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Research Article

**ANALYSIS OF DEFICIENCY OF VITAMIN B12 IN TYPE 2  
DIABETIC PATIENTS TAKING METFORMIN THERAPY**Dr Ushna Ali<sup>1</sup>, Dr Farwa Sajid<sup>1</sup>, Dr Zakia Tariq<sup>1</sup><sup>1</sup>Bahawal Victoria Hospital, Bahawalpur.

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**Abstract:**

**Introduction:** Metformin is the first therapeutic choice for management of type 2 diabetes mellitus (T2DM), as recommended by the American Diabetes Association and the European Association for the Study of Diabetes.

**Objectives:** The basic aim of the study is to analyze the deficiency of vitamin B12 in type 2 diabetic patients taking metformin therapy.

**Material and methods:** This cross sectional study was conducted in Bahawal Victoria Hospital, Bahawalpur during December 2108 to April 2019. The data was collected from 100 patients. The patients of both genders, aged between 30-80 years, diagnosed cases of Diabetes Mellitus type 2 and on metformin therapy for more than one year was included in this study. Blood was drawn for the analysis of serum. Serum B12 level was checked by Roche B12 kit.

**Results:** The data was collected from 100 patients of both genders. Mean age (years) in the study was  $54.08 \pm 13.74$  with ranges from 20 to 80 years. Distribution of gender of patient was also calculated in terms of frequency and percentage of male and female patients. Mean duration of plasma sugar level was  $16.02 \pm 3.55$  in the study. Descriptive statistics of serum vitamin B12 level was calculated in terms of mean and standard deviation. Mean serum vitamin B12 level was  $102.67 \pm 28.10$  in the study.

**Conclusion:** It is concluded that frequency of vitamin B12 deficiency is substantial in type 2 diabetic patients taking metformin therapy.

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**INTRODUCTION:**

Metformin is the first therapeutic choice for management of type 2 diabetes mellitus (T2DM), as recommended by the American Diabetes Association and the European Association for the Study of Diabetes. Metformin improves peripheral insulin sensitivity and cardiovascular mortality risk. The worldwide prevalence of DM has risen dramatically in past two decades, an estimated 30 million cases in 1985 to 285 million in 2010 and according to International Diabetes Federation it will be 438 million by the year 2030. The prevalence of type 2 DM is rising much more rapidly mainly because of reduced physical activity levels as countries are becoming more industrialized, increasing obesity and the aging of the population [1]. In 2010, the prevalence of diabetes ranged from 11.6 to 30.9% in the countries with the highest prevalence (United Arab Emirates, Saudi Arabia, Bahrain, Kuwait, Oman, and Malaysia). In the United States, diabetes is the seventh leading cause of death and a recent estimate suggested that diabetes is the fifth leading cause of death worldwide [2].

Deficiency of vitamin B12 affects both men and women in equal numbers. The prevalence of deficiency varied by age group  $\leq 3\%$  in aged 20–39 yrs,  $\approx 4\%$  in aged 40–59 yrs and  $\approx 6\%$  in aged  $\geq 70$  y. The reported prevalence of deficiency is much higher in African and Asian countries i.e 70% in Kenyan school children, 80% in Indian preschoolers, and 70% in Indian adults. Diabetes mellitus is a group of metabolic diseases characterized by high blood sugar (glucose) levels that result from defects in insulin secretion, or its action, or both [3]. Diabetes mellitus, commonly referred to as diabetes was first identified as a disease associated with "sweet urine," and excessive muscle loss in the ancient world. Elevated levels of blood glucose (hyperglycemia) lead to spillage of glucose into the urine, hence the term sweet urine [4]. Normally, blood glucose levels are tightly

controlled by insulin, a hormone produced by the pancreas. Insulin lowers the blood glucose level [5,6].

**Objectives:**

The basic aim of the study is to analyze the deficiency of vitamin B12 in type 2 diabetic patients taking metformin therapy.

**MATERIAL AND METHODS:**

This cross sectional study was conducted in Bahawal Victoria Hospital, Bahawalpur during December 2108 to April 2019. The data was collected from 100 patients. The patients of both genders, aged between 30-80 years, diagnosed cases of Diabetes Mellitus type 2 and on metformin therapy for more than one year was included in this study. Blood was drawn for the analysis of serum. Serum B12 level was checked by Roche B12 kit. The rationale to check HbA1c is to look for the control of sugars. The reports were collected by post graduate resident. The results were noted on proforma accordingly. Variables which were noted include patient's age, gender, blood sugars and serum Vitamin B12 level.

**Statistical analysis:**

The data was analyzed by SPSS software version 16. Descriptive statistics was calculated for all variables like age, gender, plasma sugar level and serum Vitamin B12 level.

**RESULTS:**

The data was collected from 100 patients of both genders. Mean age (years) in the study was  $54.08 \pm 13.74$  with ranges from 20 to 80 years. Distribution of gender of patient was also calculated in terms of frequency and percentage of male and female patients. Mean duration of plasma sugar level was  $16.02 \pm 3.55$  in the study. Descriptive statistics of serum vitamin B12 level was calculated in terms of mean and standard deviation. Mean serum vitamin B12 level was  $102.67 \pm 28.10$  in the study.

**Table 01:** Effect modifier like Age stratification with Serum Vitamin B12 level deficiency

|           |               | Serum Vitamin B12 level deficiency (<148 mpol/L) |               | p-value |
|-----------|---------------|--|---------------|---------|
|           |               | yes  | No            |         |
| Age group | 30 - 50 years | 23<br>35.4%                                      | 42<br>27.5%   | 0.241   |
|           | 51 - 80 years | 42<br>64.6%                                      | 111<br>72.5%  |         |
| Total     |               | 65<br>100.0%                                     | 153<br>100.0% |         |

**Table 02:** Effect modifier like Duration of Diabetes Mellitus stratification with Serum Vitamin B12 level deficiency

|                               |               | Serum Vitamin B12 level deficiency (<148 mpol/L) |               | p-value |
|-------------------------------|---------------|--|---------------|---------|
|                               |               | yes  | No            |         |
| Duration of Diabetes Mellitus | 5 - 7 years   | 5<br>7.7%  | 17<br>11.1%   | 0.632   |
|                               | >7 - 10 years | 21<br>32.3%                                      | 42<br>27.5%   |         |
|                               | > 10 years    | 39<br>60.0%                                      | 94<br>61.4%   |         |
| Total                         |               | 65<br>100.0%                                     | 153<br>100.0% |         |

**DISCUSSION:**

Metformin is the most prescribed anti-diabetic drug in patients with type 2 diabetes mellitus (T2DM) and hence, considered a cornerstone in the treatment of T2DM. It is an anti-hyperglycaemic agent that is usually well tolerated in most of the patients (except for mild gastrointestinal side effects) and it is characterized by excellent improvement in the cardiovascular morbidity and mortality associated with T2DM. Due to the numerous clinical benefits associated with metformin, some side effects with potential adverse health effects associated with its use are usually ignored and rarely investigated. One of such side effects is vitamin B<sub>12</sub> deficiency [7].

Vitamin B<sub>12</sub>, also called cobalamin, is a water-soluble vitamin involved in the optimal functioning of the hemopoietic, neuro-cognitive and vascular systems. It is involved in DNA synthesis, fatty acid metabolism and energy production. Vitamin B<sub>12</sub> exerts its physiological effects by facilitating the methylation of homocysteine to methionine which is later activated into S-adenosyl methionine that donates its methyl group to methyl acceptors [8]. Similarly, vitamin B<sub>12</sub> mediates the conversion of methyl malonyl coenzyme A (coA) to succinylcoA, a process when hindered, results in accumulation of serum methylmalonic acid (MMA) thereby causing defective fatty acid synthesis of the neuronal membranes [9].

Reports have shown that there is an association between metformin use and vitamin B<sub>12</sub> deficiency. However, the mechanism through which metformin induces vitamin B<sub>12</sub> deficiency (VBD) in patients with T2DM is presently unclear. Some of the suggested mechanisms include alteration in small bowel motility, which stimulates bacterial overgrowth and consequential vitamin B<sub>12</sub> deficiency [10]. Others include competitive inhibition or inactivation of

vitamin B<sub>12</sub> absorption, alteration in intrinsic factor levels and interaction with the cubulinendocytic receptor. Also, inhibition of the calcium dependent absorption of vitamin B<sub>12</sub>-intrinsic factor (IF) complex at the terminal ileum has been suggested as one of the mechanisms [11].

**CONCLUSION:**

It is concluded that frequency of vitamin B12 deficiency is substantial in type 2 diabetic patients taking metformin therapy.

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