

Original Research Article

Relationship between serum vitamin B12 level, sociodemographic variables, and medical comorbidity in psychiatric in-patients

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ABSTRACT

Background: To compare serum vitamin B12 levels in psychiatric in-patients and their caregivers and, to study the relationship between psychiatric diagnosis and vitamin B12 levels in psychiatric in-patients.

Methods: Adult psychiatric in-patients (n=103) and their adult caregiver (n=103) were enrolled in the present cross-sectional study. All participants underwent estimation of serum vitamin B12, complete blood counts, mean corpuscular volume (MCV), serum folate, and serum ferritin.

Results: Vitamin B12 deficiency was found more frequently (60.2%) in psychiatric patients compared to their caregiver (3.9%) (p=0.000). Psychiatric in-patients were significantly younger in age, with a lower level of serum vitamin B12 and folate, fewer numbers of polymorphs, and more numbers of lymphocytes in their peripheral compared to their caregivers. There was no statistically significant difference in socio-demographic variables such as food habit, gender, residence (rural/urban), and occupation between those patients who were deficient and those who were non-deficient in vitamin B12. There was no statistically significant difference between the psychiatric diagnoses and comorbidities in patients with and without vitamin B12 deficiency. Patients with vitamin B12 deficiency were also not different in terms of their psychiatric diagnosis and associated comorbidities when compared with the patient without vitamin B12 deficiency.

Conclusions: Around 60% of psychiatric inpatients have low serum vitamin B12 levels. Lifestyle-related factors and chronic medical illness likely contribute to vitamin B12 deficiency in psychiatric in-patients. Adult psychiatric patients with other medical comorbidities should be screened for vitamin B12 deficiency.

Keywords: Vitamin B12, Comorbidities, Psychiatric, In-patients, Folate, Depression, Anxiety

INTRODUCTION

Vitamin B12, also called Cobalamin, a water-soluble essential vitamin, has a vital role in DNA synthesis during cell division.¹ It is also linked with the synthesis of neurotransmitters such as dopamine and serotonin, and thus has been implicated in the pathogenesis of various neuropsychiatric disorders.² In earlier times, a one carbon hypothesis of schizophrenia was hypothesized, citing impaired transmethylation leading to an accumulation of toxic metabolites.³

Psychiatric manifestations of vitamin B12 deficiency can include depression, apathy, irritability, dementia, catatonia, delirium and hallucinations.^{4,5} Higher vitamin B12 levels are thought to be associated with more favorable outcome in depression.⁶ A study in general psychiatric in patients, Brett AS, Roberts MS⁷ reported the incidence of vitamin B12 deficiency to be 4%-6%.⁷ Neuropsychiatric abnormalities (i.e. peripheral neuropathy, dementia, cognitive impairment, subacute combined degeneration of the cord, demyelinating disorder) are reported to be present in up to 28% of

patients in the absence of any change in the hematocrit value or increase red cell mean corpuscular volume, these indices are usually the most commonly investigated for vitamin B12 deficiency. Hence vitamin B12 level estimation is warranted in such conditions.

Even though the human body can store vitamin B12 to last for up to five years, its deficiency is not very uncommon. The diagnosis is frequently made on the basis of low serum vitamin B12 level.^{8,9}

It has been asserted that carrying out vitamin B12 assay on psychiatric patients will enable doctors to cure several disabling diseases which otherwise may end in chronicity.¹⁰ Several patients have been reported in whom mental symptoms apparently responded dramatically to vitamin B12 replacement.¹¹

On the background of this information available, we hypothesized that quite a big number of psychiatric patients in our set up will have vitamin B12 deficiency and prediction of this deficiency could be done based on same socio-demographic and clinical parameters.

This study was aimed to compare serum vitamin B12 levels among different type of psychiatric illness who got admitted in psychiatric ward and to assess the relationship between psychiatric illness and vitamin B12 level.

METHODS

The design of the study was of comparative cross-sectional type. It was conducted in the Departments of Psychiatry and Biochemistry of G.B. Pant Hospital, New Delhi between January 2019 to December 2019. In this study Psychiatric patients who were admitted to the psychiatry ward of GIPMER New Delhi were included. The sample of this study was consisted of 206 participants out of them 103 were psychiatric patients and 103 were their family members.

Selection criteria

Psychiatric patients

Inclusion criteria: Patient who got admitted in the psychiatric ward. Patients who were 18 years and above.

Exclusion criteria: Those who are not consenting for the study. Those who did not have available care giver as per inclusion and exclusion criteria. Those who were already on vitamin B12 supplementation as treatment.

Care giver of psychiatric patient's

Inclusion criteria: Care-giver of patient sharing same kitchen as that of patient (who looked after the index patients most). Care-giver who was of 18 years or above.

Exclusion criteria: Those who are not consenting for the study.

Study procedure

Consecutive psychiatric patients admitted in the psychiatry ward of G. B. Pant Hospital along with their care-giver (controls), were taken up for the study, after inclusion and exclusion criteria were fulfilled. Diagnosis of psychiatric illness in psychiatric patients were made as per DSM-5 diagnostic criteria and the diagnosis was validated by the treating consultant psychiatrist. Thus, the patients were evaluated only once during this study. Information were gathered as per the Semi-structured Performa designed specifically for the study. After proper informed consent from both patients and care giver blood samples of both were taken and sent to the Department of Biochemistry, GIPMER for estimation of serum vitamin B12 level, CBC, MCV, Serum folate, Serum ferritin. The patients were then assessed and scored on the Global Assessment of Functioning (GAF) scale. Serum vitamin B12 was estimated in the department of Biochemistry, GIPMER by Roche Elecsys modular Cobas e411 using electrochemiluminescence immune assay (Manheim Germany) kits of which is commercially available from Roche. The study considered biochemical vitamin B12 deficiency when the serum concentration was below <200 pg/ml. Ethical clearance had been obtained from the institutional ethical board of MAMC, prior to the onset of the study.

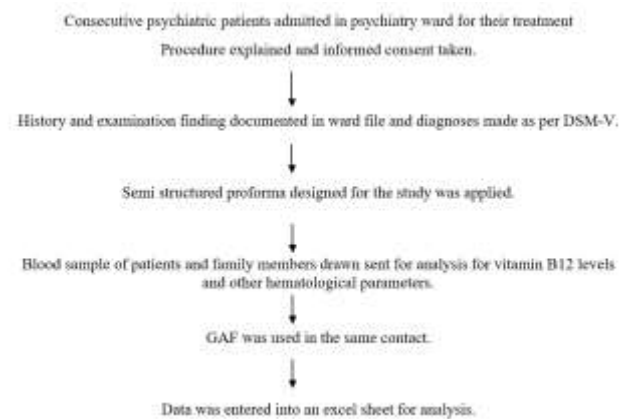


Figure 1: Data collection flow chart.

Sample size

The sample of this study consisted of 206 participants, out of which 103 were psychiatric patients and 103 were their family members.

$$N = Z_{1-\alpha/2}^2 * P(1 - P) / d^2$$

RESULTS

Majority of patients of both the group belonged to the male gender (p=0.262). Psychiatric patients were less

frequently married ($p=0.000$), more frequently jobless ($p=0.000$) and had more medical comorbidities ($p=0.01$) as compared to their care givers. Psychiatric patients in comparison to their care giver were significantly younger in age ($p=0.000$) with lower level of serum vitamin B12 ($p=0.000$), less numbers of polymorph ($p=0.037$) and more numbers of lymphocytes ($p=0.016$) in their peripheral blood and lower level of serum folate ($p=.031$). But the age and the number of polymorph and lymphocytes in peripheral blood, serum level of folate in patient with vitamin B12 deficient ($n=62$) were not different from patients without vitamin B12 deficiency ($n=41$). MCV was not different either between patients and their care givers, or between patients with vitamin

B12 deficiency and patients without vitamin B12 deficient. Vitamin B12 deficiency was found more frequently (60.2%) in psychiatric patients compared to their care giver (3.9%) ($p=0.000$). It did not find any difference in socio-demographic variables like food habit, gender socioeconomic status, residence (rural/urban) and occupation between those patients who were deficient and those who were non-deficient in vitamin B12 level. Patients with vitamin B12 deficiency were also not different in terms of their psychiatric diagnosis and associated comorbidities when compared with patient without vitamin B12 deficiency. As the serum vitamin B12 level reduced in patients with vitamin B12 deficiency, MCV got increased ($p=0.002$).

Table 1: Socio-demographic factors (categorical) between psychiatric in-patients and their care giver (n=206).

		Patients (%) (n=103)	Care givers (%) (n=103)	X ² /Fisher's Exact Test (df)	P value
Gender	Male	61 (59.2)	53 (51.5)	1.25 (1)	0.262
	Female	42 (40.8)	50 (48.5)		
Occupation	Job	36 (35.0)	41 (39.8)	17.94 (3)	0.000*
	Home maker	30 (29.1)	48 (46.6)		
	Student	22 (21.4)	4 (3.9)		
	Unemployed	15 (14.6)	10 (9.7)		
Marital status	Unmarried/divorced/widowed	37 (35.9)	12 (11.7)	16.73 (1)	0.000*
	Married	66 (64.1)	91 (88.3)		
Comorbidity	Nil	90 (87.4)	102 (99.0)	11.41 (3)	0.010*
	CAD/HTN/DM-II	5 (4.9)	1 (1.0)		
	Hypothyroidism	3 (2.9)	0 (0)		
	Seizure disorder/ Alzheimer's disorder/cervical disease	5 (4.9)	0 (0)		

CAD-Coronary artery disease, HTN-Hypertension, DM-II Diabetes mellitus type –II, *when p value <0.05 (significant).

Table 2: Difference of socio-demographic and clinical data between psychiatric in-patient and their care giver (n=206).

	Patients Mean (SD) (n=103)	Care givers Mean (SD) (n=103)	t (df)	P value
Age (yrs)	33.68 (12.13)	42.66 (12.77)	-5.17 (204)	0.000*
Education (yrs)	7.44 (4.48)	6.95 (4.92)	0.75 (204)	0.451
BMI	20.71 (3.68)	21.27 (2.72)	-1.24 (204)	0.216
Vitamin B12	212.19 (120.86)	413.60 (176.22)	-9.5 (204)	0.000*
Haemoglobin	13.40 (1.61)	13.47 (1.27)	-0.31 (204)	0.756
TLC	6433.20 (1283.72)	6551.7087 (1176.06)	-0.69 (204)	0.490
Polymorph	58.02 (8.19)	60.24 (6.85)	-2.10 (204)	0.037*
Lymphocytes	30.32 (8.00)	27.71 (7.27)	2.44 (204)	0.016*
MCV	89.77 (6.35)	89.81 (5.02)	-.049 (204)	0.961
Serum folate	9.08 (4.74)	11.83 (11.92)	-2.17 (204)	0.031*
Serum ferritin	94.54 (63.55)	106.88 (50.23)	-1.54 (204)	0.124

BMI-Body mass index, TLC-Total leukocyte count, MCV-Mean corpuscular volume, *when p value <0.05 (significant).

Table 3: Difference of state of vitamin B12 levels (normal or deficiency) between patients and care giver (n=206).

Vitamin B12 level	Patients (%), (n=103)	Care giver (%), (n=103)	X ² /Fisher's Exact Test (df)	P value
Normal	41 (39.8)	99 (96.1)	74.99 (1)	0.000*
Deficiency	62 (60.2)	4 (3.9)		

*when p value <0.05 (significant).

Table 4: Difference of socio-demographic (categorical variables) between patients with normal vitamin B12 levels and patients with deficiency of vitamin B12 levels (n=103).

		Patients with normal vitamin B12 level (%) (n=41)	Patients with deficiency of vitamin B12 level (%) (n=62)	X ² /Fisher's exact test (df)	P value
Gender	Male	21 (51.2)	40 (64.5)	1.80 (1)	0.179
	Female	20 (48.8)	22 (35.5)		
Food habit	Vegetarian	9 (22.0)	24 (38.7)	3.18 (1)	0.074
	Non vegetarian	32 (78.0)	38 (61.3)		
Residence	Urban	30 (73.2)	50 (80.6)	0.79 (1)	0.373
	Rural	11 (26.8)	12 (19.4)		
Occupation	Job	12 (29.3)	24 (38.7)	2.88 (3)	0.409
	Homemaker	12 (29.3)	18 (29.0)		
	Student	12 (29.3)	10 (16.1)		
	Unemployed	5 (12.2)	10 (16.1)		
Socio-economic status (function)	Lower	18 (43.9)	24 (38.7)	0.95 (2)	0.621
	Lower middle	18 (43.9)	26 (41.9)		
	Upper middle	5 (12.2)	12 (19.4)		
Marital-status	UM/D/W	17 (41.5)	20 (32.3)	0.90 (1)	0.341
	Married	24 (58.5)	42 (67.7)		
Family type	Nuclear	41 (100.0)	61 (98.4)	0.66 (1)	0.414
	Joined	0 (0.0)	1 (1.6)		
Religion	Hindu	22 (53.7)	37 (59.7)	0.36 (1)	0.546
	Muslim	19 (46.3)	25 (40.3)		

UM-unmarried, D-Divorced, W-Widowed.

Table 5: Difference between socio-demographic and clinical data (continuous variables) between patients with normal vitamin B12 levels and patients with deficiency of vitamin B12 levels (n=103).

	Patients with normal vitamin B12 levels mean (SD) (n=41)	Patients with deficiency of vitamin B12 levels mean (SD) (n=62)	T (df)	P value
Age (yrs)	33.24 (12.73)	33.98 (11.81)	- 0.302 (101)	0.764
Education (yrs)	6.95 (4.24)	7.77 (4.63)	-0.911 (101)	0.364
Total family income	13097.56 (13542.16)	12758.06 (10523.487)	0.143 (101)	0.887
BMI	20.55 (3.23)	20.82 (3.97)	0.372 (101)	0.711
Haemoglobin	13.08 (1.65)	13.62 (1.56)	-1.688 (101)	0.095
TLC	6373.65 (1427.46)	6472.58 (1189.73)	-0.381 (101)	0.704
Polymorph	58.46 (7.57)	57.74 (8.62)	0.436 (101)	0.664
Lymphocytes	31.19 (7.500)	29.74 (8.33)	0.901 (101)	0.370
Monocytes	5.68 (2.94)	5.46 (2.10)	0.432 (101)	0.667
MCV	88.70 (6.70)	90.48 (6.05)	0-1.403 (101)	0.164
Serum folate	9.500 (4.50)	8.81 (4.90)	0.718 (101)	0.474
Serum ferritin	105.90 (78.00)	87.04 (51.18)	1.48 (101)	0.141
GAF	46.44 (18.59)	47.44 (17.82)	-0.273 (101)	0.785

BMI-Body mass index, TLC- Total leukocyte count, MCV-Mean corpuscular volume, GAF-Global assessment of functioning scale.

Table 6: Correlation between serum vitamin B12 levels and socio-demographic and clinical data in psychiatric in-patients (n=103) and their care givers (n=103).

	Patient's serum vitamin B12 levels Pearson's correlation(p)	Care giver's serum vitamin B12 levels Pearson's correlation (p)
Age (yrs)	0.143 (0.150)	0.028 (0.780)
Education year	-0.138 (0.163)	-0.063 (0.529)
Total family income	-0.32 (0.748)	
BMI	-0.008 (0.934)	-0.01 (0.920)

Continued.

	Patient's serum vitamin B12 levels Pearson's correlation(p)	Care giver's serum vitamin B12 levels Pearson's correlation (p)
Haemoglobin	-0.167 (0.091)	0.073 (0.465)
TLC	0.161 (0.104)	-0.156 (0.115)
Polymorph	0.104 (0.294)	-0.089 (0.372)
Lymphocytes	-0.065 (0.513)	-0.141 (0.157)
Monocytes	-0.016 (0.876)	-0.099 (0.321)
MCV	-0.298 (0.002)*	0.042 (0.670)
Serum folate	0.037 (0.713)	0.118 (0.234)
Serum ferritin	0.008 (0.939)	0.189 (0.056)
GAF	-0.10 (0.921)	

BMI-Body mass index, TLC- Total leukocyte count, MCV-Mean corpuscular volume, GAF-Global assessment of functioning scale.

DISCUSSION

Majority of the psychiatric patients of this study enrolled were young, unmarried and jobless. Majority of patients were suffering from chronic mental illness like schizophrenia/schizoaffective, bipolar type-II/ major depressive disorder, neurotic/substance disorder. These illnesses themselves may helped these patients to be jobless and keep unmarried. Mental health problems affect functional and working capacity in numerous ways. Depending on the age of onset of a mental health disorder, an individual's working capacity may be significantly reduced. Mental disorders are usually one of the three leading causes of disability, together with cardiovascular disease and musculo-skeletal disorders. In the European Union (EU), mental health disorders are a major reason for granting disability pensions.¹²

Most of the mental disorders begin in adolescence and early adulthood, with these disorders now revealed as the major contributors to the burden of psychiatric illness in young people.¹³

Serum vitamin B12 level and serum folate level of psychiatric patients were significantly lower in psychiatric patients than that of their care giver. 60.2% of psychiatric patient had vitamin B12 deficiency and only 3.9% of their care giver had vitamin B12 deficiency. Hermesh et al, found 20% of their reviewed obsessive compulsive disorder patients to have low vitamin B12 level compared to control group (healthy individuals).¹⁴ Major depressive disorder patients of Levit and Joffe, similarly had observed low vitamin B12 level associated with early age of onset.¹⁵ The same authors reported (Levit and Joffe) that psychotic depression was different from non-psychotic depression in term of low vitamin B12 level.¹⁵

Only four psychiatric patients of our study had intellectual disabilities/ dementia. The authors like Renvoize et al, Rawlinson and Eagles, and Hector and Burton, reviewed cases of dementia and attributed many of them to be suffering from vitamin B12 deficiency.¹⁶⁻¹⁷

Vitamin B12 is naturally found in animal food product, including meat, poultry, shell fish, egg milk, and other

dairy products.^{18,19} As psychiatric patients and their care givers lived under the same roof and shared same food, possibly the source of vitamin B12 had less contribution and the illness itself may have contributed to vitamin B12 deficiency in the psychiatric patient.

Comorbidities like coronary artery disease, hypertension, diabetes mellitus type-II, were higher in frequency in the psychiatric patients because probably of neglect of healthy life style.²⁰⁻²²

Psychiatric patients with vitamin B12 deficiency did not differ from those without vitamin B12 deficiency in term of age of presentation, psychiatric diagnoses and comorbidities. Thus, psychiatric diagnoses and comorbidities could not be the reason for vitamin B12 deficiency in psychiatric patients. Likewise, chronic infection (because equal number of lymphocytes and polymorph in both the group), food habit (vegetarian/non vegetarian), gender difference, socioeconomic status, residence (rural/urban) and occupation could not be held responsible for vitamin B12 in psychiatric patients (62%) of our study. The studies here presented elaborate on our preliminary reports indicating that folic acid activity piles up in human serum in the presence of vitamin B12 deficiency.^{23,24} The accumulation of this folic acid activity (probably N5-methyl-tetrahydrofolic acid) provides direct evidence of deranged folic acid metabolism due to vitaminB12 deficiency. This folic acid-vitamin B12 interrelationship may explain much of the confusion in therapy of pernicious anemia, as well as the fact that the anemia of vitamin B12 and folic acid deficiencies are hematologically identical.

CONCLUSION

In the index study we found 60.2% of our index psychiatric patients had vitamin B12 deficiency in their serum. It was associated with lower level of serum folate, but not MCV. As the serum vitamin B12 level reduces in patient with vitamin B12 deficiency MCV got increased.

Vitamin B12 deficiency in psychiatric patient possibly could not be attributed to their food habit, gender, socioeconomic status, residence or occupation. It could rather be because of their unhealthy life style or chronic

illness like medical comorbidities. It has been suggested that patients with vitamin B12 deficiency should be treated with supplementation of vitamin B12 to reduce the associated morbidities.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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