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Occurrence of Vitamin B 12 Deficiency in Patients Presenting with Chronic Inflammatory Demyelinating Polyneuropathy

Hikmatullah, Asif Hashmat, Wasim Alamgir, Muhammad Ali Yousaf, Hassan Tariq*

Department of Neurology, Pak Emirates Military Hospital/National University of Medical Sciences (NUMS), Rawalpindi Pakistan, *Department of Pathology, Armed Forces Institute of Pathology/National University of Medical Sciences (NUMS), Rawalpindi Pakistan

ABSTRACT

Objective: To determine the frequency of vitamin B 12 deficiency among the patients presenting with chronic inflammatory demyelinating polyneuropathy.

Study Design: Correlational study.

Place and Duration of Study: Department of neurology, Pak Emirates Military Hospital, Rawalpindi Pakistan, from Apr 2020 to Sep 2020.

Methodology: A total of 240 patients of chronic inflammatory demyelinating polyneuropathy diagnosed by consultant neurologist were included in the study. Vitamin B 12 deficiency was diagnosed on the basis of serum B 12 levels done at chemical pathology department of laboratory of own hospital by standard method. Relationship of age, gender, body mass index and duration of chronic inflammatory demyelinating polyneuropathy was assessed with the presence of iron vitamin B 12 deficiency among the chronic inflammatory demyelinating polyneuropathy patients participating in this study.

Results: Out of 240 chronic inflammatory demyelinating polyneuropathy patients studied in the given time period, 204(85%) had no Vitamin B12 deficiency while 36(15%) had presence of clinically significant B 12 deficiency. 168(70%) patients were male while 72(30%) were female. After applying the binary logistic regression analysis, we found that longer duration chronic inflammatory demyelinating polyneuropathy had a statistically significant association with presence of vitamin B12 deficiency in the target population (p-value<0.001).

Conclusion: This study showed a high frequency of Vitamin B 12 deficiency among the patients presenting with chronic inflammatory demyelinating polyneuropathy in our hospital. Patients with longer duration of chronic inflammatory demyelinating polyneuropathy should be considered at high risk for developing the deficiency cobalamin.

Keywords: Chronic Inflammatory Demyelinating Polyneuropathy, Deficiency, Vitamin B12.

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INTRODUCTION

Chronic inflammatory demyelinating polyneuropathy (CIDP) has been diagnosed more frequent in recent years due to advancement in understanding of neurological disorders and availability of modern neuro-diagnostic modalities.[1] It involves both proximal and distal group of muscles and becomes a multisystem disorder instead of just being a neuropathy.[2] Studies so far have given an immunological etio-pathogensis of this disorder and immunoglobulins remain treatment of choice for this chronic debilitating neurological condition.[3]

Vitamin B12 or cobalamin has been an important factor in multiple metabolic pathways of human body. Its deficiency may be due to multiple causes related to decreased intake, impaired metabolism and absorption.[4] Manifestations of this important vitamin may vary in patients from being asymptomatic to severe hematological or neurological complications.[5] Neuropathies have been a well-documented manifestation of vitamin B 12 deficiency.[6] Sometime there may be same underlying immune mediated process which may be responsible for B 12 deficiency and neuropathy or Vitamin B 12 deficiency may add to the symptoms generated by primary neuropathy which may be immunological in origin.[5,6]

A lot of work has been done to look for relationship of Vitamin B 12 with various types of primary and secondary neuropathies. An interesting study was done by Roy *et al.*, in 2016 regarding Vitamin B 12 deficiency among patients having neuropathy secondary to metformin use in diabetic patients.[7] They came up with the conclusion that metformin use was related to decrease in vitamin B 12 levels leading to significant neuropathic symptoms among patients suffering from diabetes mellitus.[7] Franques *et al.*, published an important study in 2019

Correspondence: Dr Hikmatullah, Department of Neurology, Pak Emirates Military Hospital, Rawalpindi Pakistan

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highlighting that Vitamin B 12 supplementation in various form of neuropathies may reduce the symptom burden in patients therefore whatever the cause of neuropathy may be, vitamin B 12 levels may be assessed and supplementation may be done.[8] Torre *et al.,* in 2012 did a similar analysis and came up with the findings that sensory neuropathy respond quite well to cobalamin supplementation and symptoms of patients have significant reduction after adequate trial of Vitamin B 12.[9]

Advancement in diagnostics and increase in number of neurologists in past few years have revolutionized neurology in our part of the world. Chronic inflammatory demyelinating polyneuropathy has been diagnosed more frequently in last decade and also been diagnosed with other immune based disorders.[10] Vitamin B 12 deficiency may have multiple etiological factors and there may be cause and effect relationship between vitamin B 12 deficiency and CIDP. We therefore planned this study with the rationale to determine the frequency of vitamin B 12 deficiency and associated socio-demographic factors among the patients presenting with chronic inflammatory demyelinating polyneuropathy.

METHODOLOGY

This correlational study was conducted at the department of neurology in Pak Emirates Military Hospital, Rawalpindi Pakistan, from Apr 2020 to Sep 2020. Sample size was calculated by WHO Sample Size Calculator with population prevalence proportion of cobalamin deficiency in neuropathic patients as 8%.[11] Nonprobability Consecutive sampling technique was used to gather the sample. All patients between the age of 18 and 65 years diagnosed by consultant neurologist were included in the study. CIDP was diagnosed on the basis of clinical picture, cerebrospinal fluid analysis, nerve conduction studies and nerve biopsy.[12] Exclusion criteria were the patients with anemias prior to diagnosis of CIDP, malignancies (solid or hematological), severe infection or any organ failure in past six months. Patients who had already diagnosed B-12 or folate deficiency or replacement therapy, had recent surgery, had neuropathy secondary to any identifiable cause or any autoimmune disorder those who were using illicit drugs or those whose follow up was not possible were also excluded from the study.

Ethical review board committee of the hospital was approached to get the ethical approval for this study (via letter number A/28/61). Written informed consent was taken from all the potential participants of this study before the start of study after complete description of the study. Patients with CIDP fulfilling the above-mentioned inclusion and exclusion criteria presenting in the neurology OPD were included in the study. Venous blood was taken from the participants between 9 and 11 a.m. after 12 hours of fasting. Complete blood count (CBC), serum ferritin, vitamin B12, and folic acid were measured by routine methods in chemical pathology department of laboratory of our own hospital. Socio demographic variables were also collected. Variables in the study included age, BMI, gender and duration of illness. Vitamin B 12 deficiency was defined as serum cobalamin values of <100 pg/ml.[13]

Characteristics of participants and the distribution of the vitamin B 12 deficiency were described by using the descriptive statistics. Binary logistic regression analysis was done to evaluate the relationship of age, gender, BMI and duration of chronic inflammatory demyelinating polyneuropathy. All statistical analysis was performed using Statistics Package for Social Sciences version 24.0 (SPSS-24.0). Chi-square and then binary logistic regression analysis was done to look for the correlation of different variables with presence of vitamin B 12 deficiency among the study participants. Differences between groups were considered significant if *p*-values were less than or equal to 0.05.

RESULTS

Out of 240 chronic inflammatory demyelinating polyneuropathy patients studied in the given time period, 204(85%) had no Vitamin B12 deficiency while 36(15%) had presence of clinically significant B 12 deficiency. 168(70%) patients were male while 72(30%) were female. Table-I shows the general characteristics of the study participants. Mean age of the study participants was 52.24±5.512 years. Table-II shows that chi-square test reveals that long duration of illness had statistically significant relationship with vitamin B 12 deficiency (*p*-value<0.01). After applying the binary logistic regression analysis (Table-III), it was confirmed that longer duration chronic inflammatory demyelinating polyneuropathy had a statistically significant association with presence of vitamin B12 deficiency in the target population (*p*-value<0.001) while age, gender and body mass index had no such relationship with vitamin B 12 deficiency.

Table-I: Characteristics of Patients with Chronic Inflammatory Demyelinating Polyneuropathy Included in Study (n=240)

Factors	Values
Age (years)	
Mean+SD	52.24±5.512 years
Range (min-max)	31 -64 years
Gender	
Male	168(70%)
Female	72(30%)
Presence of Vitamin B 12 deficiency	
No	204(85%)
Yes	36(15%)
Duration of chronic inflammatory demyelinating polyneuropathy	
>2 years	183(76.3%)
≤ 2 years	57(23.7%)
Mean Duration of chronic inflammatory demyelinating polyneuropathy	3.57±2.91 years

Table-II: Relationship of Various Factors with Vitamin B 12 Deficiency (n=240)

	Normal levels of vitamin B 12 (n=204)	Deficiency of vitamin B 12 (n=36)	*p*-value
Age			
40 year or less	54(26.5%)	08(22.3%)	0.586
>40 years	150(73.5%)	28(77.7%)	
Gender			
Male	144(70.5%)	24(66.7%)	0.639
Female	60(29.5%)	12(33.3%)	
Body mass index			
Normal	141(69.2%)	21(58.3%)	0.210
Overweight or obese	63(30.8%)	15(41.7%)	
Duration of illness			
<2 years	167(81.8%)	16(44.4%)	<0.001
>2 years	37(18.2%)	20(55.6%)	

Table-III: The Correlated Factors Relating to Presence of Vitamin B 12 Deficiency among the Patients of Chronic Inflammatory Demyelinating Polyneuropathy

	p-value	Odds ratio	Confidence interval
			Lower-upper
Age (ref. was 40 years or less)	0.571	1.300	0.524-3.222
Duration of illness (reference was <2 years)	< 0.001	6.226	2.881-13.453
Body mass index (ref. was <25)	0.070	2.077	0.941-4.584
Gender (ref. was male)	0.455	1.363	0.605-3.070

DISCUSSION

Different types of neuropathies make a good chunk of illnesses encountered by neurologists in routine outpatient department.[2] Previously diagnosis remained ambiguous, as only clinical picture was the main stay of diagnosing these debilitating painful conditions. Recent advancement in cerebrospinal fluid markers, histopathological support and nerve conduction studies have made the diagnostic picture quite clear and neurologist in our part of the world have been diagnosing these conditions with more confidence and authority. Chronic inflammatory demyelinating polyneuropathy has been a fairly common diagnosis in our set up among all other neuropathies. Though immune based pathogenesis of CIDP has been well established still a lot of work has been going on to find other factors and comorbidities related to this chronic neuropathy.[13,14] We therefore designed this study with the rationale to determine the frequency of vitamin B 12 deficiency among the patients presenting with chronic inflammatory demyelinating polyneuropathy.

Farhad *et al.,* in 2016 performed an interesting study to look for the causes of neuropathy among patients which have been labelled as idiopathic. Their findings revealed that diabetes or impaired glucose metabolism was the commonest cause of poly-neuropathy previously labelled as idiopathic followed by CIDP and other causes. Vitamin B 12 deficiency was established as a cause in minority of the patients.[15] Mandate of our study was different from Farhad *et al.,* as we included diagnosed cases of CIDP and found that 15% of the patients diagnosed as CIDP had comorbid cobalamin deficiency.

Sachedina *et al.,* in 2013 studied progression of various neuropathies including B 12 deficiency neuropathy.[16] They concluded that idiopathic neuropathies, when followed up for some time might get diagnosed with an identifiable and treatable cause. Results of Vitamin B 12 administration without actual deficiency were debatable. We provided a baseline data that a considerable number of patients with CIDP have B 12 deficiency as well. Researchers in future may find the basis for this finding and trials may be conducted to look for improvement in these patients after administration of cobalamin.

Ricci *et al.,* published their experience of single center in 2019 regarding etiology of patients having neuropathies. Vitamin B 12 deficiency was found in 9% of the patients while CIDP was found in 8% of the patients they studied.[17] They concluded that treatable causes of chronic neuropathies, such as dysimmune neuropathies, including CIDP, and celiac disease-associated neuropathy, were common. They suggested that the utility of routine screening with blood testing for dysimmune neuropathy and celiac disease for all patients presenting with idiopathic chronic polyneuropathy in whom primary diagnostic testings

had failed to identify an etiology for the disease. Our results supported their findings as diagnosed cases of CIDP when tested for Vitamin B 12 levels, 15% were found deficient with long standing illness as a risk factor for cobalamin deficiency.

Another relevant study was published from our neighboring country China highlighting the etiological factors and clinical profile related to neuropathies which appear after stem cell transplant. Forty patients in 10 years developed the neuropathies after stem cell transplant and out of these more than 60% showed improvement in neurological symptom after the administration of vitamin B 12.[18] This highlights the fact that either immune mediated mechanism leads to neuropathy and B 12 deficiency both or one of these occurs first and might lead to other. Whatever the causative pathway may be various studies including our study showed that B 12 deficiency may be found in considerable number of patients with neuropathies other than Vitamin B 12 deficiency neuropathy including the CIDP.

It was a single center survey and data was collected from a military hospital which may not represent the whole population. Exclusion criteria included other diseases which may interfere with vitamin B 12 levels but we did not include the nutritional assessment and deficiencies which may cause vitamin B 12 deficiency. Cross-sectional study design also posed some methodological issues which may be a hindrance in generalization of the results.

CONCLUSION

This study showed a high frequency of Vitamin B 12 deficiency among the patients presenting with chronic inflammatory demyelinating polyneuropathy in our hospital. Patients with longer duration of chronic inflammatory demyelinating polyneuropathy should be considered at high risk for developing the deficiency cobalamin.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

H & AH: Data acquisition, data analysis, critical review, approval of the final version to be published.

WA & MAY: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

HT: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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