MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.59218/makrjms.2024.1.179.182

OPEN ACCESS

Key Words
Vitamin B12, mellitus, metformin and retinopathy

Corresponding Author
V. Ganesh,
Department of Pharmacology, SMIMS, Tamil Nadu, India

Author Designation
[1]Associate Professor
[2,3]Postgraduate

Received: 4 November 2023
Accepted: 25 December 2023
Published: 6 January 2024

Citation: V. Ganesh, S. Rajendra Nandha and K. Pragadeesh, 2023. Vitamin B12 deficiency in Metformin taking Patients with Type 2 Diabetes mellitus. Res. J. Med. Sci., 18: 179-183, doi: 10.59218/makrjms.2024.1.179.182

Vitamin B12 Deficiency in Metformin Taking Patients with Type 2 Diabetes Mellitus

[1]V. Ganesh, [2]S. Rajendra Nandha and [3]K. Pragadeesh
[1-3]Department of Pharmacology, SMIMS, Tamil Nadu, India

ABSTRACT
The aim of the study is to asses prevalence of vitamin B12 deficiency in diabetes patients mellitus patients taking metformin. This study was conducted in the outpatient department of General medicine in a tertiary care teaching hospital in Tamil Nadu, India. The study was done during period of June 2023 to November 2023 were included in the study. Patients diagnosed with Diabetes mellitus Type 2 and are on metformin therapy were included in the study. Baseline characteristics like age, gender and variables like duration of illness and duration of therapy with metformin were noted. The Glycosylated haemoglobin values were also included in the study variables. Out 210 patients 40 (19.04%) patients were found to be deficient in Vitamin B12 and 96 patients (45.17%) were found to vitamin B12 deficient at border line level. The daily dose of metformin in these patients ranges from 500 mg to 1500 mg (mean dose:896.36±150.4). By the above study we conclude that there is significant amount of vitamin B12 deficiency found in patient on metformin therapy.

INTRODUCTION

A large proportion of world's population is affected by diabetes mellitus, making it a major health problem[1]. Diabetes may produce long term complications like retinopathy, diabetic foot ulcer, diabetic gastriparesis.The number of cases diagnosed with type 2 diabetes mellitus is on a raise. Type 2 diabetes mellitus is controlled by oral hypoglycemic drugs and life style modifications. Among oral hypoglycemic drugs-Metformin a biguanide is the drug used as a first line pharmacotherapy in patients with Type 2 diabetes mellitus as per many Guide lines[2]. Across various studies done around the world, a significant decrease of Vitamin B12 levels were observed in patients taking metformin for Type 2 diabetes Mellitus[3]. Long-term placebo controlled studies done in the past were suggestive of decrease in vit b12 levels in patients taking metformin when compared to placebo[4]. Longer duration of therapy with metformin was found to be associated with larger amount of vitamin B12 deficiency[5]. Haematological and neurological complications associated with Vitamin B12 deficiency can be avoided in patients taking metformin if vitamin b12 deficiency detected early[6]. The vitamin B12 deficiency and diabetes related complications like peripheral neuropathy has a found to be associated in few studies[7].

MATERIALS AND METHODS

The cross sectional study was carried out in a tertiary care private teaching hospital, Kanyakumari district, India.

Inclusion criteria:

- Patients aged above 18 years of age
- Patients diagnosed with diabetes mellitus and treatment with metformin
- Patient taking metformin for the past 1 year

Exclusion criteria:

- Pateints who are vegetarian by diet
- Patients who are on treatment for GERD/Peptic ulcer disease with Proton pump inhibitors
- Patients with history of anemia
- Patients with history of gastrectomy/Ilectomy
- Pregnant woman
- Patients with infectious disaeses like Tuberculosis and HIV/hepatitis B
- Patients with history of carcinoma, kidney disease

A pilot study was conducted in the institution based on prevalence of 10% vitamin b12 deficiency in the pilot study the sample size of 210 was calculated. Data related to patient's duration of diabetes, history of metformin intake, duration of metformin intake, dose of metformin per day were collected in the outpatient department from the patient itself/ patient's attender. Blood samples were collected for analyses of Vitamin B12 levels, The level of Vitamin B12 was assessed using chemiluminescent paramagnetic microparticle immunoassay. Complete blood count and Glycosylated haemoglobin (HbA1c) were also assessed. HbA1c levels were assessed using turbidimetric inhibition immunoassay in haemolysed whole blood.

After analyses of serum vitamin B12 levels the participants were categorized into 3 categories:

- Deficient Vitamin b12 group
- Borderline deficient Vitamin b 12 group
- Normal Vitamin b 12 group

Deficient Vitamin B12 group has less than 133 pmol/L of serum Vitamin B12. The Border line deficient vitamin B 12 group have Vitamin b 12 levels between 133 to 200 pmol/L. The Normal Vitamin b 12 group contains normal levels of vitamin b 12 of more than 200 pmol/L. After analyses of blood Haemoglobin levels the patients were classified into Anemic/Non Anemic based on gender. Anemic- less than 13 g/dl in male patients and less than 12 g/dl in female patients.

Statistical analysis:

- The datas were analysed using SPSS software version 23 by IBM corp. USA
- ANOVA test was done to determine statistically significant differences in the means between the three groups
- Chi-Square test was used to analyse categorical data A $p<0.5$ is significant

RESULTS

A total of 210 patients were enrolled in the study the mean age of the participants were found to be 54.5±7 yrs (Table 1). The number of patients on Metformin therapy and having normal Vitamin b12 level of > 200 Pmol/L were 74 (35.23%) and patients

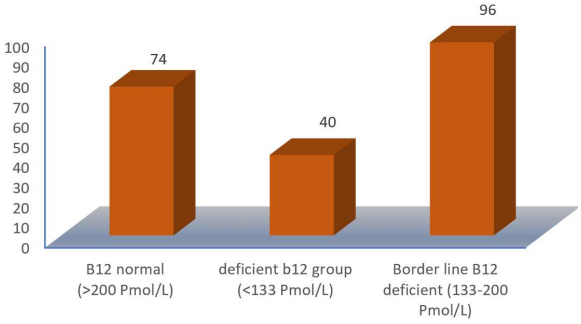

Fig. 1: No of Patients in Each group

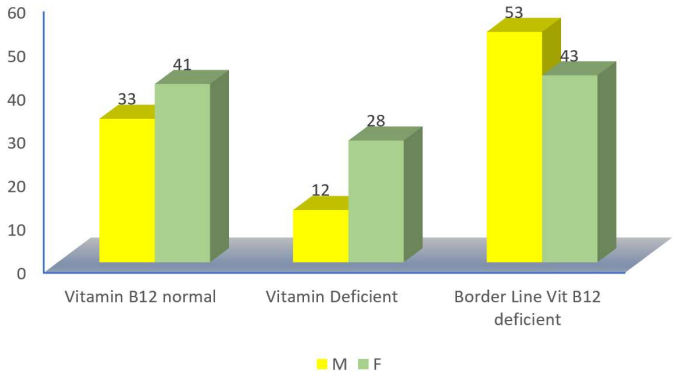

Fig. 2: Patients in Each group

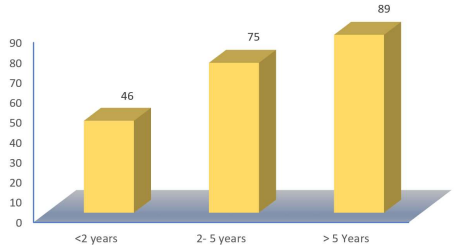

Fig. 3: No of Patients

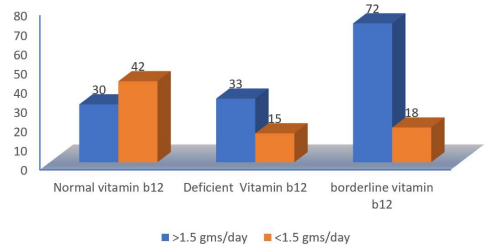

Fig. 4: Dose of Metformin Tharapy

Table 1: The mean age of the participants.

	B12 normal (>200 Pmol/L)	deficient b12 group (<133 Pmol/L)	Border line B12 deficient (133-200 Pmol/L)
No of patients in each group	74 96		40
Mean age	53.6±7.5	55.6±11.6	54.3±10.3

Table 2: The number of patients on metformin therapy.

	M	F
Vitamin B12 normal	33	41
Vitamin Deficient	12	28
Border Line Vit B12 deficient	53	43
Total	98	112

Table 3: The number of patients on metformin therapy.

Duration of metformin Therapy Years	<2 years	2- 5 years	> 5
No of patients	46	75	89

Table 4:The mean age of the participants.

Dose of metformin tharapy	Normal vitamin b12	Deficient Vitamin b12	borderline vitamin b12	p-value
>1.5 gms/day	30	33	72	<0.003
<1.5 gms/day	42	15	18	

with borderline deficiency (133-200Pmol/L) were found to be 96 in number (45.71%) (Table 1). In the 210 patients enrolled 98 (46.66 %) were found to be males and 112 (53.33%) were found to be females [Table 2]. The number of patients on metformin therapy who had deficient levels below 133 Pmol/L of vitamin B12 were found to be 40 (19.04%).

There was a high number of patients belonging to metformin dose of >1.5 gms of per day which constitutes around 33 (15.71%) vitamin B12 deficient group and 72 (34.28%) border line deficient group. The number of patients found to be anemic in the vitamin b12 normal group was 12 in number (5.71%) and the number of patients found to be anemic borderline vitamin b12 deficient group was 18 (8.57%) and the number of patients found to be anemic in vitamin B12 deficient group was 30 (14.28%). The mean Hb level in patients with normal Vitamin B12 levels is 13.6±1.5 and in vitamin b12 deficient group was found to be 12.3±1.6, In Vitamin b12 borderline deficient group was found to be 12.8±1.2 g%.

DISCUSSIONS

Our study compared the values of Vitamin B12 and metformin and duration of metformin therapy, the number of patients with vitamin b12 deficiency in minimal amount was present in male gender in contrary to study done by Aydin B, Cansu GB, Ozlu C which showed high number of male preponderance in Vitamin B12 deficiency. There is association of duration of metformin therapy and serum vitamin b12 levels in our study which is similar to study done by Kancherla *et al.*[8]. Our study we found that patients belonging to Vitamin B12 deficient group was found to have low mean haemoglobin levels but did not have any association and are insignificant. Our study found

Table 5: Patients with normal Vitamin B12 levels.

Vitamin B12 Levels	Haemoglobin	HbA1C
Normal Vitamin B12	13.6±1.5	6.3±1.5
Deficient Vitamin B12	12.3±1.6	7.6±1.2
Border Line Vitamin B12	12.8±1.2	7.3±1.3

Table 6: Metformin therapy and serum vitamin b12 levels.

Mean dose of	Normal Vitamin B12	Deficient Vitamin B12	Borderline Vitamin B12	p-value
Mean dose of metformin	1195±400mg	1495±150mg	1359±300mg	<0.005

Table 7: Patients with normal Vitamin B12.

	Normal vitamin b12	Deficient Vitamin b12	borderline vitamin b12	p-value
Mean Duration of Diabetes mellitus	2.3 ± 0.5 years	4.3 ± 1.5 years	3.5 ± 1.7	<0.005

showed that serum vitamin b12 levels were lower (<133pmol/L) (230 pmol/L± 94pmol/L)(p<0.005) in patients taking metformin for more than 5 years when compared to patients taking metformin for two to five years (276 pmol/L±73 pmol/L) similar to study conducted by Al-Fawaeir. Higher blood levels of glycosylated haemoglobulin (mean 7.6±1.2) is associated with deficiency of Vitamin B12 in our study the finding similar to study done by Aydin B11. Higher doses of metformin was found to have association with decreased serum vitamin B12 similar to study conducted by Marco Infante which suggests that a metformin dose of = 1500 mg/d (p<0.003) for a duration of at least 6 months is associated with vitamin B12 deficiency[9].

Limitations: The study was conducted in a relatively smaller number of population, a larger sample size is needed for studying to avoid errors in the study. The factor of diet was not taken into consideration in this study .It is well known that vegetarians are more prone for vitamin B12 deficiency. The other causes of low Hb deficiency was not assessed in this study.

CONCLUSION

Our study concluded that there is significant association between long term metformin usage and vitamin B12 deficiency in type to diabetes Mellitus patients.

REFRESHES

1. CM, S., K. L, S. Puli, V. TK and A. Acharya, 2013. Sensitivity pattern of bacteria causing respiratory tract infections in a tertiary care centre. Int. J. Basic. Clin. Pharmacol., 2: 590-595.
2. Kho, B.,P. C.M. and Ong, 2013. Antibiotic prescribing for upper respiratory tract infections in sarawak district hospitals. Med. J. Malaysia., 68: 136-140.
3. P.S.A., 2013. Performance Standards for antimicrobial susceptibility testing; Clinical and laboratory standards institute. Twenty. Third. Informational. supplement., Vol. 33.
4. Christopher, E., Aye, 2011. Microbiology of Lower Respiratory tract infections in benin city, nigeria. Malays. J. Med. Sci., 18: 27-31.
5. Mishra, S.K. and J. Acharya, 2012. Metallo-beta-lactamase producing gram-negative bacterial isolates. J. Nepal. Health. Res. Counc., 10: 208-213.
6. Ramana, K.V., 2014. Aetiology and Antimicrobial Susceptibility Patterns of Lower Respiratory Tract Infections (LRTI) in a Rural Tertiary Care Teaching Hospital in Karimnagar, South India. American. J. Infect. Dis. Microbiol., 1: 101-105.
7. Navaneeth, B.V., 2002. Antibiotic resistance among gram -negative bacteria of lower respiratory tract secretions in hospitalized patients. Indian. J. Chest. Dis. Allied. Sci., 44: 173-176.
8. Ali, I.,M.A. Butt, 2001. Antibiotic susceptibility pattern of bacterial isolates from patients of respiratory tract infection at 43 centers in Punjab, Pakistan J.Clin. Experiment. Pharm., Vol. 7 .10.4172/2161-1459.
9. Tripathi, C., Purti, 2014. Lower respiratory tract infections: current etiological trends and antibiogram. J. Pharm. Biomed. Sci., 4: 249-255.