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PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.398814>Available online at: <http://www.iajps.com>**Research Article****TYPE 2 DIABETES MELLITUS:**

(THE VITAMIN B12 DEFICIENCY DURING METFORMIN THERAPY)

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Dr. Hamid Nawaz Ali Memon³, Dr Imran Karim² and Dr. Zulfiqar Ali Qutrio Baloch⁴**¹Government Lyari General Hospital Karachi.²Department of Medicine, Liaquat University Hospital Hyderabad / Jamshoro.³Zulekha Hospital, Dubai United Arab Emirates .⁴Brandon Regional Hospital, Brandon, Florida.**Received:** 22 February 2016**Accepted:** 10 March 2017**Published:** 14 March 2017**Abstract:****OBJECTIVE:** To determine the frequency of vitamin B12 deficiency in patients with type 2 diabetes mellitus on metformin therapy.**PATIENTS AND METHODS:** This cross sectional descriptive study of six was conducted at Liaquat university hospital Hyderabad & Govt. Lyari general hospital Karachi. The inclusion criteria of the study were diagnosed type 2 diabetic patients of ≥ 01 year duration, already on metformin therapy, of 35-60 years of age, both gender regardless on treatment and their glycemic status. All the diabetic individuals were further evaluated for vitamin B12 deficiency. The data of all patients was analyzed in SPSS version 16.00. The frequency and percentage (%) will be calculated for vitamin B12 deficiency in type 2 diabetes mellitus on metformin therapy. The mean and standard deviation (SD) will be calculated for age, duration of diabetes mellitus and vitamin B12 level.**RESULTS:** During six months study period total one hundred diabetic patients on metformin therapy were evaluated for vitamin B12 deficiency. The mean \pm SD for age, fasting and random blood glucose, hemoglobin A1C and vitamin B12 level for overall population was 52.87 ± 6.87 , 159.74 ± 6.96 and 266.32 ± 8.92 , 9.08 ± 2.74 and 85.23 ± 72.54 respectively. The vitamin B12 deficiency was observed in 61% with male gender predominance (63%). The hemoglobin A1c was raised in 47 (68.1%) vitamin B12 deficient individuals.**CONCLUSION:** Type 2 diabetics on metformin therapy were observed to have low vitamin B12 level**Keywords:** Diabetes mellitus, Vitamin B12, and Metformin**Corresponding Author:****Dr. Nisar Ahmed Shah***,

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INTRODUCTION:

Diabetes mellitus is an endocrine disorder associated with multisystem complications [1-6]. Pakistan is estimated to have seven million people with diabetes and by the year 2025 expected fifteen million people diabetes representing a twofold increase[7].

Vitamin B12 deficiency is a common disorder and leads to neuropathy present as impaired sensation in the limbs [8-10].The diabetic neuropathy symptoms correlates to impaired vibration and position due to vitamin B12 deficiency and such neuronal presentation usually confused with neuropathy due to diabetes mellitus [11,12]. Identification of etiology is important because vitamin B12 supplements can improve the neurologic complaints despite of glycemic status [13,14]. The reported prevalence of vitamin B12 deficiency in type 2 diabetes mellitus is 50% in the study by Jawa A, et al [15]. In regard to vitamin B12 levels, this study was focused on metformin associated vitamin B12 deficiency in diabetic population as has been reported that with long term treatment metformin lowers vitamin B12 levels [16].

Literature regarding the vitamin B12 deficiency still scarce in Pakistan; This multi-institutional study evaluate the frequency of vitamin B12 deficiency in diabetic patients already on metformin regimen as early evaluation can reduce life threatening complication of vitamin B12 deficiency.

PATIENTS AND METHODS:

This cross sectional descriptive study of six was conducted at Liaquat university hospital Hyderabad / Jamshoro & Govt. Lyari general hospital Karachi.

The inclusion criteria of the study were diagnosed type 2 diabetic patients of ≥ 01 year duration, already on metformin therapy, of 35-60 years of age, both gender regardless on treatment and their glycemic status while the exclusion criteria were patient already on folic acid or vitamin B12 therapy, malignancy, malabsorption syndrome, hypothyroidism and non cooperative individuals. This study was conducted on the patients with history of type 2 diabetes mellitus (diagnosed cases) for more than one year duration admitted in medical ward. A consent was taken from all patients for participation in the study and all the diabetic participants were further evaluated for vitamin B12 deficiency (considered when serum vitamin B12 concentration < 100 pg/ml). The data was collected on pre-designed proforma and all the financial burden of the study will be paid by the collaboration of whole research team. The data was analyzed in SPSS 16, the frequency and percentage (%) will be computed for categorical variables while mean \pm SD was also calculated for quantitative (numerical) variables (duration of diabetes mellitus and vitamin B12).

RESULTS:

During six months study period total one hundred diabetic patients on metformin therapy were evaluated for vitaminB12 deficiency. The mean \pm SD for age, fasting and random blood glucose, hemoglobin A1C and vitamin B12 level for overall population was 52.87 ± 6.87 , 159.74 ± 6.96 and 266.32 ± 8.92 , 9.08 ± 2.74 and 85.23 ± 72.54 respectively. The results are presented in Table 1-5.

Table 1: The Age and Gender Distribution

	AGE (yrs)	GENDER		Total
		Male	Female	
35-39		14	3	17
		22.2%	8.1%	17.0%
40-49		24	22	46
		38.1%	59.5%	46.0%
50-60		25	12	37
		39.7%	32.4%	37.0%
Total		63	37	100
		100.0%	100.0%	100.0%

*P-value=0.05; (significant)

Table 2: The Gender and Vitamin B12

	GENDER	VITAMIN B12 DEFICIENCY		Total
		Yes	No	
	Male	43	20	63
		70.5%	51.3%	63.0%
	Female	18	19	37
		29.5%	48.7%	37.0%
Total		61	39	100
		100.0%	100.0%	100.0%

*P-value = 0.04 (significant)

Table 3: The Gender and Duration Of Diabetes Mellitus

	GENDER	DURATION (yrs)			Total
		1-2	3-4	>5	
	Male	23	23	17	63
		79.3%	59.0%	53.1%	63.0%
	Female	6	16	15	37
		20.7%	41.0%	46.9%	37.0%
Total		29	39	32	100
		100.0%	100.0%	100.0%	100.0%

*P-value = 0.03 (significant)

Table 4: The Gender and Hemoglobin A1C

	GENDER	HBA1C		Total
		Raised	Normal	
	Male	45	18	63
		65.2%	58.1%	63.0%
	Female	24	13	37
		34.8%	41.9%	37.0%
Total		69	31	100
		100.0%	100.0%	100.0%

*P-value: 0.49 (non significant)

Table 5: The Vitamin B12 Deficiency and Hemoglobin A1C

	VITAMIN B12 DEFICIENCY	HBA1C		Total
		Raised	Normal	
	Yes	47	14	61
		68.1%	45.2%	61.0%
	No	22	17	39
		31.9%	54.8%	39.0%
Total		69	31	100
		100.0%	100.0%	100.0%

*P-value: 0.03 (significant)

DISCUSSION:

Vitamin B12 usually not screened by majority of physicians prescribed metformin. In present study the mean vitamin-B12 levels among overall population was 85.23 ± 72.54 (SD) pg/ml. The metformin associated vitamin B 12 deficiency leads to peripheral neuropathy in subjects with diabetes mellitus usually mistaken as diabetic peripheral neuropathy. Except kidney and liver impairment guidelines advised the metformin use as the initial oral hypoglycemic drug along with dietary modification modifications [17]. Metformin decreases the serum B12 levels, the observation reported formerly by several studies [18-24]. The risk to acquire vitamin B12 deficiency superimposed by advanced age, dosage and duration of metformin therapy [25]. Decrease in vitamin B12 absorption after metformin usage typically initiate within few months [26]. Although clinical features of B12 deficiency appears in five to ten years as large hepatic stores is available naturally that not rapidly depleted [27]. The mechanisms of metformin induced vitamin B12 deficiency includes bowel motility alterations that causes overgrowth of bacteria and leads to deficiency of B12 [28]. Calcium associated vitamin B12 absorption and intrinsic factor complex in the terminal ileum blocked by metformin and can be reversed with calcium supplementation. Thus, it has been suggested that vitamin B12 level should be monitored annually especially who are on metformin. Proper education and cost-effective measures on metformin should convey to patients at community level and vitamin B12 supplementation is sufficient to cover vitamin B12 desire in diabetic population taking metformin.

CONCLUSION:

The diabetic patients on metformin therapy were observed to have low vitamin B12 level; hence vitamin B12 therapy is beneficial for type 2 diabetics patients taking metformin

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