

Original Article**A STUDY OF VITAMIN B12 DEFICIENCY IN TYPE-II DIABETIC PATIENTS ON METFORMIN THERAPY IN EASTERN REGION OF NEPAL*****Gopal Mishra¹, Pawan Kumar Lal Das², Dipesh Karki¹, Roshna Shrestha¹**¹Department of Internal Medicine, ²Department of Physiology, B&C Medical College Teaching Hospital and Research Centre Birtamod, Jhapa, Nepal**Submitted: 23rd – October-2024, Revised: 20th – November- 2024, Accepted:10th-December-2024****DOI: <https://doi.org/10.3126/mjen.v3i2.73050>****ABSTRACT****Background**

Diabetes mellitus, a metabolic disorder marked by elevated blood glucose level, requires effective management to prevent complications. Metformin, a common frontline treatment for type -II diabetes, is linked to Vitamin B12 deficiency, which may trigger severe health disorders like anemia and neurological problems if remain undiagnosed for a longer duration. This study aims to assess the prevalence of Vitamin B12 deficiency among type 2 diabetic patients on metformin therapy. The objective is to assess the distribution of patients affected by this deficiency and understand how metformin therapy influences B12 levels among these patients³. The Study was conducted at B&C Medical College Teaching Hospital and Research Center, Birtamod, Jhapa, Nepal.

Methods

A total of 200 diabetes patients on metformin were included in the study. Patients were included if they were diagnosed with type -II diabetes, were currently undergoing metformin therapy, and had been on the medication for at least 6 months. Data collected comprised patient age, gender, duration of metformin use, and serum vitamin B12 levels measured using chemiluminescence immunoassay (CLIA). Vitamin B12 deficiency was defined as serum levels <200 pg/mL, insufficiency as 200-300 pg/mL, and sufficiency as >300 pg/mL. Statistical analysis involved descriptive statistics and Chi-square tests.


RESULTS

Out of the 200 diabetic patients taking metformin, 45% exhibited Vitamin B12 deficiency based on serum levels (<200 pg/mL), 30% had insufficient Vitamin B12 levels (200–300 pg/mL), and 25% had sufficient levels (>300 pg/mL). Deficiency rates were similar across genders but higher in patients over 47 years. A significant correlation was observed between longer metformin use and lower Vitamin B12 levels.

CONCLUSION

The results highlight a prominent rate of Vitamin B12 deficiency among diabetes patients prescribed metformin, especially in older patients and those on long-term therapy. Routine monitoring of vitamin B12 levels is recommended for these patients to prevent serious complications and improve health outcomes.

Keywords: Metformin, Therapy, Type-II Diabetes Mellitus, Vitamin B12 deficiency

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INTRODUCTION

Diabetes mellitus, an enduring metabolic disorder with high blood sugar levels affects millions worldwide and requires ongoing management to prevent complications. Metformin, a first-line oral hypoglycemic agent, is widely prescribed for the treatment of type-II diabetes due to its efficiency, safety profile, and cost-effectiveness^{1,4}. Nonetheless, prolonged use of metformin has been linked to Vitamin B12 deficiency an often overlooked complication that can lead to significant health issues if not addressed promptly^{2,3}.

Vitamin B12, commonly called cobalamin, plays a vital role in red blood cell production, nervous system function, and DNA synthesis^{6,7}. Deficiency in this essential vitamin can result in hematologic abnormalities such as megaloblastic anemia and neuropsychiatric manifestations including peripheral neuropathy, cognitive disturbances, and mood disorders^{1,3,6}. The occurrence of vitamin B12 deficiency in individuals taking metformin is a particular concern due to its insidious onset and the potential for irreversible damage if left untreated¹⁷.

At B&C Medical College Teaching Hospital and Research Center, Birtamod, Jhapa, Nepal, a large number of diabetes patients are managed with metformin. However, the extent of vitamin B12 deficiency in these patients remains unclear. Understanding the prevalence and correlated factors of vitamin B12 deficiency in these patients is crucial for guiding clinical practice and improving patients wellbeing.

This research aims to examine the prevalence of vitamin B12 deficiency in patients with diabetes mellitus on metformin treatment at B&C Hospital. By identifying the magnitude of this issue among affected patients, we hope to raise awareness about the importance of monitoring vitamin B12 levels in the patients on metformin and to suggest potential strategies for prevention and management of deficiency related hematopoietic and neurological disorders. The findings from this study will provide valuable insights into the need for routine screening, supplementation and ultimately enhancing the quality of care for diabetic patients.

METHODS

This perspective cross-sectional study was carried out at B&C Medical College Teaching Hospital and Research Center, with ethical approval obtained from the Institutional Review Committee (IRC No :- 00212024). The study included all diabetic patients of out-patient (OPD) and in-patient (IPD) departments, on metformin treatment for a minimum of six months. Data were Collected from electronic health records between January 2024 and June 2024, focusing on patients demographics, duration of metformin

therapy, and estimation of vitamin B12 levels 9, 10. The inclusion criteria were Type-II diabetic patients on metformin for a minimum of 6 months, Age 18 years and older, willingness to participate and provide consent. Exclusion criteria were patients with dietary Vitamin B12 deficiency (e.g., strict vegetarians), patients with conditions that impair Vitamin B12 absorption, such as malabsorption syndromes, chronic gastritis, pernicious anemia, or gastrointestinal surgeries (e.g., gastrectomy), patients with autoimmune diseases such as celiac disease, those on Vitamin B12 supplementation or other medications affecting B12 levels. The study included 200 patients who met the inclusion criteria. Data was obtained from the hospital's central laboratory records. For each patient, the following information was collected: age, gender, duration of metformin use, and serum vitamin B12 levels. Serum vitamin B12 levels were measured using a chemiluminescence immunoassay (CLIA) technique. Vitamin B12 deficiency was defined as serum levels less than 200 pg/mL, insufficiency as levels between 200-300 pg/mL, and sufficiency as levels greater than 300 pg/mL. The collected data was then compiled and analyzed using Microsoft Excel 2019 and SPSS (Statistical Package for the Social Sciences) version 29.0.0. Descriptive statistics were utilized to summarize the data, calculating means and standard deviations (SD) for continuous variables, along with frequencies and percentages for categorical variables. Statistical significance was assessed using the Chi-Square test, with a p-value of less than 0.05 considered significant.

During this study, several potential confounding factors were identified and accounted for to ensure the accuracy of the results. These factors, which could influence Vitamin B12 levels independently of metformin use, include:

Other Medications: Certain medications that patients may be using in conjunction with metformin can also impact Vitamin B12 absorption. For example, proton pump inhibitors (PPIs) or H2 receptor antagonists, often used for managing gastroesophageal reflux disease (GERD), reduce stomach acid, which is essential for the assimilation of Vitamin B12. This could lead to Vitamin B12 deficiency independently of metformin use, potentially confounding the observed relationship.

Alcohol Consumption: Excessive alcohol intake is another factor that could influence Vitamin B12 levels. Chronic alcohol consumption can impair the absorption of Vitamin B12 by damaging the gastrointestinal lining. Therefore, it could confound the study's findings if not adequately controlled.

Gastrointestinal Conditions: Patients with chronic gastrointestinal diseases, like Crohn's disease or celiac disease, may have impaired Vitamin B12 absorption. If these conditions are not accounted for,

they could serve as confounders in assessing the true impact of metformin on B12 Levels.

Duration of Diabetes: The duration of diabetes itself may impact Vitamin B12 levels. Longer-standing diabetes could lead to autonomic neuropathy, which affects the gut and absorption processes. Patients with longer disease duration could thus have lower B12 levels, independently of metformin use. Adjustments were made to account for these potential confounders to ensure the results accurately reflected the implications of Metformin consumption for Vitamin B12 levels.

RESULTS

The study included 200 diabetes patients on metformin therapy at B&C Medical College Teaching Hospital and Research Center over a six-month period. The gender distribution was nearly equal, with 49% males and 51% females (Table-1). The majority of patients were aged between 47-62 years (41%) and over 62 years (33%) (Table-2). Serum vitamin B12 levels indicated that 37.5% of patients had deficiency (<200 pg/mL), 17% had insufficiency (200-300 pg/mL), and 45.5% had sufficient levels (>300 pg/mL) (Figure-1)¹³.

The mean Vitamin B12 levels were 57.3 ± 28.67 pg/mL for males and 55.14 ± 14.91 pg/mL for females. The distribution of Vitamin B12 deficiency was similar across genders, with 36 males and 39 females being deficient. Additional, 12 males and 22 females had insufficient levels, while 50 males and 41 females had sufficient levels (Table-3). Age-wise distribution showed that younger age groups (18 and 19-30 years) had relatively lower deficiencies, while older patients, particularly those over 47 years, showed a higher prevalence of deficiency (Table-4)¹⁶. Among the different age groups, the highest deficiency was observed in the >62 years group, with 32 out of 66 patients followed by the 47-62 years group, with 26 out of 82 patients. For the age group 31-46 years, 14 patients were deficient, and for the age group 19-30 years, 3 patients were deficient. Only one patient in the 18 year age group had insufficient levels of Vitamin B12. The study also found a significant correlation between the duration of metformin use and lower Vitamin B12 levels, indicating that prolonged metformin therapy increases the risk of deficiency. Peripheral neuropathy and Ineffective erythropoiesis were notably higher among patients with Vitamin B12 deficiency, underscoring the clinical relevance of monitoring and managing Vitamin B12 levels in this population^{11,14}.

Table 1: Percent distribution of patients according to gender (N=200)

Gender	Numbers	Percent (%)	Mean \pm SD
Male	98	49	57.3 \pm 28.67
Female	102	51	55.14 \pm 14.91

Table 2: Percent distribution of patients according to age groups (N=200)

Age group (years)	Numbers	Percent (%)	Mean \pm SD
18	1	0.5	3 \pm 0
19-30	9	4.5	27.77 \pm 1.78
31-46	42	21	39.35 \pm 4.27
47-62	66	33	53.96 \pm 4.87
>62	82	41	75.27 \pm 28.58

The study included 200 diabetes patients on metformin therapy at B&C Medical College Teaching Hospital and Research Center over a six-month period. The gender distribution was nearly equal, with 49% males and 51% females

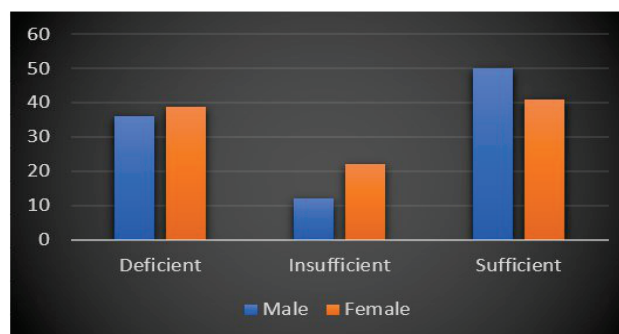


Figure 1: Distribution of Vitamin B 12 levels in diabetic patients according to gender (N=200)

The distribution of Vitamin B12 was similar across genders, with 36 males and 39 females being deficient. Additional, 12 males and 22 females had insufficient levels, while 50 males and 41 females had sufficient levels

Table 3: Distribution of patients according to Vitamin B12 levels (N=200).

Vitamin B12 levels	Numbers	Percent (%)	Mean \pm SD
Sufficient	91	45.5	58.88 \pm 25.49
Deficient	75	37.5	56.3 \pm 14.62
Insufficient	34	17	52.88 \pm 17.53

The Vitamin B12 deficiency rate of 37.5%, coupled with 17% of patients having insufficient levels, indicates that more than half of the diabetic patients on metformin are at risk of deficiency or insufficiency. Table 3 provides a detailed distribution of Vitamin B12 levels among 200 diabetes patients undergoing metformin therapy. The overall findings reveal that 37.5% of patients were classified as deficient (serum levels <200 pg/mL), while 17% were insufficient (200-300 pg/mL), and 45.5% had sufficient levels (>300 pg/mL).

Table 4: Distribution of Vitamin B12 levels in patients according to age groups (N=200)

Age Groups (Years)	Sufficient	Deficient	Insufficient
18	0	0	1
19-30	3	3	3
31-46	22	14	6
47-62	28	26	10
>62	38	32	14

When analyzed by gender, 36 males and 39 females fell into the deficient category, with a notable number of females also showing insufficiency. Age group analysis indicated that the highest deficiency rates were found in patients over 62 years, highlighting a concerning trend among older demographics. Conversely, younger patients (those aged 18 and 19-30 years) exhibited lower deficiency rates (table-4). These results underscore the critical need for regular monitoring of Vitamin B12 levels, especially for patients on long-term metformin therapy, to prevent deficiencies that can significantly impact health outcomes.

DISCUSSION

This study's findings revealed a significant occurrence of Vitamin B12 deficiency among diabetic patients receiving metformin treatment at B&C Medical College Teaching Hospital and Research Center. The nearly equal gender distribution with slightly higher female representation (51%) and the concentration of patients in the older age groups (47-62 years and >62 years) provided a comprehensive demographic overview of the study population.

The Vitamin B12 deficiency rate of 37.5%, coupled with 17% of patients having insufficient levels, indicates that more than half of the diabetic patients on metformin are at risk of deficiency or insufficiency²². This is consistent with prior research findings that have suggested metformin to interfere with Vitamin B12 absorption, particularly with prolonged use⁵.

Gender-specific analysis revealed comparable rates of deficiency between males and females, suggesting that gender does not significantly influence the risk of Vitamin B12 deficiency in this population. Nevertheless, the higher mean levels observed in males (57.3 pg/mL) compared to females (55.14 pg/mL) could point to slight physiological differences that require further studies to elaborate the observation.

Age-wise, the study indicated well documented trend showing that the tendency of Vitamin B12 deficiency rises with the age. The highest prevalence of defi-

ciency in the >62 years group (26 out of 66 patients) and the 47-62 year group (32 out of 82 patients) underscored the need for targeted screening and intervention strategies for older patients. The lower deficiency rates in younger age groups highlighted a potential age-related decline in Vitamin B12 levels, possibly exacerbated by prolonged metformin therapy. The exact mechanisms underlying metformin-induced vitamin B12 deficiency are still not fully understood, However, the mechanisms are thought to cause vitamin B12 deficiency mainly through altered vitamin B12 absorption from ileum and metabolism²³. The link between prolonged metformin therapy and decreased Vitamin B12 levels reinforces the importance of regular monitoring for patients on long-term metformin therapy^{4,9,11}. The findings of other studies had shown a higher prevalence of hematologic and neuropsychiatric manifestations among Vitamin B12 deficient patients, further emphasize the clinical implications of these deficiencies^{5,13,14}. Regular screening for Vitamin B12 levels should be integrated into the management plan for diabetic patients on metformin, especially for those with prolonged use and older age⁸.

CONCLUSION

The study underscores a significant prevalence of Vitamin B12 deficiency in diabetic patients using metformin. Older age and longer duration of metformin use being significant risk factors. Given the serious health implications of serum vitamin B12 deficiency, routine monitoring of serum vitamin B12 levels can be integrated into the clinical management of diabetes patients on metformin therapy. Early diagnosis and appropriate supplementation of vitamin B12 can help alleviate potential hematologic and neuropsychiatric complications, improving patient outcome and quality of life.

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Conflict of Interest : None

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