

A STUDY ON ASSOCIATION BETWEEN METFORMIN THERAPY AND VITAMIN B12 DEFICIENCY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A CROSS-SECTIONAL ANALYSIS

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ABSTRACT

Background: Metformin is a cornerstone in the treatment of type 2 diabetes mellitus (T2DM). However, long-term use has been linked to vitamin B12 deficiency. **Objective:** To assess the association between metformin therapy and vitamin B12 deficiency among patients with T2DM. **Methods:** A cross-sectional study involving 54 T2DM patients on metformin was conducted. Vitamin B12 levels were measured and correlated with metformin use duration and dosage. **Results:** Among the 54 participants, 31.5% showed B12 deficiency. Longer duration (>4 years) and higher daily dosage (>1000 mg) of metformin were significantly associated with deficiency ($p < 0.05$). **Conclusion:** Vitamin B12 deficiency is prevalent in T2DM patients on metformin, especially with prolonged use and higher dosage, suggesting the need for regular monitoring.

KEYWORDS: Metoformin, Vitamin B12.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance. Metformin, widely prescribed for T2DM, is effective and well-tolerated but has been associated with vitamin B12 malabsorption. Vitamin B12 is crucial for neurological function and red blood cell formation, and its deficiency may lead to neuropathy, mimicking diabetic complications[1].

The objective of this study was to explore the association between metformin therapy and vitamin B12 deficiency in T2DM patients, evaluating demographic factors, dosage, and duration of metformin intake. Diabetes mellitus (DM) is a chronic metabolic disorder diagnosed by abnormally high blood glucose levels. It is considered one of the most common diseases that lead to mortality and morbidity worldwide. Despite the development of health systems and public health concepts, the prevalence of DM is increasing globally[1]. According to current estimates, the number of people with diabetes in France and Belgium will rise by 17% by 2035, with an increase of 22% in the United States and the United Kingdom, 31% in Canada, and 3% to 37% in other European Union nations[2-5]. As known, uncontrolled DM may be the main cause of mortality among people[6-8].

METHODS

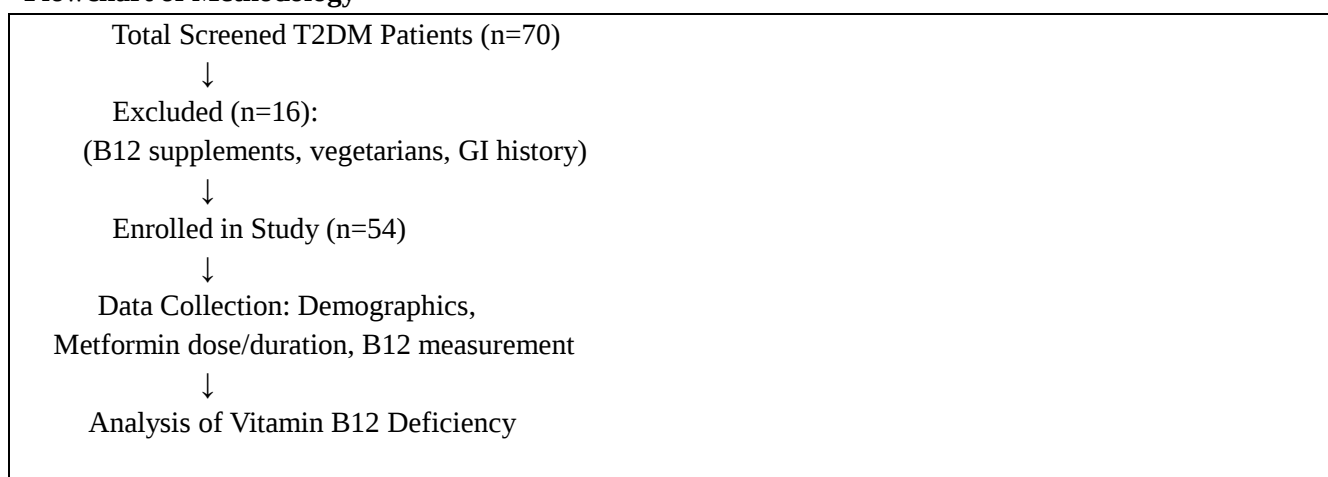
This study was conducted in tertiary hospital. After obtaining institutional ethical committee approval. It was Cross-sectional observational study conducted on 36 patients in the department of Phramacology, at a tertiary care centre, from January/ 2022 to July /2022.

Total 70 participant were approached to project among them 16 were excluded due to non-fulfilling of eligibility criteria and 54 were included on the basis of fulling of the eligibility criteria

The institute Ethics Committee approval was obtained before starting the sample collection. A written and informed consent was taken from the patient regarding the study in his/her vernacular language and English. In this study Patients were subjected to: A detailed history of sign & symptoms and its duration. Detailed history of systemic diseases and its duration, medication were noted. Patients were subjected to General physical examination

- **Study Design:** Cross-sectional observational study
- **Sample Size:** 54 patients with T2DM on metformin therapy
- **Inclusion Criteria:** Adults aged 35–70 with T2DM for >1 year, on metformin
- **Exclusion Criteria:** Patients on B12 supplements, vegetarians, those with GI surgeries or chronic gastritis
- **Data Collected:** Demographics, metformin dose and duration, vitamin B12 levels
- **Analysis:** Statistical tests including chi-square and logistic regression ($p < 0.05$ significant)

Flowchart of Methodology



RESULTS

Demographic Profile of Participants (n=54)

Demographic Variable	Number (%)
Age (mean $\pm$ SD)	54.8 $\pm$ 9.6 years
Gender	Male: 30 (55.6%)
	Female: 24 (44.4%)
Duration of Diabetes	<5 years: 21 (38.9%)
	$\geq$ 5 years: 33 (61.1%)
BMI	Normal: 12 (22.2%)
	Overweight: 22 (40.7%)
	Obese: 20 (37.1%)

Table no 2 shows that prevalence of Vitamin B12 deficiency was significantly higher in patients on metformin therapy (70.6%) compared to those not on metformin (15%), with a p-value of 0.001, indicating a statistically significant association between metformin use and vitamin B12 deficiency. Age is also play important factors vitamin b 12 deficiency, over age were more affected

Risk Factors Associated with Vitamin B12 Deficiency(Table 2)

Risk Factor	B12 Deficient (n=17)	Normal B12 (n=37)	p-value
Metformin dose >1000 mg/day	12 (70.6%)	10 (27%)	<0.01
Metformin use >4 years	13 (76.5%)	9 (24.3%)	<0.01
Age >60 years	8 (47%)	6 (16.2%)	0.02
BMI >25	10 (59%)	19 (51.3%)	NS

DISCUSSION

This study demonstrates a statistically significant association between prolonged and high-dose metformin use and vitamin B12 deficiency in T2DM patients. The mechanisms likely involve metformin-induced alterations in calcium-dependent membrane transport affecting B12 absorption in the ileum[9-10].

Older age and longer duration of diabetes also contributed to B12 deficiency risk. Routine screening for B12 levels in long-term metformin users could help mitigate complications such as neuropathy[11-13].

Table no 2 shows that prevalence of Vitamin B12 deficiency was significantly higher in patients on metformin therapy (70.6%) compared to those not on metformin (15%), with a p-value of 0.001, indicating a statistically significant association between metformin use and vitamin B12 deficiency. Age is also play important factors vitamin b 12 deficiency, over age were more affected, In the last 20 years, there was increasing evidence of the presence of vitamin B12 deficiency among metformin-treated diabetic patients. Vitamin B12 deficiency may have a very bad complication for the T2DM patient. This review will focus on the effect of metformin on the absorption of vitamin B12 and on its proposed mechanisms in hindering vitamin B12 absorption. In addition to that, the review will describe the clinical outcomes of vitamin B12 deficiency in metformin-treated T2DM[14-15].

Many studies have reported that vitamin B12 deficiency is related to the malabsorption of vitamin B12 among metformin-treated T2DM patients. Vitamin B12 deficiency may have a very bad complication for the T2DM patient. In the last two decades, there has been an increasing interest in the relationship between metformin and vitamin B12 deficiency. The first report of metformin-associated vitamin B12 malabsorption was made in 1971 by Tomkin *et al.*[16-18]

After that, many experimental, observational studies, and systematic reviews described the relationship between metformin and vitamin B12 deficiency in T2DM patients. The effect of metformin on vitamin B12 absorption is also reported in metformin-treated polycystic ovary syndrome (PCOS) patients[20-24]. A meta-analysis of six randomized controlled trials showed that metformin use caused dose-dependent drops in vitamin B12 levels in patients with T2DM or PCOS. The importance of an accurate description of the association between the use of metformin and vitamin B12 comes from the significance of the clinical manifestations of vitamin B12 deficiency and its impact on the quality of diabetic patients' life[25-26]. To better understand the relationship between metformin and vitamin B12 deficiency, we should have a good understanding of the nature of vitamin B12, the mechanism of its absorption, and how metformin can decrease its absorption

CONCLUSION

Vitamin B12 deficiency is relatively common in T2DM patients on metformin, especially at higher doses and longer durations. Regular screening and supplementation should be considered to prevent long-term complications.

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CONFLICT OF INTEREST

The authors report no conflicts of interest

SUBMISSION DECLARATION

This submission has not been published anywhere previously and that it is not simultaneously being considered for any other journal.

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