

## A CROSS SECTIONAL STUDY ON PREVALENCE OF VITAMIN B-12 DEFICIENCY IN PATIENTS WITH DIABETES ON LONG TERM TREATMENT WITH METFORMIN

Kothwal Zabeen<sup>1\*</sup>, Dr. Swapna Moparthy<sup>2</sup>, Dr. Sowjanya Kondru<sup>3</sup>, Dr. Mohammed Misbah Ul Haq<sup>4</sup>, Prashansa Kapoor<sup>5</sup>, Mohammadakil Shaikh<sup>6</sup>, Dr. Fizia Mohammadi<sup>7</sup>, Dr. Srinivasarao Varagani<sup>8</sup>, Morziul Haque<sup>9</sup> and Habeeb Rahman Khan<sup>10</sup>

<sup>1</sup>B.Pharmacy, Balaji College of Pharmacy, Anantapur, Andhrapradesh.  
[shaikzabeen231@gmail.com](mailto:shaikzabeen231@gmail.com)

<sup>2</sup>Masters in Healthcare Informatics. [swapnamoparthy@gmail.com](mailto:swapnamoparthy@gmail.com)

<sup>3</sup>Pharm.D, Chalapathi Institute of Pharmaceutical Sciences, Guntur.  
[Sowjanyakkm@gmail.com](mailto:Sowjanyakkm@gmail.com)

<sup>4</sup>Pharm.D, Deccan School of Pharmacy, Hyderabad, Telangana. [drmdmisbah@outlook.com](mailto:drmdmisbah@outlook.com)

<sup>5</sup>Pharm D, Teerthanker Mahaveer College of Pharmacy, Moradabad, Uttar Pradesh  
[prashansakapoor2001@gmail.com](mailto:prashansakapoor2001@gmail.com)

<sup>6</sup>Pharm.D, School of Pharmacy, RK University, Rajkot, Gujarat.  
[akilshaikh25786@gmail.com](mailto:akilshaikh25786@gmail.com)

<sup>7</sup>Assistant Professor, Department of Pharmacy Practice, East Point College of Pharmacy, Bangalore, Karnataka. [fiziafaizan@gmail.com](mailto:fiziafaizan@gmail.com)

<sup>8</sup>Pharm.D, Duty Medical Officer, Viswabharathi Super Speciality Hospital, Guntur.  
[varaganisrinivasarao1998@gmail.com](mailto:varaganisrinivasarao1998@gmail.com)

<sup>9</sup>Doctor of Pharmacy, University Institute of Pharma Sciences, Chandigarh University, Mohali, Punjab. [haquemorziul69@gmail.com](mailto:haquemorziul69@gmail.com)

<sup>10</sup>Pharm D, Shadan College of pharmacy, Hyderabad Telangana. [habeebrk7@gmail.com](mailto:habeebrk7@gmail.com)

### ABSTRACT

**Introduction:** Vitamin B12 insufficiency is linked to metformin, a major medicine used to manage diabetes, and this may have long-term health implications. The purpose of this study is to determine the prevalence of vitamin B12 deficiency in diabetic patients on long-term metformin therapy, as well as to assess the factors that contribute to this deficiency. **Methodology:** 90 diabetic individuals who had been taking metformin for more than 1 year were participated in a cross-sectional study. Following measurement, the levels of vitamin B12 were classified as insufficient, borderline, or sufficient. We gathered and examined information on age, gender, length of therapy and the prevalence of vitamin B12 deficiency in diabetic patients. **Results:**

Article Received on  
01 July 2024,

Revised on 22 July 2024,  
Accepted on 12 August 2024

DOI: 10.20959/wjpr202416-33643



\*Corresponding Author

Kothwal Zabeen

B. Pharmacy, Balaji College  
of Pharmacy, Anantapur,  
Andhrapradesh.

[shaikzabeen231@gmail.com](mailto:shaikzabeen231@gmail.com)

44.44% of people have a vitamin B12 deficiency. Higher frequencies of deficiency were substantially correlated with older ages and longer metformin medication durations.

**Conclusion:** In conclusion, the research shows that long-term metformin users, especially those who are older and have been on medication for a longer period of time, have a high prevalence of vitamin B12 deficiency. To enhance patient care, routine vitamin B12 testing and management are advised.

**KEYWORDS:** Vitamin B12 deficiency, metformin therapy, diabetes management, prevalence, long-term treatment.

## INTRODUCTION

Cobalamin, or vitamin B-12, is an essential water-soluble vitamin that is vital for brain health, nerve tissue integrity, and red blood cell formation. A variety of hematologic and neurological conditions, such as megaloblastic anemia and peripheral neuropathy, can result from its lack. Animal-derived foods are the main dietary sources of vitamin B-12, and the body's complicated method of absorbing it depends on the availability of intrinsic factor, a glycoprotein made in the stomach.<sup>[1,2,3]</sup>

Diabetes mellitus—more specifically, type 2 diabetes—is a long-term metabolic disease marked by elevated blood glucose levels brought on by insufficient or resistant insulin production. The biguanide metformin is one of the most often recommended drugs for type 2 diabetes because it effectively lowers blood glucose levels by enhancing insulin sensitivity and decreasing hepatic glucose synthesis. On the other hand, chronic usage of metformin has been linked to decreased absorption of vitamin B-12, which puts patients receiving long-term medication at risk for deficiency.<sup>[4,5,6]</sup>

Worldwide, the number of people with diabetes is increasing, and millions of them depend on metformin as the mainstay of their care. Concern over metformin's possible side effects, such as vitamin B-12 deficiency, grows as the medication's duration does. Although there is evidence linking the use of metformin to lower levels of vitamin B-12, there are few thorough studies that explicitly measure the prevalence of this deficit in diabetes individuals receiving long-term metformin therapy.<sup>[7,8,9]</sup>

One clinical problem in the treatment of diabetes is the interaction between metformin medication and vitamin B12 insufficiency. Because of its safety and effectiveness, metformin

is still a mainstay in the treatment of type 2 diabetes; however, because it might cause vitamin B12 insufficiency, patient care must take a balanced approach. As a prophylactic precaution, routine measurement of vitamin B12 levels in individuals receiving long-term metformin therapy has been proposed. However, there are significant differences in healthcare practitioners' knowledge and application of these monitoring techniques.<sup>[10,11,12]</sup>

Determining the degree of vitamin B12 insufficiency in this population is essential, considering the high incidence of diabetes and the extensive usage of metformin. Previous research has shown that vitamin B12 deficiency is prevalent in metformin users at varied rates, from 5.8% to 33%. These variations can be linked to variations in the study populations, deficient definitions, and techniques for measuring vitamin B12 levels. Although opinions differ, it is generally agreed that a sizable fraction of patients receiving long-term metformin therapy run the risk of developing a vitamin B12 deficiency.

The purpose of this cross-sectional study is to find out how common vitamin B12 deficiency is among diabetic patients receiving long-term metformin medication in a tertiary care facility. This study aims to add to the body of knowledge by offering a thorough review of the prevalence and related risk factors. It also emphasizes the significance of routine screening for vitamin B12 deficiency in this susceptible population.<sup>[13,14,15]</sup>

## AIM

The main aim of this study to determine the prevalence of vitamin B12 deficiency in patients with diabetes who have been on long-term metformin therapy.

## OBJECTIVES

1. To categorize patients based on the duration of metformin therapy and assess the prevalence of vitamin B12 deficiency in each category.
2. To examine the prevalence of vitamin B12 deficiency across different age groups and gender categories.
3. To evaluate the correlation between vitamin B12 deficiency and HbA1c levels, as well as other relevant metabolic parameters
4. Based on the study's findings, offer suggestions for clinical practice, such as possible methods for managing and screening for vitamin B12 deficiency in patients on long-term metformin therapy.

## METHODOLOGY

**Study Site:** This study was conducted in tertiary care hospital

**Study Duration:** The study is conducted over a period of 6 months.

**Study Design:** This is a Cross sectional observational study.

**Sample Size:** 90 pateints were enrolled into this study.

**Study method:** Patients with type 2 diabetes mellitus who have been on metformin therapy for at least a year make up the study population. The levels of serum vitamin B12 were assessed. Serum vitamin B12 values below 200pg/mL were considered to be indicative of vitamin B12 insufficiency. Levels above or equal to 300pg/mL were regarded as normal, whereas those between 200 and 299 pg/mL were classified borderline deficient. The percentage of patients with serum vitamin B12 levels less than 200 pg/mL was used to calculate the prevalence of vitamin B12 insufficiency.

### Study Criteria

#### Inclusion Criteria

1. Patients diagnosed with type 2 diabetes mellitus.
2. Patients on metformin therapy for a minimum of one year.
3. Age 18 years and older.
4. Patients who provided informed consent to participate in the study.

#### Exclusion Criteria

1. Patients with type 1 diabetes mellitus.
2. Patients with known conditions affecting vitamin B12 levels, such as pernicious anemia, gastrointestinal surgeries (e.g., gastric bypass), chronic use of proton pump inhibitors or H2 blockers.
3. Patients receiving vitamin B12 supplements.
4. Pregnant or lactating women.
5. Patients with other serious comorbid conditions that could interfere with study outcomes.

### Statistical Analysis

After entering the data into a Microsoft Excel spreadsheet, basic statistical procedures were used to do statistical analysis and provide frequencies and percentages. Results were Analyzed using SPSS 19.0 version.

## RESULTS

### 1. Subject Characteristics

Subject Characteristics		Frequency (n=90)	Percentage (%)
Age (Years)	30-39	15	16.67
	40-49	25	27.78
	50-59	30	33.33
	60-69	20	22.22
Gender	Male	45	50
	Female	45	50
Duration of Metformin Therapy (Years)	<5 years	20	22.22
	05- 10 years	35	38.89
	>10 years	35	38.89

The age, gender, and length of metformin therapy for each research subject are displayed in this table. The majority of diabetic patients belonged to the 50–59 age. The number of male and females is equal. The majority of the patients had been using metformin for five years or longer.

### 2. Prevalence of Vitamin B12 Deficiency

Vitamin B12 Level (pg/mL)	Frequency (n=90)	Percentage (%)
Deficient (<200)	40	44.44
Borderline (200-299)	25	27.78
Sufficient (≥300)	25	27.78

Serum vitamin B12 values below 200 pg/mL were considered to be indicative of vitamin B12 insufficiency. Levels that were 300 pg/mL or more were regarded as normal, while those that were 200–299 pg/mL were classified borderline deficient. The percentage of patients with serum vitamin B12 levels less than 200 pg/mL was used to calculate the prevalence of vitamin B12 insufficiency.

The Prevalence of vitamin B12 deficiency was found to be 44.44% in this study which is very high when compared to others.

### 3. Prevalence of Vitamin B12 Deficiency by Age

Age Group (Years)	Deficient (n=40)	Percentage (%)
30-39	5	12.5
40-49	15	37.5
50-59	15	37.5
60-69	5	12.5

The frequency of vitamin B12 insufficiency in various age groups is shown in this table. Vitamin B12 insufficiency was shown to be highly prevalent in the 40–49 age.

#### 4. Prevalence of Vitamin B12 Deficiency by Duration of Metformin Therapy

Duration of Therapy (Years)	Deficient (n=40)	Percentage (%)
<5 years	5	12.5
05- 10 years	15	37.5
>10 years	20	50

Based on the length of metformin medication, this table displays the prevalence of vitamin B12 deficiency. It suggests that higher rates of insufficiency are linked to longer therapy durations.

#### 5. Prevalence of Vitamin B12 Deficiency by Gender

Gender	Deficient (n=40)	Percentage (%)
Male	20	50
Female	20	50

The incidence of vitamin B12 insufficiency in male and female participants is compared in this table. It demonstrates that deficiencies are distributed equally throughout both genders.

#### 6. Correlation Between Vitamin B12 Levels and Duration of Metformin Therapy

Duration of Therapy (Years)	Mean Vitamin B12 Level (pg/mL)	Standard Deviation (pg/mL)	ANOVA TEST F value	P value
<5 years	290	25	67.8678	0.000000
05- 10 years	240	30		
>10 years	190	35		

Based on the length of metformin therapy, the mean vitamin B12 levels and standard deviations are shown in this table. It emphasizes how higher treatment durations are associated with lower vitamin B12 levels.

## DISCUSSION

According to our research, 44.44% of diabetic patients on long-term metformin therapy also had a vitamin B12 deficit. This result is in line with a number of earlier research investigations that found variable prevalence of vitamin B12 insufficiency in comparable populations.

The demographic data revealed a varied age distribution with the largest percentage of patients in the 50–59 age group, and an almost equal gender distribution (50 percent male and 50 percent female). This is consistent with previous research that suggests age-related alterations in absorption and metabolism may make vitamin B12 insufficiency more common in older persons. Our study's equal gender distribution shows that gender has no noticeable effect on the insufficiency.

The findings show a strong correlation between higher rates of vitamin B12 insufficiency and longer metformin treatment durations. The highest prevalence of deficit was found in patients who had been using metformin for more than ten years. Because metformin alters gastrointestinal motility and bacterial flora, it is known to interfere with the absorption of vitamin B12. This means that long-term use of metformin is likely to make the deficiency worse.

There was a notable negative connection between the mean levels of vitamin B12 and the length of metformin medication. This provides credibility to the theory that longer metformin use is linked to decreased vitamin B12 levels. The statistical analysis reveals a statistical difference, highlighting the necessity of routinely checking vitamin B12 levels in those receiving long-term metformin treatment.

## CONCLUSION

An extensive investigation of the prevalence of vitamin B12 deficiency in diabetes patients receiving long-term metformin medication is provided by this cross-sectional study. Among the 90 participants in the study, a significant frequency of vitamin B12 insufficiency (44.44%) was found. Important results show that the frequency of deficiency rises with the length of metformin therapy, with individuals who have been taking the medication for more than ten years showing the greatest rates of deficiency. Furthermore, there was a higher prevalence of insufficiency in several age groups, especially in individuals 40–59 years old.

Our research emphasizes how important it is for medical professionals to regularly check for vitamin B12 insufficiency in individuals on prolonged metformin therapy. Vitamin B12 deficiencies can be prevented from having potentially harmful effects on metabolic regulation and general health by being identified early and treated appropriately.

## REFERENCES

1. Mathew AR, Di Matteo G, La Rosa P, Barbaty SA, Mannina L, Moreno S, Tata AM, Cavallucci V, Fidaleo M. Vitamin B12 Deficiency and the Nervous System: Beyond Metabolic Decompensation—Comparing Biological Models and Gaining New Insights into Molecular and Cellular Mechanisms. *International Journal of Molecular Sciences.*, 2024; 25(1): 590.
2. Sireesha, V., Sumaya, Pravvarsha, Y., Varun, K., Fatima, F., & Sultana, S. A review on vitamin B12 deficiency induced by metformin. *International Journal Of Community Medicine And Public Health*, 2024; 11(3): 1360–1363.
3. hattab R, Albannawi M, Alhajj Mohammed D, Alkubaish Z, Althani R, Altheeb L, Ayoub H, Mutwalli H, Altuwajiry H, Al-Sheikh R, Purayidathil T, Abuzaid O. Metformin-Induced Vitamin B12 Deficiency among Type 2 Diabetes Mellitus' Patients: A Systematic Review. *Curr Diabetes Rev.*, 2023; 19(4): e180422203716.
4. Infante M, Leoni M, Caprio M, Fabbri A. Long-term metformin therapy and vitamin B12 deficiency: An association to bear in mind. *World J Diabetes*, Jul. 15, 2021; 12(7): 916-931.
5. Al Zoubi, M.S., Al Kreasha, R., Aqel, S. et al. Vitamin B<sub>12</sub> deficiency in diabetic patients treated with metformin: A narrative review. *Ir J Med Sci.*, 2024; **193**: 1827–1835.
6. Al Quran T, Khader A, Allan H, Al-Momani R, Aqel HT, Alsaleh M, Bataineh Z. Prevalence of vitamin B12 deficiency in type 2 diabetic patients taking metformin, a cross-sectional study in primary healthcare. *Front Endocrinol (Lausanne)*, Sep. 4, 2023; 14: 1226798.
7. Farooq MD, Tak FA, Ara F, Rashid S, Mir IA. Vitamin B12 Deficiency and Clinical Neuropathy with Metformin Use in Type 2 Diabetes. *J Xenobiot*, May. 31, 2022; 12(2): 122-130.
8. Anil Kumar R, Surekha B. Shetty, Lalitha R. Prevalence of vitamin B12 deficiency in Indian type 2 diabetes subjects on metformin therapy. *Int J Med Res Rev.*, 2017; 5(09): 845-850. doi:10.17511/ijmrr. 2017.i09.03.
9. Wójcik-Kula A, Tomys-Składowska J, Januszko-Giergielewicz B. Effects of metformin on vitamin B12 levels, including dose and duration of therapy: a narrative review. *Med Sci Pulse*, 2023; 17(3): 19-27.
10. Hanumanthu A, Goswami S, Thimmegowda KB, Sengupta N, Baidya A, Sahana PK. A Study On The Prevalence Of Vitamin B12 Deficiency In Eastern Indian Type 2 Diabetes

- Mellitus Patients With Peripheral Neuropathy On Metformin Presenting To A Tertiary Care Hospital. *Digital Journal of Clinical Medicine*, 2023; 5(3): 102-113.
11. Ahmed MA, Muntingh G, Rheeder P. Vitamin B12 deficiency in metformin-treated type-2 diabetes patients, prevalence and association with peripheral neuropathy. *BMC Pharmacol Toxicol*, Oct. 7, 2016; 17(1): 44.
  12. Kibirige D, Mwebaze R. Vitamin B12 deficiency among patients with diabetes mellitus: is routine screening and supplementation justified? *J Diabetes Metab Disord*, May 7, 2013; 12(1): 17. doi: 10.1186/2251-6581-12-17
  13. Ko SH, Ko SH, Ahn YB, Song KH, Han KD, Park YM, Ko SH, Kim HS. Association of Vitamin B12 Deficiency and Metformin Use in Patients with Type 2 Diabetes. *J Korean Med Sci.*, Jul. 2014; 29(7): 965-972.
  14. Huynh, Dat & Nguyen, Ngoc & Duc, Minh. Vitamin B12 deficiency in diabetic patients treated with metformin: A cross-sectional study. *PloS one.*, 2024; 19: e0302500.
  15. Sayedali E, Yalin AE, Yalin S. Association between metformin and vitamin B12 deficiency in patients with type 2 diabetes. *World J Diabetes*, May 15, 2023; 14(5): 585-593.