

Frequency of Vitamin B12 in Patients with Diabetic Peripheral Neuropathy

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ABSTRACT

Objective: To determine the frequency of vitamin B12 deficiency in patients with diabetic peripheral neuropathy

Study Design: Descriptive / cross sectional study

Place and Duration of Study: This study was conducted at the Department of Medicine, HMC Peshawar from Jan to Dec 2016.

Materials and Methods: A total of 135 patients were studied by using (22%) 8 proportion of vitamin B12 deficiency in patients with diabetes, 95% confidence level and 7% margin of error using WHO software for sample size. The SPSS latest version was used to analyze the data. For continuous data while for categorical one frequencies and %ages were calculated and the dated was prepared in tabulated form

Results: In this study 135 diabetics fulfilling the inclusion criteria were enrolled. We found mean age 56 years with SD $\pm$ 1.34. Fifty six percent cases were male and rest of 44% patients female. Mean duration of diabetes was 20 years with standard deviation $\pm$ 1.26. Twenty six percent patients had S Vit B12 level $<$ 200 pg/ml and 74% patients had S Vitamin B12 level $>$ 200pg/ml. On this basis S Vit B12 Deficiency was found in 26% patients while 74% patients didn't had S Vit B12 Deficiency.

Conclusion: Patients with diabetes have both clinical and biochemical prevalence of vitamin B12 deficiency. Homocysteine and methylmalonic acid levels can estimate B12 deficiency and diabetic and non-diabetic.

Key Words: Vita B₁₂ deficiency; Diabetes mellitus; Diabetic peripheral neuropathy

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INTRODUCTION

Diabetes mellitus is an increasing global health problem worldwide. Currently it was guessed that 366 million population is suffering from diabetes and it may reach as high as 552 million in 2030, making diabetes as the major health problem an public health threat around the globe^{1, 2}.

Complications of diabetes are resulting in increased morbidity, mortality and enormous health costs. Diabetic peripheral neuropathy (DPN) is a serious microvascular complication of diabetes³. American Diabetes Association mentions the involvement of nervous system about 60-70 % in diabetics which may be from mild to severe form⁴. Several distinct clinical syndromes of DPN have been delineated, the most common being distal symmetrical sensorimotor polyneuropathy (DSPN).

Symptomatic patients with DSPN typically present with numbness and tingling of the distal extremities, often described as a stocking-glove neuropathy⁵.

Painful neuropathy is also common in the form of burning, dysesthesia, allodynia and severe, short-lasting lancinating pains. All types of pain usually worsen at night. In the later stages of disease there is severe sensory loss, small muscle wasting of the hands and feet, sensory ataxia, loss of tendon reflexes, and neuropathic arthropathy (Charcot joints). In advanced cases, it can lead to foot ulceration, infection and lower limb amputation. More than 60% of non-traumatic lower-limb amputations occur in patients with diabetes⁶.

Although longstanding hyperglycemia and its associated metabolic derangements is the most important etiological risk factor for the onset and progression of micro-vascular complications of diabetes including DPN, some patients may still develop these complications even with good glycemic control. Therefore other risk factors and comorbid conditions might be associated with the causation and severity of DPN, and sometimes nondiabetic neuropathies might be present in these patients. Vitamin B12 deficiency is a potential comorbidity that should be considered in patients with DPN^{7,8,9}.

Vitamin B12 Deficiency may present with signs and symptoms that may be due to peripheral nervous system or spinal cord involvement¹⁰. Vitamin B12 deficiency – induced neuropathy may be confused with DPN. In 28% of such patients there will be no anemia or macrocytosis. Clinical manifestations like paresthesias or numbness, impaired vibration and position sense, absent ankle reflexes, ataxia, and muscle weakness may

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pose a diagnostic challenge, if they are the presenting features of B12 deficiency in patients with diabetes¹¹.

The objective of this study is to determine the frequency of vitamin B12 deficiency in our local population with diabetes and having peripheral neuropathy. This study will be first of its kind and will give us local statistics about the problem as no local data is available on similar objective so far.

MATERIALS AND METHODS

The study was descriptive cross-sectional and was carried out in Medicine department HMC, Peshawar. The duration was one year from Jan to Dec 2016, after approval from ethical committee HMC. Both male and female patients with age 40 years and above; and with diagnosis of diabetes and having peripheral neuropathy were included in the study. Patients with pernicious anemia, pancreatic insufficiency, inflammatory bowel disease, tuberculous enteritis, mal-absorption syndrome, taking metformin, proton pump inhibitors and oral or parental B12 supplementation were excluded from the study.

The study was carried out after permission of ethical committee HMC. Patients fitting to the inclusion were selected and biodata and relevant information filed on Proforma. We took Comprehensive history and did thorough clinical assessment in all cases. A careful scrutiny of past medical records was carried out for each patient. From all patients after observing strict aseptic technique, 5cc of venous blood was obtained and was immediately sent to hospital laboratory for the measurement of vitamin B12 level. All the laboratory investigations were done under supervision of expert pathologist fellow of CPSP and using same standard laboratory equipment.

All data was filed and assessed in SPSS version 16.0. Mean + SD was measured for continuous variables like age, serum B12 and duration of diabetes. Frequencies and percentages were calculated for categorical variables like gender and vitamin B12 deficiency. Vitamin B12 deficiency was assessed for different age range, gender and duration of diabetes to observe the outcome. Eventually the results were presented in tabulated form.

RESULTS

In this study carried out at HMC medical units a total of 135 patients were assessed to know about the vit B status in diabetic patients with peripheral neuropathy and results assessed.

Age distribution in 135 patients were found as 7(5%) cases in age group 40-45 years, 28(21%) cases 46-50 years, 55(41%) cases 51-55 years, 38(28%) cases 56-60 years and 7(5%) cases in age above 60 years. We found mean age of 56 years with SD $\pm$ 1.34 (Table 1).

Table No.1: Age-wise distribution of Diabetic Neuropathy (n=135)

Age in Years	Frequency	Percentage
40-45	7	5
46-50	28	21
51-55	55	41
56-60	38	28
61-65	7	5
Total	135	100

We found 76(56%) cases as male and 59(44%) cases as female out of total 135 cases.

Duration of diabetes among 135 patients was analyzed as 15(11%) patients had diabetes from 1-10 years, 66(49%) patients had diabetes from 11-20 years, 51(38%) patients had diabetes from 21-30 years and 3(2%) patients had diabetes more than 30 years. Mean duration of diabetes was 20 years with standard deviation $\pm$ 1.26 (Table 2).

Table No 2: Duration of diabetes (n=135)

Duration of Diabetes	Frequency	Percentage
1-10 years	15	28
11-20	66	49
21-30	51	38
>30 years	3	2
Males	113	84

Mean duration of diabetes was 20 years with SD $\pm$ 1.26. S Vitamin B12 level among 135 patients was analyzed as 35(26%) patients had S Vitamin B12 level < 200 pg/ml while 100(74%) patients had S Vitamin B12 level > 200pg/ml. Mean S Vitamin B12 level was 250 pg/ml with standard deviation $\pm$ 2.41 (Table 3).

Table No. 3: S. Vitamin B12 Level (n=135)

S. Vitamin B ₁₂ Level	Frequency	Percentage
< 200 pg/ml (Deficient)	35	26
> 200 pg/ml (not deficient)	100	74
Total	135	100

Mean S Vitamin B₁₂ level was 250 pg/ml with SD $\pm$ 2.41.

S Vitamin B12 Deficiency among 135 patients was analyzed as S Vitamin B12 Deficiency was found in 35(26%) patients while 100(74%) patients didn't had S Vitamin B12 Deficiency.

Association of S Vitamin B12 Deficiency with age group was analyzed as in 35 cases of S Vitamin B12 Deficiency, one case was in age group 40-45 years, 4 in group 46-50 years, 11 in 51-55 years, 14 in 56-60 years and 5 cases in age more than 60 years (Table 4).

Table No. 4: Association of S. Vitamin B12 deficiency in age group (n=135)

Age/ S. B12 Def	40-45 years	46-50	51-55	56-60	>60	Tot
Def	1	4	11	14	5	35
Non Def	6	24	44	24	2	100
Total	7	28	55	38	7	135

Association of S Vitamin B12 Deficiency with gender distribution was analyzed as in 35 cases of S Vitamin B12 Deficiency, 21 patients were male while 14 patients were female.

Association of S Vitamin B12 Deficiency with duration of diabetes was analyzed as in 35 cases of S Vitamin B12 Deficiency, 9 patients had diabetes from 11-20 years, 23 patients had diabetes from 21-30 years and 3 patients had diabetes from more than 30 years.

DISCUSSION

This study was carried out at HMC medical units Peshawar and we assess 135 diabetic with peripheral neuropathy for vit B12 deficiency. In our study we found 26% of type 2 DM with deficiency of B12 which is showing difference from other international study and possibly this difference was the result of the generalization of our study as compared to others¹².

Diabetic neuropathy is the frequently occurring complications just like other complications like nephropathy and vasculopathy and even more. Neuropathy in Diabetics ranges from mild to severe. Though multiple risk factors are contributing to Diabetic neuropathy, this study did confirm the significant role of vitamin. This statement has indirectly been confirmed by previous studies where they found that vitamin B12 supplementation can reduce somatic and autonomic neuropathy and therefore treating these patients with additional B12 will reduce significantly the neuropathy and hence result in the better outcome in diabetic with neuropathy^{13,14}.

We also investigated for the serum level of methylmalonic acid and homocysteine levels to make our diagnosis more accurate. And good thing about these markers is that accuracy of Vitamin B12 deficiency detection increases and even it gives clue about early tissue B12 deficiency. Though this study used MMA acid and HC levels but other studies have been conducted to know about its levels in B12 deficient elder adults rather than a complication of DM and they found B12 deficiency ranging from as low as 5 to as high as 28%, which is showing some resemblance in percentage to our study. There was difference of age related to B12 deficiency. The age difference was mostly aligning with other studies but there was difference in some of the studies where the age was less¹⁵. Therefore, it shows that there is a definite role of

Diabetes on serum level of B12 and MMA HC level is helpful in assessing its level.

There is close association of B12 deficiency and chronic user of antidiabetic metformin. Its long use by patients having DM case have deficit and ultimately low B12 level and megaloblastic anemia^{16,17,18}. Some studies have attributed to the higher doses and longer duration of treatment¹⁹. We had not looked for other associations of B12 deficit due to restricted inclusion criteria.

A group of diabetics who are have poor diabetes control and such patients must be started with early B12 supplementation to avoid earliest neuropath development. The age group of our study population closely simulated to the population of a study conducted at United States of America¹⁹. In short majority of our patients were representing day care ones. Being the primary objective of our study was to look for deficiency of B12, therefore this cross sectional study was the most suitable; but we could not study other aspects and to know about other risk factor leading to this problem²⁰.

CONCLUSION

Patients with diabetes have both clinical and biochemical prevalence of vitamin B12 deficiency. Homocysteine and methylmalonic acid levels can estimate B12 deficiency and diabetic and non-diabetic.

Author's Contribution:

Concept & Design of Study:	Muhammad Bilal Khattak
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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Leon AP, Perez G. Tuberculosis and diabetes in southern Mexico Epidemiology / health services psychosocial research. Diabetic Care 2004;27: 1584-90.
2. Forouhi NG, Wareham NJ. Epidemiology of diabetes. Medicine 2014; 42 (12): 698-702.
3. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diab Care 2004;27(5): 1047-53.
4. Pflipsen MC, Oh RC, Saguil A, Seehusen DA, Seaquist D, Topolski R. The prevalence of vitamin

- B12 deficiency in patients with type 2 diabetes: a cross-sectional study. *J Am Board Fam Med* 2009; 22(5): 528-34.
5. Jayabalan B, Low LL. Vitamin B supplementation for diabetic peripheral neuropathy. *Singapore Med J* 2016;57(2): 55-59.
 6. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2005; 28: S37-42.
 7. Andres E, Loukili NH, Noel E. Vitamin B12 deficiency in elderly patients. *CMAJ* 2004;171: 251-9.
 8. Head KA, Peripheral neuropathy: pathogenic mechanisms and alternative therapies. *Altern Med Rev* 2006; 11: 294-329.
 9. Farvid MS, Homayouni F, Amiri Z, Adelmanesh F. Improving neuropathy scores in type 2 diabetic patients using micronutrient supplementation. *Diabetes Res Clin Pract* 2011;93: 86-94.
 10. Atkinson MA, Eisenbarth GS. Type 1A diabetes: new perspectives on disease pathogenesis and treatment. *Lancet* 2001; 358: 221-9.
 11. Jacobs AM, Cheng D. Management of diabetic small-fiber neuropathy with combination L-methylfolate, methylcobalamin, and pyridoxal 5'-phosphate. *Rev Neurol Dis* 2011; 8: 39-47.
 12. Pflipsen M, Oh R, Saguil A, Seehusen D, Topolski R: The Prevalence of Vitamin B12 Deficiency in Patients with Type 2 Diabetes: A Cross-Sectional Study. *J Am Board Fam Med* 2009;22: 528-34.
 13. Bell D: Metformin-induced vitamin B12 deficiency presenting as a peripheral neuropathy. *South Med J* 2010;103: 265-7.
 14. Ting R, Szeto C, Chan M, Ma K, Chow K: Risk Factors of Vitamin B12 Deficiency in Patients Receiving Metformin. *Arch Int Med* 2006;166: 1975-9.
 15. Loikas S, Koskinen P, Irjala K: Vitamin B12 deficiency in the aged: a population-based study. *Age and Ageing* 2007; 36: 177-83.
 16. Shobhaa V, Tareya S, Singh R: Vitamin B12 deficiency and levels of metabolites in an apparently normal urban south Indian elderly population. *Indian J Med Res* 2011, 134: 432-9.
 17. Klee G: Cobalamin and folate evaluation: measurements of methylmalonic acid and homocystein vs vitamin B12 and folate. *Clin Chem* 2000;46: 1277-83.
 18. Sun Y, Lai M, Lu C: Effectiveness of Vitamin B12 on Diabetic Neuropathy: Systematic Review of Clinical Controlled Trials. *Acta Neurol Taiwan* 2005;14: 48-54.
 19. Talaei A, Siavash M, Majidi H, Chehrei A: Vitamin B12 may be more effective than nortriptyline in improving painful diabetic neuropathy. *Int J Food Sci Nutr* 2009;60: 71-6.
 20. Khan MA, Wakefield GS, Pugh DW. Vitamin B12 deficiency and diabetic neuropathy. *Lancet* 1969; 2: 768-70.