JPSIM Journal of Pakistan Society of Internal Medicine

Original Article

Frequency of Vitamin B12 Deficiency in Type 2 Diabetics Treated With Metformin

Bushra Faiz,[1] Imran Taqi,[1] Javeid Iqbal,[1] Muhammad Asim Rana,[2] Kifayat Ullah Malik,[1] Muhammad Fawad Ali[1]

Services Hospital Lahore, Bahria International Hospital Lahore

Abstract

Objective: To determine the frequency of vitamin B12 deficiency in patients of type 2 diabetes Mellitus on metformin treatment.

Methodology: This Descriptive Cross sectional study was conducted over six months. A total of 225 cases from the Department of Medicine, Bahria International Hospital Lahore and Services Hospital Lahore who fulfilled inclusion criteria & exclusion criteria were registered. Cobas e411 analyzer was used to determine serum vitamin B12 levels and DXC600 analyzer was used to measure Glycosylated hemoglobin (HbA1c) level.

Results: Out of 225 patients, 56.0 %(n=126) enlisted in group of 30-50 years age and 44.0 %(n=99) enlisted in group of 51-70 years age and mean age was calculated as 49.01±7.45 year. There were 60.0 %(n=135) male whereas 40.0 %(n=90) were females. Frequency of 12.4% was noted as cobalamin deficiency in patients of type 2 diabetes mellitus taking metformin treatment.

Conclusion: This study elaborated that a significant frequency of patients with diabetes mellitus on metformin treatment have decreased vitamin B12 levels. Diabetic patients with neuropathic symptoms should be evaluated for vitamin B12 deficiency.

Keywords: Metformin, Vitamin B12 deficiency, Type 2 diabetes

How to cite this:

Faiz B, Taqi I, Iqbal J, Rana MA, Malik KU, Ali MF. Frequency of Vitamin B12 Deficiency in Type 2 Diabetics Treated With Metformin. J Pak Soc Intern Med. 2026;7(4): 345-348

Corresponding Author: Dr. Imran Taqi **Email:** drimrantaqi@gmail.com

Received: 13-03-2026 **Revised:** 06-09-2026 **Accepted:** 04-11-2026 **DOI:** https://doi.org/10.70302/jpsim.v7i4.2668

2709-8729/© 2026 The Author(s). Published by JPSIM on behalf of Pakistan Society of Internal Medicine, Lahore, Pakistan. This is an open access article under the CC BY 4.0 license https://creativecommons.org/licenses/by/4.0/

Introduction

Diabetes mellitus is a disorder due to dysregulated blood glucose metabolism leading to high blood sugar levels. In western countries it is very common and affects 5-10% of adults.[1] In Pakistani population type 2 diabetes Mellitus is prevalent currently about 11.77%.[2]

Main contributing factors leading to increased prevalence of type 2 diabetes Mellitus are decreased physical activity, obesity & more use of carbohydrate rich diet.[3] Metformin is mostly prescribed antidiabetic drug used often as initial medicine for type 2 diabetics. It is recommended by EASD and ADA guidelines as first line treatment.[4] However, many published medical evidences and articles suggest correlation between extended duration use of metformin and cobalamin deficiency.[5]

A previous article signified the decreased vitamin B12 levels in diabetic patients on metformin treatment to a frequency of 17.4%.[6] in another study it was 28.1%.[7] In Pakistan Raheel Iftikhar and others documented vitamin B12 deficiency in 31% of cases.[8] Whereas in another study it was 13.9%.[9]

The rationale of this study is that there is significant variation of frequency of vitamin B12 deficiency in national and international studies so a local study should be done. Our study will help to formulate guidelines related to vitamin B12 testing and treatment in diabetic patients.

Methodology

This Descriptive Cross sectional study was performed over a period of six months in Department of Medicine, Bahria International Hospital Lahore and Services Hospital Lahore. A total of 225 cases were calculated by taking 95% as level of confidence and 5% as margin in error and entering expected percentage of vitamin B12 deficiency as 13.9%[9] in

diabetic cases taking metformin sample technique done was non-probability and Consecutive method of Sampling.

Patients who met the inclusion & exclusion criteria were registered.

Inclusion & Exclusion criteria: All diagnosed cases of diabetics taking metformin >=1gram/day , Aged 30-70 years of either gender were included while all diagnosed cases of vitaminB12 deficiency and taking its management (on history and medical record), Crohn's disease, ulcerative colitis or disease affecting terminal ileum, gastrectomy, proton pump inhibitors, H2-receptor antagonists or vitamin B12 use in past 4 weeks were excluded.

After approval from hospital ethics committee, study was initiated. Informed consent was obtained. Patients biodata like Age, gender, weight, height, BMI of patients, dose and duration of metformin use were registered on a proforma. Blood samples were drawn and Cobas e411 analyzer by electro chemiluminescence immunoassay was used to measure Vitamin B12 levels. DXC600 analyzer was used to determine Glycosylated hemoglobin (HbA1c). The Tests were done by a pathologist in hospital laboratory. The data was analyzed in SPSS version for 22.0. Mean and standard deviation was analyzed for age, weight height and BMI of the patients. Frequencies and percentages were calculated for qualitative variables like gender and vitamin B12 deficiency (as per operational definition). Data was Stratified for age, gender, BMI and duration of treatment of diabetes with metformin. After data stratification chi-square testing was done to see the significance. P value less than or equal to 0.05 was regarded as statistically important.

Results

Total of 225 patients fulfilling inclusion & exclusion criteria were to establish the percentage of patients of cobalamin deficiency (vitamin B12) in patients of type 2 diabetes mellitus on metformin treatment. Age distribution of the patients was done, it showed that out of 225 patients, 56.0 %(n=126) enlisted in group of 30-50 years age and 44.0 %(n=99) enlisted in group of 51-70 years age and mean age was calculated as 49.01±7.45 year.

Gender distribution of the patients was done; it showed that 60.0 %(n=135) were male whereas 40.0 %(n=90) were females.

Frequency of Cobalamin deficiency in patients of type 2 diabetes mellitus taking metformin treatment was 12.4%

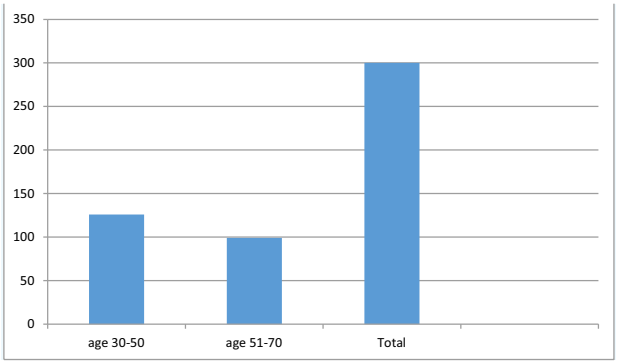


Figure 1: *Age Distribution.*

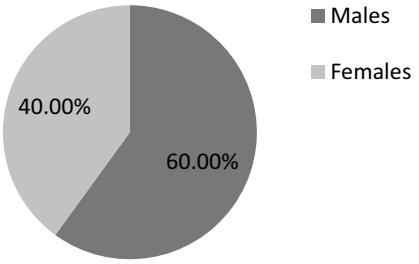


Figure 2: *Gender Distribution.*

Table 1: *Distribution of Vitamin B12 deficiency N=225*

Vitamin B12 Deficiency	n	%
Yes	28	12.4
No	197	87.6
Total	225	100

Stratification for percentage of cobalamin deficiency in patients of type 2 diabetes mellitus taking metformin with respect to age was done using chi-square test showed that in age group 30-50 years 7.1%(n-16) and in 51-70 years 5.3%(n-28) had vitamin B12 deficiency**.** Stratification for percentage of cobalamin deficiency in patients of type 2 diabetes mellitus on metformin with respect to duration of metformin use was done using chi- square test showed that 12 cases in metformin use duration 1 year and 16 cases in > 1 year metformin use had vitamin B12 deficiency.

Discussion

Metformin has been recommended as the first choice for treatment for type 2 diabetic patients and endorsed by The American Diabetes Association, international diabetic federation and the European Association for the Study of Diabetes. Published articles from many national studies and interventional studies have depicted that cobalamin deficiency can be related to metformin. It has been noted that Cobalamin deficiency is present in 9% to 52% of people with

T2DM and has been associated to metformin use for a longer duration.[12] In this study, out of 225 patients, 56.0 %(n=126) enlisted in group of 30-50 years age and 44.0 %(n=99) enlisted in group of 51-70 years age and mean age was calculated as 49.01±7.45 year. Males were 60.0 %(n=135) whereas females were 40.0 %(n=90). Frequency of Cobalamin deficiency in type 2 diabetics on metformin therapy was 12.4%.

Table 2: *Stratification of Cobalamin Deficiency among Patients for age and duration of Metformin use. (n= 225)*

Variable			Cobalamin deficiency		Total	p-value
			Yes	No		
Age group (Years)	30-50	n	16	110	126	0.89
		%	7.1	48.9	56	
	51-70	n	12	87	99	
		%	5.3	38.7	44	
Duration of Metformin Use (Years)	<1	n	12	86	98	0.94
		%	5.3	38.2	43.6	
	≥1	n	16	111	127	
		%	7.1	49.3	56.4	
Total		n	28	197	225	-
		%	12.4	87.6	100	

De Jager et.al in a study published that the negative effect of metformin treatment on cobalamin level becomes prominent with extended duration of metformin therapy. This has been attributed to alteration in small intestinal motility (which leads to overgrowth of bacteria resulting in cobalamin deficiency), decrease in intrinsic factor values, modification in cubulin endocytic receptor and blockage of the calcium dependent cobalamin-intrinsic factor complex at the site of terminal small intestine.10 It has been narrated that 1000mg daily dose of metformin results in a ratio of 2.88 increased chance of cobalamin deficiency.[11]

Osifo et al. conducted a study8 on serum cobalamin levels in 240 Nigerians showed a mean vitamin B12 value in males of 554 pmol/L versus 615 pmol/Lin females. But, no value as cut-off for vitamin B12 deficiency was described. The mean total serum cobalamin level of 210.22 pg/mL and 273.57 pg/mL for on metformin treatment group and metformin-naïve groups, respectively,

(p = 0.0001) was narrated in this study, with vitamin B12 deficiency considered as values under 200 pg/mL.[10]

In a study done by Miyan et.al. Demonstrated low hemoglobin levels in patients on metformin treatment as analyzed with patients not on metformin. In prior studies, the significant correlation between B12deficiency and decreased Hemoglobin level was also noted.

A research article from Qatar, however, claimed no association between metformin treatment and cobalamin deficiency or diabetic neuropathy. De Groot-Kamphuis et al also narrated a lower frequency of neuropathy in diabetic patients on metformin as matched with patients on no metformin therapy.[12] Recently American diabetic association recommends screening of serum cobalamin levels in diabetic patients with neuropathy but previously no such guidelines were there to highlight this problem.[13]

Conclusion

This study Elaborated that a significant percentage of type 2 diabetes mellitus patients taking metformin therapy have decreased serum cobalamin levels. So, Doctors must be aware of this correlation of metformin with cobalamin deficiency. Patients with diabetic neuropathy should be investigated for low cobalamin levels.

Ethical Approval: The IRB/EC approved this study via letter no. IRBEC//BIH/076-2024 dated February 04, 2026.

Conflict of Interest: None

Funding Source: None

Authors' Contribution

IT: Conception.

BF, MFA: Design of the work.

JI, MAR, KUM: Data acquisition, analysis, or interpretation.

BF, JI, MAR, KUM: Draft the work.

IT, MFA: Review critically for important intellectual content.

All authors approve the version to be published.

All authors agree to be accountable for all aspects of the work.

References

1. Raffel LJ, Goodarzi MO. Diabetes Mellitus. Reference Module in Biomedical Research 2014; available at: h http://dx.doi.org/10.1016/B978-0-12-801238-3.05558-6

2. Meo SA, Zia I, Bukhari IA, Arain SA. Type 2 diabetes mellitus in Pakistan: Current prevalence and future forecast. J Pak Med Assoc. 2016; 66(12):1637-42.
3. Rehman K, Akash MS. Mechanisms of inflammatory responses and development of insulin resistance: How are they interlinked? J Biomed Sci 2016; 23(1):87.
4. Sanchez-Rangel E, Inzucchi SE. Metformin: clinical use in type 2 diabetes. Diabetologia 2017; 60(4):1586-93.
5. 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 2016;17(1):44.
6. Kang D, Yun JS, Ko SH, et al. Higher prevalence of metformin-induced vitamin B12 deficiency in sulfonylurea combination compared with insulin combination in patients with type 2 diabetes: a cross-sectional study. PLoS One 2014;9(10): e109878.
7. 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 2016;17(1):44.
8. Iftikhar R, Kamran SM, Qadir A, Iqbal Z, bin Usman H. Prevalence of Vitamin B12 deficiency in patients of type 2 diabetes mellitus on metformin: a case control study from Pakistan. Pan Afr Med J. 2013; 16(10):67
9. Rauf A, Khan M, Arshad A. Frequency of Vitamin B12 Deficiency in patients with Type 2 Diabetes Mellitus Taking Metformin. Pak J Med Health Sci. 2015; 9(1):1316-8.
10. Owhin SO, Adaja TM, Fasipe OJ, Akhideno PE, Kalejaiye OO, Kehinde MO. Prevalence of vitamin B12 deficiency among metformin-treated type 2 diabetic patients in a tertiary institution, South-South Nigeria. SAGE open Med. 2019; 7:2050-31211-9853433.
11. Miyan Z, Waris N. Association of vitamin B12 deficiency in people with type 2 diabetes on metformin and without metformin: a multicenter study, Karachi, Pakistan. BMJ Open Diab Res Care. 2020;8(1): e001151.
12. De-Jager J, Kooy A, Lehert P. Long term treatment with metformin in patients with type 2 diabetes and risk of vitamin B-12 deficiency: randomized placebo-controlled trial. BMJ. 2010;340:c2181.
13. Osifo BO, Lukanmbi FA, Bolodeoku JU. Reference values for serum folate, erythrocyte folate and serum cobalamin in Nigerian adolescents. Trop Geogr Med. 1986; 38(3): 259–64.