



ISSN: 2395-7476

IJHS 2024; 10(2): 90-92

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Received: 10-02-2024

Accepted: 16-03-2024

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## Prevalence of vitamin B12 deficiency in type 2 diabetic patients: A review

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DOI: <https://doi.org/10.22271/23957476.2024.v10.i2b.1605>

### Abstract

Vitamin B<sub>12</sub> also named as Cobalamin, is a water-soluble vitamin. It acts fundamental role in Neurological function, Optimal Haemopoiesis and DNA Synthesis. The deficiency of Vitamin B<sub>12</sub> features as the haematological and neuro cognitive dysfunction. Diabetic patients have been demonstrated highly prevalent of Vitamin B<sub>12</sub> deficiency. The purpose of the current study to review the literature related to the prevalence of Vitamin B<sub>12</sub> deficiency in type 2 diabetic patients. The studies assess that the prevalence of Vitamin B<sub>12</sub> deficiency is ranges about 5.8 to 52% in diabetic patients. Such as the study of D. Malla *et al* reported as high as 50.95% prevalence of Vitamin B<sub>12</sub> deficiency in diabetic patients. However, the patients enrolled in the study are on metformin treatment. Several Studies reported that the deficiency of Vitamin B<sub>12</sub> may associated with the treatment of Metformin and old age population. Metformin is known as the initial hypoglycaemic drug to treat Type 2 Diabetes Mellitus. It prescribed by many health practitioners as front-line treatment for T<sub>2</sub>DM. It is used as monotherapy or combined with other drugs according to the need with some of the mild or self-limiting side effect of the drug. However, studies reported that the prevalence of vitamin B<sub>12</sub> deficiency is highly associated with dose and duration of metformin treatment in diabetic patients. Old age population may associate due to the low absorption capacity of the micronutrient in that period of lifecycle. The deficiency of vitamin B<sub>12</sub> leads to various complication related to peripheral neuropathy which diagnose as diabetic neuropathy. The literature indicates the necessity of screening status of serum Vitamin B<sub>12</sub> in patient of diabetes regularly will help to be aware.

**Keywords:** Vitamin B12, diabetes mellitus, metformin, old age, diabetic neuropathy

### Introduction

Diabetes is one of the globally known chronic disease that affects people wellbeing. It can be classified in type 1, type 2, Gestational Diabetes, and MODY. The major driver of epidemic of Diabetes are the Type 2 Diabetes Mellitus, which have 90% of all diabetic cases. Type 2 are insulin dependent Diabetes mellitus. It generally occurs due to inactive lifestyle, stress, overweight, and obesity. The prevalence of diabetes patients in 20-79 age group in India is about 74.2 million in 2021 said Mansukh Mandaviya, Union Minister of Health and Family Welfare to the Lok Sabha December 3, 2021. The uncontrolled diabetes can lead to many acute and chronic complications. Research studies indicates that the Vitamin B<sub>12</sub> deficiency is a potential comorbidity in the diabetic patients. Studies found that the prevalence of vitamin B<sub>12</sub> deficiency in diabetic patients has been higher than normal population. (A. Satyanarayana *et al*, 2011) <sup>[28]</sup>.

Vitamin B<sub>12</sub> also named as Cobalamin, is a water-soluble vitamin important for various biological functions in the eukaryotes. Vitamin B<sub>12</sub> acts as neurotrophic factor which have the fundamental role in Neurological function, Optimal Haemopoiesis, DNA Synthesis and participating to functional restorations. (Rana Ali Hamdi, 2021) <sup>[25]</sup> There are two main function of vitamin B<sub>12</sub> appears to have in eukaryotes: act as cofactor for the methyl-malonyl-CoA mutase and methionine synthase enzyme. Methyl-malonyl-CoA mutase requires Vitamin B<sub>12</sub> in a step of catabolism of ketogenic amino acid and in the odd chain fatty acids oxidation. Vitamin B<sub>12</sub> requires in the form of 5-deoxyadenosyl cobalamin for the conversion of mitochondrial enzyme Methyl-malonyl-CoA mutase in the succinyl-CoA. As methionine formation is essential for the hundred methylation process.

(Rétey, 1982) [27] Methionine synthase catalyses the conversion of homocysteine by the transfer of Methyl group from Methyl-tetrahydrofolate into Methionine with the help of vitamin B12 in the form of Methyl-cobalamin (Allen, 2012) [2]. These functions are very crucial for human health. The dietary requirement for normal human health is 2.2µg/day for an adult Male/Female (Acc. To ICMR, RDA, 2020).

Vitamin B<sub>12</sub> deficiency can lead to various complications in the body. The main features of vitamin B<sub>12</sub> deficiency are the haematological and neuro cognitive dysfunction. Vitamin B<sub>12</sub> deficiency is a major issue for diabetic patients, especially for the old age population and those on metformin treatment. The long-term duration of the treatment and the high drug dose affect the serum level of vitamin B12 in diabetic patients due to the malabsorption of the micronutrient. Ting *et al.* shown that long-term metformin treatment results in malabsorption of vitamin B12, resulting in a roughly 30% decrease in vitamin B12 levels.

The current study has the aim to review the literature related to the topic and identify the studies reported about the prevalence of Vitamin B<sub>12</sub> in Diabetic Patients.

### Prevalence of Vitamin B<sub>12</sub> Deficiency in Diabetic Patients

Vitamin B12 deficiency is a well-known health issue, it does not appear to have received the same attention as deficiencies in other micronutrients like iron, calcium or vitamin D. Vitamin B12 have many dominant roles in the different biological process in the body. It has the potential to be useful as antioxidants, act as neurotropic factor and also play an important role in the utilization of carbohydrates due to which the deficiency of the micronutrient increases the risk of hyperglycaemia. In the study of Chow *et al* reported that Vitamin B-12 is beneficial for the management of glucose because in a vitro-investigations have shown that animal's deficiency in the vitamin B<sub>12</sub> had reduced levels of glutathione and enzyme activity. (FB Chow *et al*, 1957) [9].

The study of vitamin B12 deficiency in diabetic patients has been a subject of investigation, with many studies demonstrating an association of vitamin B12 deficiency in type 2 diabetes mellitus. Several studies metabolically confirmed that the high prevalence of Vitamin B<sub>12</sub> deficiency in diabetes Mellitus. The studies assess the prevalence of Vitamin B<sub>12</sub> Deficiency to range from 5.8% to 52%. (Ahmed *et al.*, 2016) [1] Such as the study of D. Malla *et al* reported as high as 50.95% prevalence of Vitamin B12 deficiency in T2DM patients. However, the patients enrolled in the study are on metformin treatment. Furthermore, a study of Pflipsen *et al.* concluded that 22% prevalence of vitamin B12 deficiency in diabetic patients. As per the study's findings, 86.4% of patients are receiving metformin medication and the majority of responders are elders. Additionally, the study suggests that patients with the deficiencies have the medical history of long-term disease. The association of vitamin B<sub>12</sub> deficiency with diabetes is highlighted in several studies and most of the studies concluded that long term metformin treated patients are more prevalent to the micronutrient deficiency. It is beyond dispute that the primary factor linked to vitamin B12 deficiency in patients with type 2 diabetes is the use of metformin treatment. Metformin is known as the initial hypoglycaemic drug to treat Type 2 Diabetes Mellitus. It prescribed by many health practitioners as front-line treatment for T<sub>2</sub>DM. It is used as monotherapy or combined with other drugs according to the need with some of the mild or self-limiting side effect of the drug. Old age population

may associate due to the low absorption capacity of the micronutrient in that period of lifecycle.

Vitamin B12 deficiency is considered a potential comorbidity that is often ignored, putting many diabetic people at risk for developing particular conditions. (Pflipsen *et al.*, 2009) [22] Many studies have documented that Vitamin B12 deficiency highly prevalent in diabetic patients especially with neuropathy. Diabetic neuropathy refers to a range of nerve damage conditions associated with diabetes mellitus. Around 30% of diabetic individuals over forty years of age report experiencing neuropathy, a relative health problem caused by a vitamin B12 shortage that manifests as decreased sensory sensitivity in the feet. (National Diabetes Statistic Report, Aug 2017) The symptoms of diabetic neuropathy are similar to those of ataxia, paraesthesia, impaired coordination, and proprioception, which has been connected to a vitamin B12 deficit. (Lindenbaum J *et al*, 1988) [19] According to Alvarez *et al.*, the prevalence of vitamin B12 deficiency in diabetic patient with neuropathy is 17%. They discovered an inverse correlation between vitamin B12 levels and diabetic neuropathy. The study also found that the relationship between lower vitamin B12 levels and male sex characteristics and metformin dosage. (Alvarez *et al*, 2019) [4] This study found significance difference in men compared to women. However, a study concluded that the high prevalence of the micronutrient in women (Alharbi *et al*). Vitamin B12 insufficiency was not shown to differ based on gender in the majority of studies. Moreover, the reviewed literatures indicates that the Type 2 Diabetes Mellitus were significantly associated with increased risk of vitamin B12 deficiency. Thus, further information about the prevalence and correlation of vitamin B12 insufficiency risk in diabetic patients is provided by this review.

### Conclusion

Several studies have evidence that the vitamin B12 deficiency highly prevalent in diabetic patients with neuropathy and high risk of the deficiency induced by metformin therapy. Many studies also reported that old age factor related to lower the vitamin B12 level in diabetic patients. So, the regular screening of vitamin B12 in diabetic patients is necessary to monitor the micronutrient level in blood particularly with diabetic neuropathy patients and those on long duration and high dose of metformin treatment. It is recommended that healthcare professionals remain cognizant of these adverse effects at all times. Annual screening was generally recommended in most of the reviewed papers. Additionally, multivitamin empirical medication should be investigated as a means of lowering the incidence of lowering the micronutrient level.

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