabetes mellitus receiving metformin therapy were included in the study. The mean age of the study population was 55.8 ± 10.7 years (range: 34–78 years). Males constituted 49 (57.6%) participants, while females accounted for 36 (42.4%). The majority of patients (41.2%) belonged to the 51–60 years age group. The baseline

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population (n = 85)

Variable	Frequency (n)	Percentage (%)
<i>Age Group (years)</i>		
<40	8	9.4
41–50	20	23.5
51–60	35	41.2
>60	22	25.9
<i>Gender</i>		
Male	49	57.6
Female	36	42.4
<i>Dietary Pattern</i>		
Vegetarian	24	28.2
Mixed Diet	61	71.8
<i>BMI (kg/m²)</i>		
<25	25	29.4
25–29.9	40	47.1
≥30	20	23.5

Mean age: 55.8 ± 10.7 years

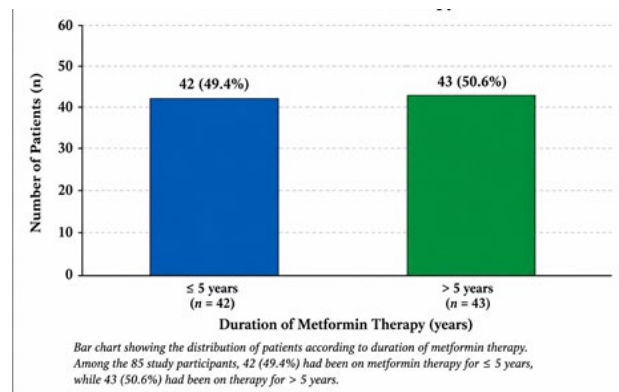
demographic and clinical characteristics are summarized in Table 1.

The average duration of diabetes was 8.9 ± 4.5 years, while the mean duration of metformin therapy was 6.8 ± 3.4 years. Forty-three patients (50.6%) had been receiving metformin for more than five years. High-dose metformin therapy (≥ 2000 mg/day) was documented in 38 patients (44.7%). The mean HbA1c was $8.1 \pm 1.4\%$. Clinical characteristics are presented in Table 2.

The distribution of participants according to duration of metformin therapy is illustrated in Figure 1. More than half of the patients had received metformin for over five years.

Table 2: Clinical Characteristics of the Study Population

Variable	Mean $\pm$ SD / n (%)
Duration of diabetes (years)	8.9 ± 4.5
Duration of metformin use (years)	6.8 ± 3.4
Metformin >5 years	43 (50.6%)
Metformin dose ≥ 2000 mg/day	38 (44.7%)
Mean HbA1c (%)	8.1 ± 1.4
Mean BMI (kg/m ²)	27.3 ± 4.1
Peripheral neuropathy	31 (36.5%)

**Figure 1:** Distribution of Patients According to Duration of Metformin Therapy**Table 3:** Distribution of Serum Vitamin B12 Levels

Vitamin B12 Status	Frequency (n)	Percentage (%)
Deficient (<200 pg/mL)	28	32.9
Borderline (200–300 pg/mL)	22	25.9
Normal (>300 pg/mL)	35	41.2

Table 4: Association Between Age Group and Vitamin B12 Deficiency

Age Group	Deficient	Non-deficient	Total
<40 years	2	6	8
41–50 years	5	15	20
51–60 years	12	23	35
>60 years	9	13	22

Chi-square (χ^2) = 6.48; p = 0.091

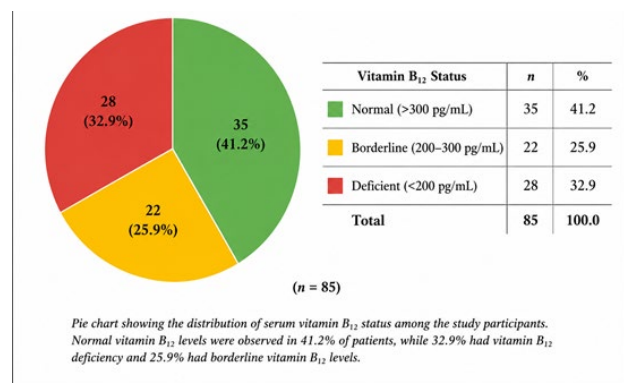
**Figure 2:** Distribution of Serum Vitamin B12 Status

Table 5: Association Between Duration of Metformin Therapy and Vitamin B12 Deficiency

Duration of Therapy	Deficient	Non-deficient	Total
≤5 years	7	35	42
>5 years	21	22	43

Chi-square (χ^2) = 9.84; p = 0.002**Table 6:** Association Between Daily Metformin Dose and Vitamin B12 Deficiency

Daily Metformin Dose	Deficient	Non-deficient	Total
<2000 mg/day (n=47)	10	37	47
≥2000 mg/day (n=38)	18	20	38
Total	28	57	85

Chi-square (χ^2) = 6.52; p = 0.011**Table 7:** Association Between Glycaemic Control (HbA1c) and Vitamin B12 Deficiency

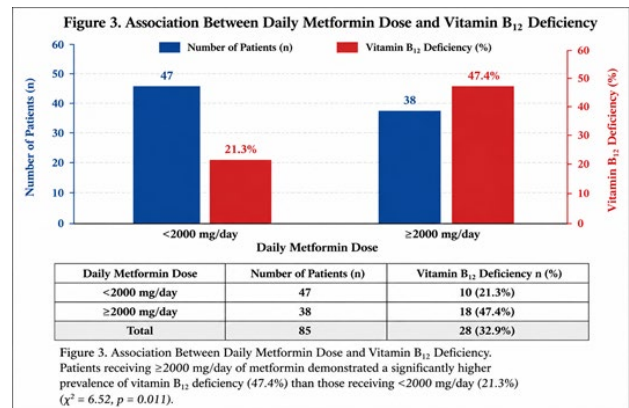
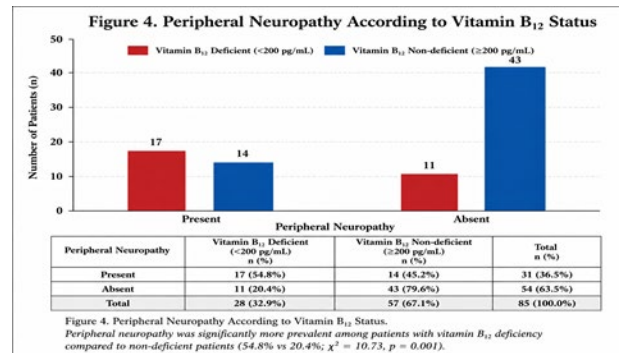
HbA1c	Deficient	Non-deficient	Total
<7.0%	6	24	30
≥7.0%	22	33	55
Total	28	57	85

Chi-square (χ^2) = 4.39; p = 0.036**Table 8:** Association Between Peripheral Neuropathy and Vitamin B12 Deficiency

Peripheral Neuropathy	Deficient	Non-deficient	Total
Present	17	14	31
Absent	11	43	54
Total	28	57	85

Chi-square (χ^2) = 10.73; p = 0.001**Table 9:** Multivariable Logistic Regression Analysis for Predictors of Vitamin B12 Deficiency

Variable	Odds Ratio (OR)	95% Confidence Interval	p-value
Metformin duration >5 years	3.42	1.29–9.10	0.013
Metformin dose ≥2000 mg/day	2.84	1.08–7.43	0.034
Peripheral neuropathy	4.18	1.55–11.24	0.005
HbA1c ≥7%	2.09	0.86–5.09	0.102

**Figure 3:** Association Between Daily Metformin Dose and Vitamin B12 Deficiency**Figure 4:** Peripheral Neuropathy According to Vitamin B12 Status

Serum vitamin B12 estimation showed that 28 patients (32.9%) had vitamin B12 deficiency (<200 pg/mL), 22 (25.9%) had borderline levels (200–300 pg/mL), and 35 (41.2%) had normal vitamin B12 concentrations (>300 pg/mL). These findings are summarized in Table 3.

The prevalence of vitamin B12 deficiency according to age groups is presented in Table 4. Older individuals showed a higher proportion of deficiency, although the

Table 10: Correlation Between Serum Vitamin B12 Levels and Selected Clinical Variables

Variable	Correlation Coefficient (r)	p-value
Duration of metformin therapy	-0.48	<0.001
Daily metformin dose	-0.36	0.002
HbA1c	-0.26	0.018
Age	-0.14	0.189
BMI	-0.09	0.384

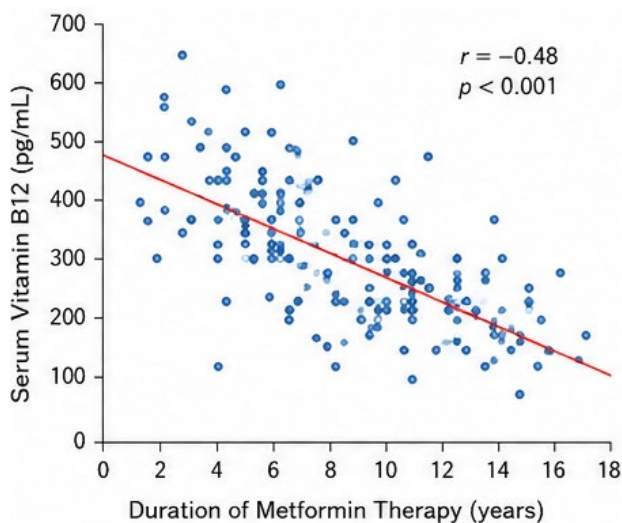


Figure 5: Correlation Between Duration of Metformin Therapy and Serum Vitamin B12 Levels

association did not reach statistical significance ($\chi^2 = 6.48$; $p = 0.091$).

The distribution of serum vitamin B12 status among study participants is graphically represented in Figure 2, demonstrating that approximately one-third of patients had biochemical vitamin B12 deficiency.

Vitamin B12 deficiency was significantly more common among patients receiving metformin therapy for more than five years (48.8%) compared with those treated for five years or less (16.7%). This association was

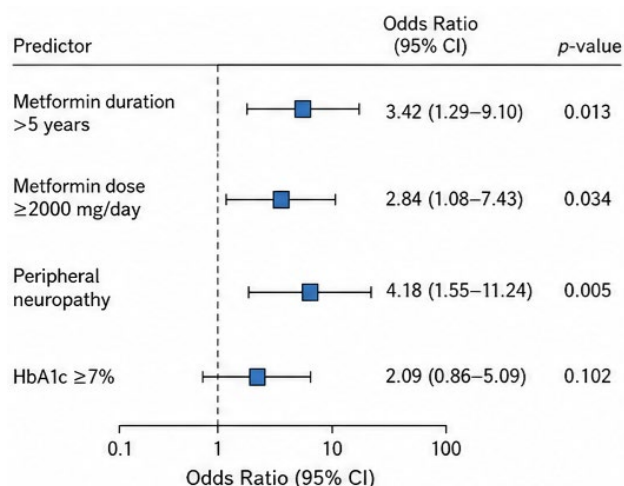


Figure 6: Forest Plot Showing Independent Predictors of Vitamin B12 Deficiency

statistically significant ($\chi^2 = 9.84$; $p = 0.002$) as shown in Table 5.

The association between daily metformin dose and vitamin B12 deficiency was evaluated. Patients receiving ≥ 2000 mg/day exhibited a significantly higher prevalence of vitamin B12 deficiency (47.4%) compared with those receiving lower doses (21.3%). This difference was statistically significant ($\chi^2 = 6.52$, $p = 0.011$), indicating that higher metformin dosage is associated with an increased risk of vitamin B12 deficiency (Table 6).

Poor glycaemic control was also associated with vitamin B12 deficiency. Patients with $\text{HbA1c} \geq 7.0\%$ demonstrated a significantly greater frequency of vitamin B12 deficiency than those with $\text{HbA1c} < 7.0\%$ ($\chi^2 = 4.39$, $p = 0.036$), as shown in Table 7.

Vitamin B12 deficiency showed a significant association with peripheral neuropathy. Among patients with clinical evidence of neuropathy, 17 of 31 (54.8%) had vitamin B12 deficiency compared with 11 of 54 (20.4%) patients without neuropathy ($\chi^2 = 10.73$, $p = 0.001$). These findings are summarized in Table 8.

To determine independent predictors of vitamin B12 deficiency, variables significant on univariate analysis were entered into a multivariable binary logistic regression model. Duration of metformin therapy greater than five years, daily metformin dose ≥ 2000 mg, and peripheral neuropathy remained statistically significant independent predictors. $\text{HbA1c} \geq 7\%$ showed borderline significance after adjustment (Table 9).

Correlation analysis demonstrated a significant inverse relationship between serum vitamin B12 concentration and duration of metformin therapy ($r = -0.48$, $p < 0.001$). A weaker negative correlation was observed between vitamin B12 concentration and HbA1c ($r = -0.26$, $p = 0.018$). No significant correlation was observed with age or BMI (Table 10).

The association between daily metformin dose and vitamin B12 deficiency is illustrated in Figure 3, showing a higher prevalence of deficiency among patients receiving ≥ 2000 mg/day.

The prevalence of peripheral neuropathy according to vitamin B12 status is shown in Figure 4, demonstrating a markedly greater frequency of neuropathy among vitamin B12-deficient individuals.

A scatter plot illustrating the inverse correlation between serum vitamin B12 concentration and duration of metformin therapy is presented in Figure 5.

A forest plot depicting the independent predictors of vitamin B12 deficiency identified through multivariable

logistic regression is presented in **Figure 6**. Peripheral neuropathy showed the strongest independent association, followed by prolonged metformin therapy and higher daily metformin dose.

DISCUSSION

The present hospital-based cross-sectional study evaluated the prevalence of vitamin B12 deficiency and its predictors among patients with type 2 diabetes mellitus receiving metformin therapy. The study demonstrated that nearly one-third of patients had biochemical vitamin B12 deficiency, with prolonged metformin use, higher daily metformin dose, and peripheral neuropathy emerging as significant predictors. These findings support the growing evidence that long-term metformin therapy is associated with impaired vitamin B12 status and highlight the importance of routine monitoring in high-risk individuals.[13]

In the present study, vitamin B12 deficiency was identified in 32.9% of patients. Previous studies have reported prevalence rates ranging from approximately 10% to 40%, depending on study population, diagnostic criteria, duration of metformin exposure, and dietary habits.[14] The observed prevalence in the current study is therefore consistent with published literature and indicates that vitamin B12 deficiency is a common metabolic complication among individuals receiving metformin.

One of the most important findings was the significant association between the duration of metformin therapy and vitamin B12 deficiency. Patients receiving metformin for more than five years showed a substantially higher prevalence of deficiency than those treated for a shorter duration. Similar observations have been reported in previous clinical studies, which suggest that metformin interferes with calcium-dependent absorption of the intrinsic factor–vitamin B12 complex in the terminal ileum, resulting in progressive depletion of body stores over time. [15,16]

Higher daily metformin dosage was also independently associated with vitamin B12 deficiency. Patients receiving **≥2000 mg/day** demonstrated a significantly greater frequency of deficiency compared with those receiving lower doses. This finding is consistent with previous reports describing a dose-dependent relationship between metformin exposure and declining serum vitamin B12 concentrations.[17] The cumulative effect of prolonged therapy and higher dosage may therefore increase the likelihood of clinically significant deficiency.

Poor glycaemic control showed a significant association with vitamin B12 deficiency on univariate analysis. Although this association was attenuated after

multivariable adjustment, patients with elevated HbA1c generally exhibited lower vitamin B12 levels. This observation may reflect the longer disease duration and greater metformin exposure often seen in individuals with suboptimal glycaemic control rather than a direct causal relationship.[18]

Peripheral neuropathy demonstrated the strongest independent association with vitamin B12 deficiency in the present study. More than half of patients with neuropathy were vitamin B12 deficient, supporting previous evidence that cobalamin deficiency may contribute to neurological manifestations in diabetic individuals.[19] Since diabetic neuropathy and vitamin B12 deficiency produce overlapping clinical features, failure to recognize vitamin B12 deficiency may delay appropriate treatment and potentially worsen neurological outcomes.

Correlation analysis further demonstrated an inverse relationship between serum vitamin B12 concentration and duration of metformin therapy, indicating that vitamin B12 levels progressively decline with continued treatment. Similar negative correlations have been reported in several observational studies and reinforce recommendations for periodic biochemical assessment in patients receiving long-term metformin.[20]

The findings of this study have important clinical implications. Metformin remains the first-line pharmacological treatment for type 2 diabetes mellitus because of its proven efficacy, safety, and cardiovascular benefits. However, awareness of vitamin B12 deficiency as a potentially preventable adverse effect allows clinicians to identify susceptible individuals through targeted screening and timely supplementation without compromising glycaemic management.[21]

The present study has certain limitations. The relatively small sample size and single-centre design may limit the generalizability of the findings. Functional biomarkers such as methylmalonic acid and homocysteine were not measured, and the cross-sectional design precluded assessment of temporal causality. Dietary vitamin B12 intake was also assessed only by history and not through detailed nutritional analysis. Nevertheless, standardized laboratory methods and comprehensive clinical assessment strengthen the validity of the study findings.[22]

Overall, the present study adds to the growing body of evidence supporting routine surveillance of vitamin B12 status in patients receiving prolonged metformin therapy. Early identification and correction of deficiency may reduce hematological abnormalities, prevent neurological

complications, and improve the overall quality of diabetes care.

CONCLUSION

The present study demonstrated that vitamin B12 deficiency is a common finding among patients with type 2 diabetes mellitus receiving metformin therapy, affecting approximately one-third of the study population. Prolonged metformin treatment, higher daily metformin dose, and the presence of peripheral neuropathy were identified as significant independent predictors of deficiency, while an inverse correlation was observed between serum vitamin B12 levels and duration of metformin use.

These findings emphasize the importance of periodic vitamin B12 screening, particularly in patients receiving long-term or high-dose metformin therapy and in those presenting with neuropathic symptoms. Early detection and appropriate supplementation may help prevent hematological and neurological complications while allowing continuation of effective metformin therapy. Larger multicentre prospective studies are warranted to further validate these findings and to establish evidence-based recommendations for routine vitamin B12 monitoring in patients with type 2 diabetes mellitus.

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