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Original Research Article

# Vitamin B12 Deficiency in Type 2 Diabetic Subjects on Metformin Vs Metformin with Proton Pump Inhibitors in Tertiary Care Hospital, Mysore

**Layajeeth Shaam[1], S.S. Ramesh[2]**

[1]Postgraduate, Department of General Medicine, Mysore Medical College and Research Institute, Mysore
[2]Professor, Department of General Medicine, Mysore Medical College and Research Institute, Mysore

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**Corresponding Author: Dr. S.S. Ramesh**
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**Abstract:**

**Introduction:** Diabetes is a common co morbidity which is rising in prevalence in the modern era. Metformin is the foundation of treatment of type 2 DM. Most of the current international guidelines including American Diabetes Association state that Metformin should be the first line oral therapy prescribed. Proton Pump Inhibitors are also commonly used in patients with type 2 diabetes on Metformin, considering the gastrointestinal side effects of Metformin. This study is focusing on looking at the prevalence of VIT B12 deficiency in diabetics on Metformin VS Metformin with PPI.

**Methods:** This study was conducted on 74 diabetics on metformin and 74 diabetics on metformin with PPI meeting inclusion and exclusion criteria. Patients were subjected to VIT B12 levels estimation. The data collected are entered in excel sheet and analysed using descriptive statistics namely mean, standard deviation, percentage and depicted in the form of frequency tables, figures, and graphs.

**Results:** In the present study, the mean age in metformin group was 58.05 ± 8.70 and mean age in Metformin + PPI was 55.9 ± 7.55 years. (p=0.02) Majority of the patients belonged to the age group of 51to 60 years in the present study. Assuming the normal range of Vit B12 as 200-835 pg/mL we observed no association of administration of metformin with PPI and vitamin B12 deficiency in the present study. Based on vitamin B12 levels. Out of 47 patients having vitamin B12 <200, 23 patients (31.1%) were in Group A and 24 patients (32.4%) were in Group B. Out of 101 patient shaving vitamin B12 >200, 51 patients (68.9%) were in Group A and 50 patients (67.6%) were in Group B. The distribution of the subjects based on vitamin B12 was statistically not significant. (p=0.86)

**Conclusion:** Diabetes affects a significant number of the population, with a large number of them being on metformin, as a first line medicine unless contraindicated. A significant number of them are also on PPI in view of the gastrointestinal effect so metformin. Vitamin B12 deficiency is known to occur in patients on metformin, which was also seen in this study, but there is conflicting evidence to the role PPI in causing Vit B 12 deficiency. This study also did not find statistically significant Vit B 12 deficiency when metformin was combined with PPI. Further large scale studies are necessary in this regards.

**Keywords:** PPI Proton Pump Inhibitors, DM Diabetic Mellitus.



## Introduction

Diabetes is a common co morbidity which is rising in prevalence in the modern era.1 out of 6 people with diabetes in the world is from India. India stands 2nd place when it comes to number of diabetic persons in a country. There are estimated 101 million cases of diabetes in adult population of India.

The prevalence in urban areas ranges between 10.9% and 14.2% and prevalence in rural India was3.0-7.8%. [1] Metformin is one of the most widely used oral hypoglycemic agents. Most of the current global clinical practice recommendations, including those of the American Diabetes Association, the European Association for the Study of Diabetes, propose that metformin, if there are no contraindications, should be initiated with concurrent lifestyle modifications at initial diabetes diagnosis. [2,6]

There is general consensus that gastric acid–lowering drugs, including proton pump inhibitors (PPIs) and H2-receptor antagonists (H2RAs), and the anti-diabetes drug metformin can reduce circulating vitamin B-12 concentrations with prolonged use.[3,5,7] Although the clinical significance of vitamin B 12 deficiency related to metformin and PPI treatment is debatable, monitoring for vitamin B12 has been recommended for patients with type 2 diabetes, especially those on long-term metfor-

min and PPI treatment. Clinically, vitamin B12 deficiency could lead to altered mental status, megaloblastic anaemia, and neurological damage. Unfortunately, diabetic neuropathy symptoms can overlap with paraesthesia, impaired vibration sensation and proprioception. Therefore, peripheral neuropathy due to vitamin B 12 deficiency may be confused with diabetic peripheral neuropathy or may contribute to the aggravation of diabetic peripheral neuropathy. The progression of neurologic damage due to vitamin B12 deficiency can be stopped by early detection and treatment with cobalamin supplementation.

However, if this occurrence is misdiagnosed as diabetic neuropathy, permanent neurological damage may occur.

As metformin has been prescribed worldwide and treatment periods increase, the prevalence of metformin-induced vitamin B12 deficiency may have also significantly increased. The prevalence of Vitamin B 12 deficiency varies from 5.8% to 30% undergoing long term treatment with Metformin. Furthermore an observational study demonstrated 22% higher chance of developing Vitamin V12 deficiency with Metformin use and concomitant use of Proton Pump Inhibitors. [4]

Because of paucity of data on Indian patients with Type 2 Diabetes using Metformin and Metformin with Proton Pump Inhibitors, this study will attempt to establish causal relationship between use of Metformin and PPI with vitamin B12 deficiency.

**Objectives**

- To study the prevalence of vitamin B 12 deficiency in type 2 diabetic subjects on metformin
- To study the prevalence of vitamin B 12 deficiency in type 2 diabetic subjects on metformin with PPI.

**Methods**

- Patients visiting the OPD/ Patients admitted in department of general medicine, Krishnarajendra hospital, Mysore.
- A primary source of information technique with observational method is adopted on blood samples collected.

**Table 1: Distribution of the mean serum Vitamin B12 between the groups**

| Groups | N | Minimum | Maximum | Mean | S.D | Mean diff | p value |
|---|---|---|---|---|---|---|---|
| Group A | 74 | 92.0 | 656.0 | 309.54 | 164.51 | | |
| Group B | 74 | 97.0 | 1158.0 | 359.26 | 210.57 | -49.71 | 0.112 |

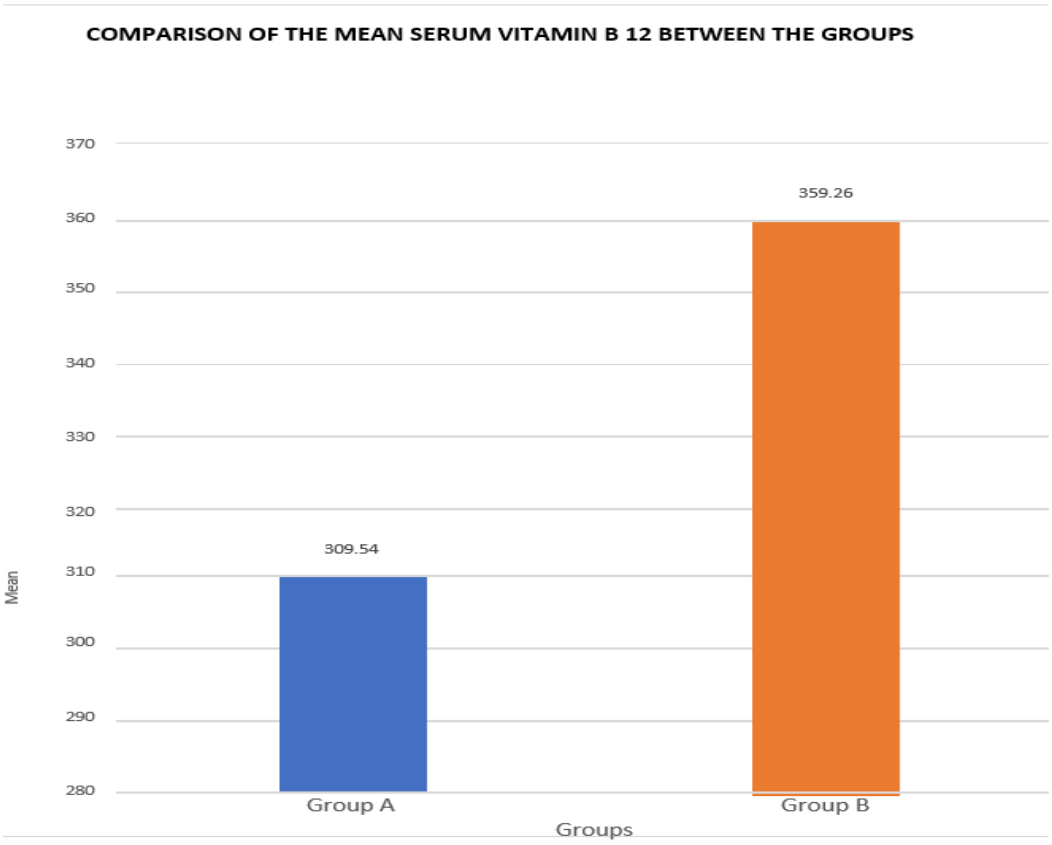


**Figure 1: Distribution of the mean serum Vitamin B12 between the groups**

**Table 1: Distribution of the Subjects Based on Vitamin B12**

| VitB12 | | Groups | | Total |
|---|---|---|---|---|
| | | Group A | Group B | |
| <200 | Count | 23 | 24 | 47 |
| | % | 31.1% | 32.4% | 31.8% |
| >200 | Count | 51 | 50 | 101 |
| | % | 68.9% | 67.6% | 68.2% |
| Total | Count | 74 | 74 | 148 |
| | % | 100.0% | 100.0% | 100.0% |
| Chi-squarevalue-0.031, P value- 0.860 | | | | |

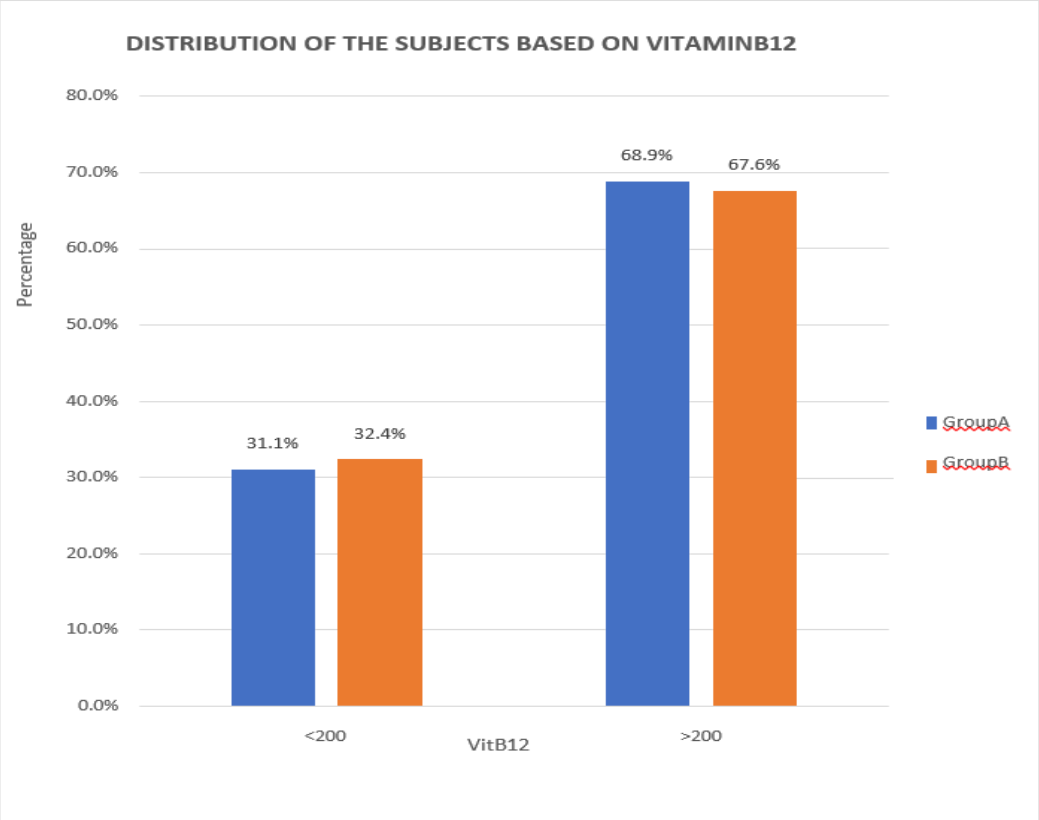


**Figure 1: Distribution of the subjects based on Vitamin B12**

## Discussion

The mean age in metformin group was 58.05 ± 8.70 and mean age in Metformin + PPI was 55.9 ± 7.55 years. (p=0.02) Majority of the patients belonged to the age group of 51 to 60 years in the present study. (p=0.10) 43 patients (29.1 %) were females, of which, 20 (27%) were in Group A and 23 (31.1%) were in Group B. 105 patients (70.9 %) were males, of which, 54 (73%) were in Group A and 51 (68.9%) were in Group B. Majority of the patients (33.8%) had a duration of DM for 1 to 3years,of which, 27% were on metformin for a period of 2 to 3years.The mean duration of DM was 7.81±5.81 and in Group B was 6.45±4.69. (p=0.11) The mean duration of metformin was 7.8±5.8 and in Group B was 6.45±4.66.(p=0.14) The mean HbA1C in Group A was 9.61±8.48 and in Group B was 9.19±0.59.(p=0.67) Out of 74 patients, the duration of PPI was 6 to 12 months in 37 patients (50%), 13 to 24 months in 25 patients (33.8%) and 25 to 48 months in12 patients (16.2%). The mean serum vitamin B12 in Group A was 309.54 ± 164.51 and in Group B was 359.26 ± 210.57. Using independent sample T test, the comparison of mean serum vitamin B12 was not statistically significant.(p=0.11)

Assuming the normal range of Vit B12 as 200-835 pg/mL we observed no association of administration of metformin with PPI and vitamin B12 deficiency in the present study. Based on vitamin B12 levels. Out of 47 patients having vitamin B12 <200, 23 patients (31.1%) were in Group A and 24 patients (32.4%) were in Group B. out of 101 patients having vitamin B12 >200, 51 patients (68.9%) were in Group A and 50 patients (67.6%) were in Group B. The distribution of the subjects based on vitamin B12 was statistically not significant. (p=0.86)

Comparison of the mean serum Vitaminb12 between the groups using independent sample T test.

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