



TO ASSESS THE LEVEL OF VITAMIN B12 IN PATIENTS WITH TYPE - II DIABETES MELLITUS ON METFORMIN

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ABSTRACT

Background: A characteristic of diabetes mellitus is usually high blood sugar levels. The absence of insulin results in an increase in blood sugar levels. Metformin is primarily used for the treatment of T2DM. Metformin by controlling blood glucose level decreases complications related to long term diabetes mellitus. Metformin blocks the absorption of Vitamin B12 from abdomen leading to its deficiency in body. The aim of this study is to assess the level of Vitamin B12 in patients with Type II diabetes mellitus treated with metformin.

Materials & Methods: This Analytical cross sectional study was conducted in the Parul Sevashram, Hospital, Vadodara. We enrolled 100 type II diabetics on metformin therapy since past 1 year and aged 35-70 years and 100 healthy patients to analyze their blood glucose and serum vitamin B12 levels.

Results: The Mean \pm S. D of RBS of group-1 was 168.24 \pm 79.44 mg/dl, group-2 was 108.77 \pm 14.81 mg/dl. The Mean \pm S.D of Vitamin B12 of group-1 was 246.36 \pm 118.50 pg/ml, group-2 was 484.72 \pm 172.96 pg/ml. we found Strong negative correlation between Plasma blood glucose and Vitamin B12 in cases, having statistical sig P value = 0.0001 and r value was - 0.607.

Conclusion: In the process of our study, we found a significant negative correlation between vitamin B12 insufficiency and using of metformin as a T2DM treatment. So, it is advisable that diabetes patients on metformin should undergo regular follow up for estimation of vitamins level to prevent further complications leading to better management.

Keywords: Type II Diabetes mellitus, Metformin, Vitamin B12 deficiency, Oral Anti-diabetic drug

INTRODUCTION:

Chronic diabetes mellitus is defined by hyperglycaemia carried on by a complete or partial absence of insulin. A characteristic of diabetes mellitus is usually high blood sugar (glucose) levels. The absence of insulin results in an increase in blood sugar levels. Overtime, this causes significant damage to the neurological system, eyes, kidneys, blood vessels, heart, and eyes [1, 2].

Blood sugar levels are out of balance, and the body either doesn't create enough insulin or resists it, which results in Type II Diabetes Mellitus [3] the most prevalent kind of diabetes is type II diabetes mellitus. Blood glucose, which is mostly obtained from the food we eat, is the main source of energy. Insulin, a hormone made in the pancreas, aids in the movement of glucose into cells for use as energy. Patients with type II diabetes tend to be older or in their middle years. People with type II diabetes who are 45 years of age or older, have a family history of the condition, are overweight, or are obese. Monitoring blood pressure, cholesterol, and blood sugar levels regularly, are all essential parts of controlling type II diabetes mellitus. In

addition to adhering to your diabetes treatment plan, you might need to take diabetic medication in the form of pills or other dosage forms [4].

Metformin blocks the absorption of vitamin B12 through a mechanism that has not been established but could be due to interference with the calcium dependent binding of the intrinsic factor vitamin B12 complex in the terminal ileum [5].

Two of the vitamin B12's crucial functions include maintaining healthy nerve cells and aiding in the creation of DNA and RNA, the body's genetic material [6].

This study's objective is to provide insight study of vitamin B12 levels in subjects with type II diabetes on metformin therapy. Therefore, early identification of a lack of vitamin B12 will cause immediate therapy for such patients in the form of B12 supplementation.

MATERIAL & METHOD:

This was an analytical cross sectional study carried out in Parul Sevashram Hospital Affiliated to Parul Institute of Medical Sciences & Research, Parul University, Vadodara from October 2022 to March

2023. Approval of institutes Scientific Review Committee Institutional Ethics Committee for Human Research (PU-IECHR) was obtained. 100 type II diabetics on metformin therapy since past 1 year and aged 35-70 years of both sexes were enrolled in this study from Medicine OPD of Parul Sevashram Hospital, Vadodara, also 100 healthy volunteers were enrolled as control group.

The inclusion criteria for cases & controls were as follows: Patients having type –II DM since past 1 year and on metformin therapy and having age between 35-70 years and for Controls: Patients relatives and our Laboratory Staff were taken as Age and Sex Matched Healthy Controls. While patients suffering from chronic kidney disease, pregnant women, & Newly Diagnosed Type-II Diabetic patients were excluded out from our study.

Informed Consent of Subjects was obtained for Participation in the Study and for blood Collection. Venous Blood Sample was collected in plain vacutainer for estimation of serum vitamin B12 and in fluoride vacutainer for estimation of plasma blood glucose. Plasma blood glucose was estimated by GOD-POD method on fully automated biochemistry analyzer, while serum vitamin B12 was estimated on CLIA based analyzer.

Statistical Analysis

The data was statistically analysed using the independent T-test to find out the significance difference between the groups. Pearson's correlation coefficient (r value) was used to find out correlation between parameters of the study group. All the data were expressed in terms of Mean \pm S.D. p value < 0.05 was considered as statistically significant All Statistical analysis was done using SPSS Statistics 26 Software.

RESULT:

In this study 200 subjects were enrolled out of which 100 patients were diagnosed with type II diabetes mellitus since past 1 years and were on metformin, having age between 35-70 years. 100 healthy controls having age between 35-70 years were also enrolled.

Based on diagnosis of diabetes mellitus subjects were divided into two groups

Group 1: cases

Group 2: controls

Table 1, shows that Mean \pm S.D of age of group-1 was 49.66 ± 10.10 years, group-2 was 47.68 ± 9.95 years. There was no statistical difference found in mean age of both groups ($p = 0.807$). The Mean \pm S.D of RBS of group-1 was 168.24 ± 79.44 mg/dl, group-2 was 108.77 ± 14.81 mg/dl. There was statistical increase in mean RBS level of cases. ($P = 0.0001$) The Mean \pm S.D of Vitamin B12 of group-1 was 246.36 ± 118.50 pg/ml, group-2 was 484.72 ± 172.96 pg/ml. There was statistical

decrease in mean Vitamin B12 level of cases. (P = 0.0001).

Figure 1, shows the comparison of age between the study groups there was no statistical difference found in mean age of both groups. (p = 0.807).

Figure 2, shows the comparison of blood sugar level between the study groups there was statistical increase in mean RBS level of cases. (P = 0.0001).

Figure 3, shows the comparison of serum vitamin B12 between the study groups there

was statistical decrease in mean Vitamin B12 level of cases. (P = 0.0001).

Table 2, shows Strong negative correlation between Plasma blood glucose and Vitamin B12 in cases, having statistical sig P value = 0.0001 and r value was -0.607 with 95% Confidence interval of -0.7182 to -0.4667.

Figure 4, shows Strong negative correlation between Plasma blood glucose and Vitamin B12 in cases, having statistical sig P value = 0.0001 and r value was -0.607 with 95% Confidence interval of -0.7182 to -0.4667.

Table 1: Physical Characteristics & Lab Parameters of study subjects

Variables	Group – 1 (n = 100) Mean ±S.D	Group – 2 (n = 100) Mean ±S.D	P Value
Age (Years)	49.66 ± 10.10	47.68 ± 9.95	0.807
Males	42 (42%)	48 (48%)	-
Females	58 (58 %)	52 (52%)	-
RBS (Mg/dl)	168.24 ± 79.44	108.77 ± 14.81	0.0001**
Serum Vitamin B12 (pg/ml)	246.36 ±118.50	484.72 ±172.96	0.0001**

** (Highly Significant)

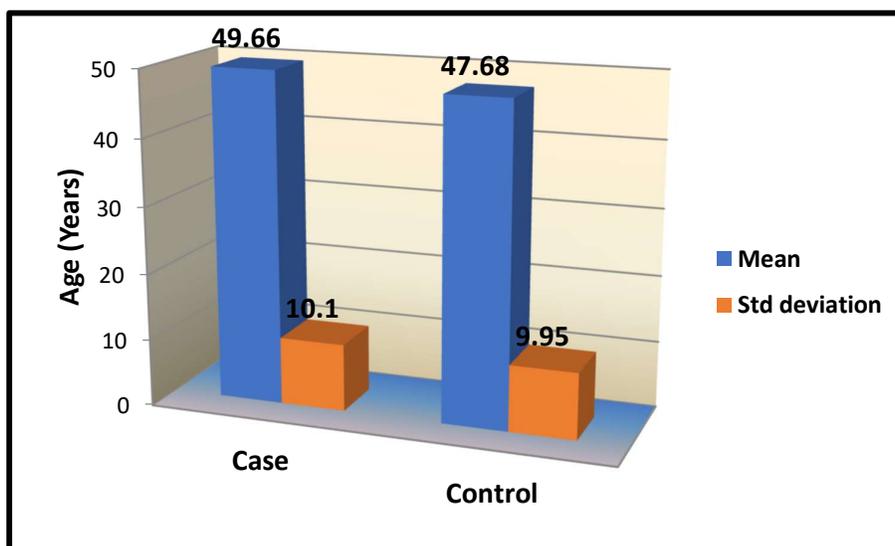


Figure 1: Shows Mean ± S.D of Age in study groups

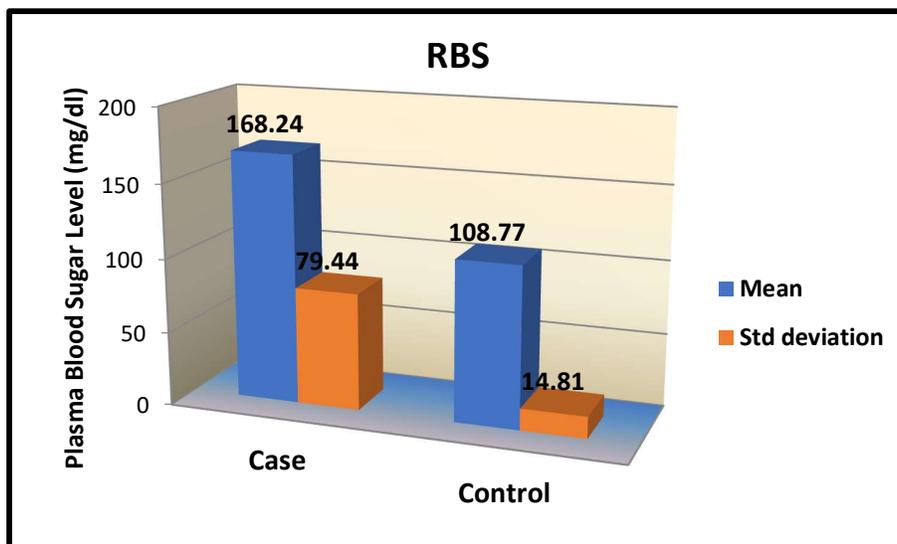


Figure 2: Shows Mean ± S.D of Random blood sugar in study groups

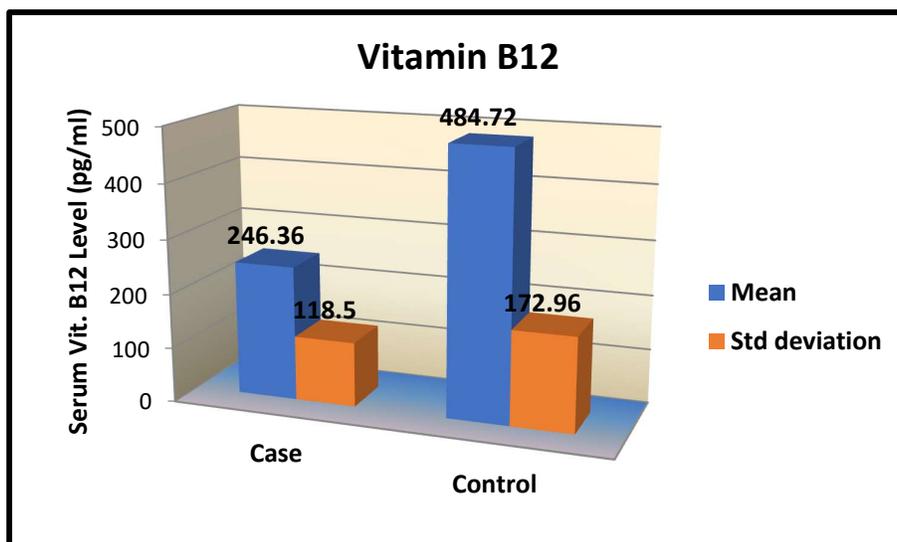


Figure 3: Shows Mean ± S.D of Serum Vitamin B12 in study groups

Table 2: Correlation of Vitamin B12 with RBS in cases

Parameter	Coefficient of Correlation (r)	95% Confidence Interval	P Value
RBS	-0.607	-0.7182 to-0.4667	0.0001**

** (Highly Significant)

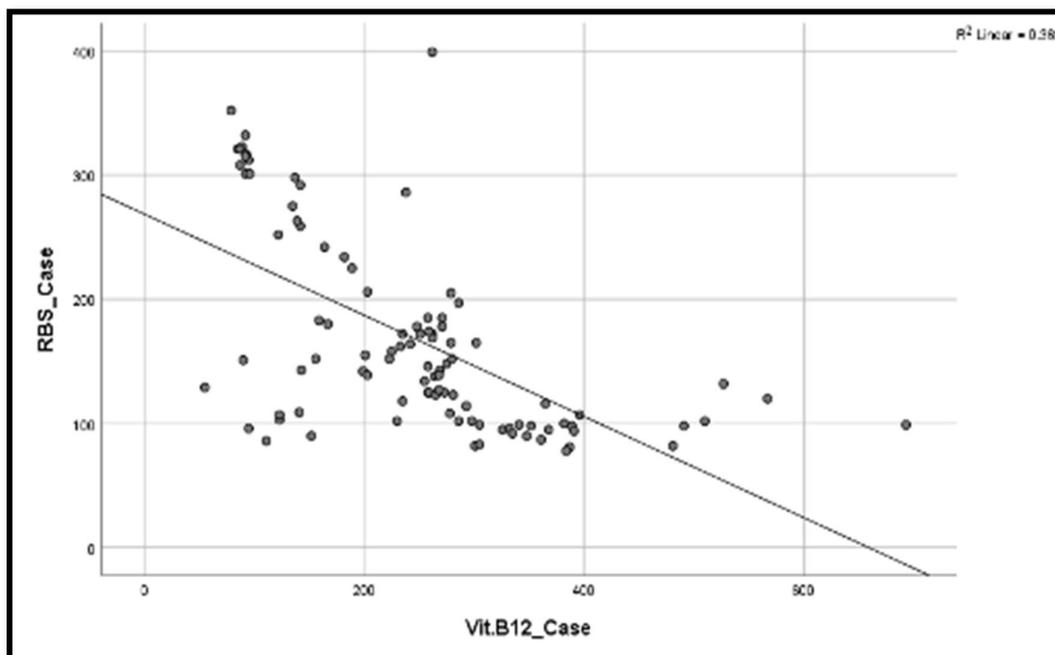


Figure 4: Shows Correlation of Vitamin B12 with RBS in cases

DISCUSSION:

In this study 200 subjects were enrolled out of which 100 patients were diagnosed with type II diabetes mellitus since past 1 years and were on metformin, having age between 35-70 years. 100 healthy controls having age between 35-70 years were also enrolled.

In this study all participants were between the age group of 35-70 years. The Mean \pm S.D of age in group-1 was 49.66 ± 10.10 years, group-2 was 47.68 ± 9.95 years. There was no significant difference found in age between cases and controls. Similar results of Age were found in study done by Rose Zhao-Wei Ting, *et al.* in 2006 [9], Jolien de jager, *et al.* in 2010 [10], Jose

Maria Calvo Romero, *et al.* in 2012 [19], Groot-Kamphuis DM, *et al.* in 2013 [11], Sun-Hye Ko, *et al.* in 2014 [12].

In our study the Mean \pm S.D of RBS in group-1 was 168.24 ± 79.44 mg/dl, group-2 was 108.77 ± 14.81 mg/dl. ($p= 0.0001$) p -values were statistically significant for RBS in both cases and controls. In contrast to our study no study did comparison of RBS, we did comparison of RBS between cases and controls. Instead Following studies done by Sun-Hye Ko, *et al.* in 2014 [12] they have compared FBS in cases and controls with significant p -value.

In our study Mean \pm S.D of serum vitamin B12 in group-1 was 246.36 ± 118.50 pg/ml,

group-2 was 484.72 ± 172.96 pg/ml. In present study serum vitamin B12 levels were decreased in cases compared to controls with statistically significant p-value ($p=0.0001$). Similar results of Vitamin B12 were found in study done by Rose Zhao-Wei Ting, *et al.* in 2006 [9], Jolien de jager, *et al.* in 2010 [10], Sun-Hye Ko, *et al.* in 2014 [12], Vanita R Aroda, *et al.* in 2016 [14], Shaik A Hussain, *et al.* in 2020 [20].

Contradictory to present study, following study did not find statistical significant difference of serum vitamin B12 between cases and controls - Adnan Khan, *et al.* in 2017 [18], G.Prakash, *et al.* in 2020 [21], K.S. Akinlade, *et al.* in 2015 [13], Viswa S, *et al.* in 2020 [16], Corina Metaxas, *et al.* in 2018 [15].

In our study we did correlation of RBS with Vitamin B12 in type II diabetes mellitus cases. In present study a significant negative correlation was observed between RBS and Vitamin B12. ($p=0.0001$) ($r= -0.607$) In contrast to our study no study did correlation between RBS and Vitamin B12. Instead, they did correlation between metformin dose and Vitamin B12.

Limitations of present study were:

- Limitation of our study was that we only measured serum vitamin B12 levels and not estimated levels of homocysteine and folic acid. Estimation of homocysteine level

would also be helpful in correlating cardiac issues associated with B12 deficiency.

- Only the impact of metformin treatment is measured, not that of other anti-diabetic medications.

CONCLUSION:

In the process of our study, we found a significant negative correlation between vitamin B12 insufficiency and using of metformin as a T2DM treatment. So, it is advisable that diabetes patients on metformin should undergo regular follow up for estimation of vitamins level to prevent further complications leading to better management.

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DECLARATIONS:

Ethical approval: Approval by- Parul University's Institutional Ethics Committee on Human Research (PU-IECHR).

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