ORIGINAL ARTICLE

Low serum vitamin B12 is significantly associated with depression: A cross sectional observational study

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ABSTRACT

Vitamin B12 plays a vital role in the prevention of psychological disorders. Studies have reported the positive impact of vitamin B12 supplementation on cognitive functions. However, epidemiological research on the prevalence of depression in the vitamin B12-deficient adult population is still insufficient. Thus, the present study investigates the prevalence of depression among the vitamin B12-deficient 400 adult participants, whose serum vitamin B12 status was below 200pg/mL, aged between 18 years to 60 years. The sociodemographic profile, anthropometric assessment and presence or absences of clinical symptoms were recorded via self-administered questionnaire. Participants were divided in Vitamin B12 insufficient and deficient group. Depression was screened by Beck- Depression Inventory II (BDI-II) scale, with 21-item self-administered survey. The study reported, 16% participants were from deficient group (serum vitamin B 12 below 150 pg/ml) with mean age 43.2±10.5 years. Depressive symptoms were found inversely associated with serum vitamin B12 levels. A significant association (at $p<0.05$) was found with age (chi sq=44.09, d.f.= 2, and p=0.001), gender (chi sq=7.91, d.f.= 1, and p=0.0048), body mass index (chi sq=12.97, d.f.= 2, and p=0.022), metformin usage (chi sq=8.31, d.f.= 2, and p=0.015), religion (chi sq=7.54, d.f.= 2, and p=0.022), income group (chi sq=5.71, d.f.= 2, and p=0.04), food preferences (chi sq=18.95, d.f.= 2, and p=0.00007) and clinical symptoms. The odds (CI) of depression among vitamin B12 deficient participants were found 5.88 (2.81-12.32), making it an independent predictor of depression. After adjusting with confounding variables, the association remained the same. The study revealed that the adult population with reduced vitamin B12 levels has higher probabilities of developing depression, and the chances increased with age. Thus, early detection and low cost supplementation should be implemented to combat vitamin B12 deficiency and its complications.

Key words:
Beck- Depression Inventory II, vitamin B12 deficiency, s-Adenosylmethionine, depression, sign and symptoms.

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INTRODUCTION

Water soluble vitamins, particularly those of the Vitamin B group, are essential for various biochemical and physiological functions. Although these vitamins are required in minimal amounts, deficiency of them may cause, anaemia, neurological disorders, abnormal growth, fatigue, anxiety, and stress.[1] Vitamin B12 deficiency is highly prevalent in the older population, and its deficiency is associated with poor or delayed antidepressant therapeutic response. This leads to the highest death rates and the conditions impose a significant strain on the healthcare system.[2] Vitamin B12 acts as a co-factor in methylation reaction for converting homocysteine to methionine, followed by S-Adenosylmethionine (SAM), which acts as a universal donor of methyl group for purine synthesis. The deficiency of vitamin B12 causes altered metabolism of neurotransmitters, phospholipids, and oxidative stress.[3] These neurotoxic effects can lead to mood swings, cognitive impairments, anxiety, and depression. In addition to the serum vitamin B12 levels, other sociodemographic profiles, body mass index, presence of co-morbid diseases, and food preferences also play a major role in its deficiency. The presence of Type-II diabetes, when treated with metformin, can cause low serum B12 levels, due to abnormal absorption[1]. Since animal food products are the richest sources of cobalamin, a study has reported a positive association between a meatless diet and depressive symptoms. Other than this, gastric atrophy, inflammatory bowel diseases, gastric bypass, or poor dietary intake of vitamin B12 can lead to low serum vitamin levels.[4-6]

Depression creates a range of psychological and physical symptoms, such as thoughts of worthlessness, being overburdened, miserable, lacking confidence, muscle discomfort, and headache, all of which decrease the patient's capabilities and well-being. In the past, older people were more likely to experience depression, but the scenario is changing as a result of lifestyle disorders and the rise in concomitant conditions. Furthermore, anti-depressive drugs such as selective serotonin reuptake inhibitors (SSRA) or tricyclic antidepressants (TCA), are used for treatment, however, prolonged usage of these drugs can lead to major adverse reactions including violent behaviour, suicidal thoughts, psychosis, or irregular bleeding.[7] The supplementation of vitamin B12 increases the effectiveness of anti-depressive drugs.[8-10] Several experimental researches have been conducted in the past to establish the role of vitamin B12 in recovery from depression. However, the presence of depressive symptoms in the vitamin B12 deficient population has not yet been studied. The occurrence of depression is not limited to the elderly population, but due to lifestyle changes and innovative dietary preferences, depressive symptoms are increasing in young and middle-aged adults as well. Therefore, to address these issues and early detection of depression, the study was conducted cross-sectionally on 400 individuals between the ages of 18 and 60. The aim was to investigate the association between vitamin B12 deficiency and depressive symptoms in the Indian population, where wide dietary diversity and religious practices are being followed. Furthermore, the study also assessed the correlation with various sociodemographic risk factors.

METHODOLOGY

Study participants and procedure

This cross-sectional study was conducted at the primary to tertiary care multi-specialty Sharda Hospital, Greater

Noida, India, equipped with an Indian Council of Medical Research, India (ICMR) approved Central Laboratory. The hospital is co-located with the School of Medical Sciences, Sharda University, under the Medical Council of India, Ministry of Health and Family Welfare, Government of India. The hospital provides the facility for thorough medical check-ups as recommended by health care practitioners for both males and females. For the study, ethical approval was obtained from the Institutional Ethical Committee, School of Medical Sciences, Sharda University, Greater Noida, India. The medical records of 430 patients between the age group 18 years to 60 years with a known serum vitamin B12 deficiency (vitamin B12<200pg/ml), between March 2022 to November 2022, were acquired for this investigation.

The data was screened and adopted after primary filtration based on medical diagnosis. Pregnant, lactating women, patients with chronic illnesses such as tuberculosis, pneumonia, cancer, hepatitis, and HIV, and patients with B12 supplementation, individuals above 60 years and below 18 years, were excluded from the study. After applying the excluding and including criteria, 410 individuals were found to be suitable for the study. However, 10 individuals, did not respond, thus the study was conducted on 400 patients. The sample size was calculated based on the prevalence of vitamin B12 using the following formula[11]:

$n = z^2 * p * (1 - p) / e^2$

Where: z = 1.96 for a confidence level (α) of 95%,

p = proportion (expressed as a decimal),

e=margin of error.

The objectives, parameters, and structure of the study were explained to potential volunteers. All participants gave their consent in writing after being fully informed. Serum vitamin B12 level was measured by electron chemiluminescence immunoassay. The demographic information (age, gender, marital status, socioeconomic status, religion, family type, education, geographical location, and employment), anthropometric data as well as the presence of clinical symptoms and illnesses, such as diabetes, drug dosage, and depression were gathered through a self-administered questionnaire.

Sociodemographic Characteristics

All participants were divided into two broader categories: Deficient group (serum vitamin B12≤150pg/mL) and Insufficient group (serum vitamin B12 between 151pg/mL to 200pg/mL). The socio-demographic profiles (age, gender, marital status, socioeconomic status, religion, family type, education, geographical location, and employment) of participants were collected via a semi-structured questionnaire. The questionnaire was internally validated via a pilot study, as per the approach adopted earlier by other researchers[7]. Gender was classified into male and female, and marital status was categorized into married, unmarried, and married discord (separated, widows, conflict), Socioeconomic status categories were based on revised B G Prasad's classification[12] and divided into three categories: High Income Group (HIG), Middle Income Group (MIG) and Lower Income Group (LIG). Educational status was divided as per the highest education level of the participants, geographical location was classified as per their residential address into urban and rural areas.

Anthropometric Assessment

The weight of all the participants was checked using a digital weight balance with 0.1 kg weight accuracy. Participants were asked to stand straight, barefoot with minimum clothing. The height was measured using a stadiometer and participants were asked to stand straight,

barefoot, head straight in Frankfurt position, heels touching the walls. Body Mass Index (BMI) was calculated by the ratio of weight in kilogram to the square of height measured in meters (Kg/mt^2). The BMI was categorized into 4 categories as per WHO: Participants with a BMI<18.5 were classified as Underweight, a BMI between 18.5 to 24.9 was Normal, 25.0 to 29.9 were classified as Overweight, and BMI >30 were called Obese.[13]

Clinical Examination

Physical symptoms and indicators of vitamin B12 insufficiency were examined clinically. The list of symptoms brought on by the lack of vitamin B12 was included in the questionnaire. Patients underwent a physical examination, and questions on the presence or absence of symptoms were marked using two options, Yes and No respectively.

Mental Health Assessment

The Beck Depression Inventory-II (BDI II) scale[14] was used to record depressive symptoms and psychiatric problems. The scale consists of a collection of 21 self-reported group questions, including, 5 typical vitamin B12 deficient depressive symptoms, such as worthlessness, sadness, self-dislike, fatigue, and disturbed sleep patterns. The answers were rated on a 4-point scale ranging from 0 (does not relate to me at all) to 3 (I encounter the issue frequently). The participants were instructed to pick one statement against each question that describes their feelings and symptoms over the last 3 weeks. If more than 2 statements applied equally well, circling the highest number was recommended. The participants with scores>20, were considered to have depressive symptoms, and scores>31, were considered to have severe depression.

Statistical Analysis

Sociodemographic and anthropometric characteristics were explained by descriptive analysis. The baseline characteristics of continuous variables were expressed in mean ± standard deviation. Comparison of sociodemographic characteristics between the two categories of vitamin B12 (deficient and insufficient) and the prevalence of clinically significant depression were analyzed using the chi-square test, for the categorical variables. Logistic regression was used to calculate the Odd Ratio (OR) at 95% confidence intervals (CI) for clinical symptoms and depression according to vitamin B12 levels. Models were adjusted for age, gender, religion, locality, BMI, food preferences, alcohol intake, sleep duration, marital status, and symptoms. All statistical analysis was performed by SPSS (IBM, SPSS version 23.0) and $p<0.05$ was considered significant for all variables.

RESULTS

Baseline Characteristics of Participants

The study involved 400 participants (68.5% female and 31.5% male), whose baseline vitamin B12 levels were below 200pg/ml (Table 1). Among all 400 participants, 16% were deficient (Vitamin B12 below 150pg/ml) with a mean age of 43.2±10.5 years, and 84% had insufficient vitamin B12 levels (Vitamin B12 between 151.00 – 200pg/ml) with a mean age of 38.69±8.45 years. As per the data depicted in Table 1, in both, deficient and insufficient groups, the majority of participants followed Hinduism (71.9% and 73.8%, respectively) and were vegetarian (84.4% and 60.1%, respectively). The majority of participants were overweight (43.8%) in deficient group. Although a non-significant association was found between education status and serum vitamin B12 levels, 81.3% and 83% were educated above intermediate

for both deficient and insufficient categories, respectively.

Vitamin B12 status showed a significant association with age (chi sq=13.58, d.f.= 2, and *p*=0.001), family income (chi sq=5.71, d.f= 2, and *p*=0.04), food preferences (chi sq=14.30, d.f= 2, and *p*=0.0007), gender (chi sq=8.34, d.f= 1, and *p*=0.003) and locality (chi sq=3.88, d.f= 2, and *p*=0.048).

Table 1. Sociodemographic characteristics of study participants according to vitamin B12 levels

Parameters	Total N (%)	Serum Vitamin B12 status		*p* value
		Deficient [Vitamin B12 (<150 pg/ml)]	**Insufficient** [Vitamin B12 (151-200 pg/ml)	
N (%)[a]	400	64 (16%)	336 (84%)	
Female	274 (68.5)	34 (53.12)	240 (71.42)	0.003*
Male	126 (31.5)	30 (46.87)	96 (28.57)	
Religion				
Hindu	294 (73.5)	46 (71.875)	248 (73.80)	0.824
Muslim	90 (22.5)	16 (25)	74 (22.02)	
Others	16 (4)	2 (3.125)	14 (4.17)	
Locality				
(Locality) Rural	250 (62.5)	33 (51.5625)	217 (64.58)	0.048*
Urban	150 (37.5)	31 (48.4375)	119 (35.41)	
BMI(kg/mt2)				
normal	164 (41)	20 (31.25)	144 (42.85)	0.36
obese	36 (9)	6 (9.375)	30 (8.92)	
overweight	144 (36)	28 (43.75)	116 (34.52)	
underweight	56 (14)	10 (15.62)	46 (13.69)	
Age Group				
18-30years	106 (26.5)	12 (18.75)	94 (27.97)	0.001*
31-45years	150 (37.5)	16 (25)	134 (39.88)	
46-60 years	144 (36)	36 (56.25)	108 (32.14)	
Alcohol intake				
No	300 (75)	50 (78.125)	250 (74.40)	0.556
Yes	100 (25)	14 (21.875)	86 (25.59)	
Education				
Intermediate and above	333 (83.25)	53 (82.8125)	280 (83.33)	0.514
Primary and secondary school	67 (16.75)	12 (18.75)	55 (16.36)	
Family Income				
HIG (>5L)	92 (23)	22 (34.375)	70 (20.83)	0.04*
LIG (Less than 2L)	66 (16.5)	8 (12.5)	58 (17.26)	
MIG (2-5L)	242 (60.5)	34 (53.125)	208 (61.90)	
Food Preference				
Eggetarian	52 (13)	2 (3.125)	50 (14.88)	0.0007*
Non vegetarian	92 (23)	8 (12.5)	84 (25)	
Vegetarian	256 (64)	54 (84.375)	202 (60.11)	
Metformin Usage(mg/d)				
0 (No metformin)	150 (37.5)	6 (9.375)	144 (42.85)	0.000002*
>1000	170 (42.5)	38 (59.375)	132 (39.28)	
500-1000	80 (20)	20 (31.25)	60 (17.85)	

Sociodemographic characteristics are represented in numbers with percentage [n (%)]. Significance was calculated using X^2 test, with 95% CI. *Values are significant.

Prevalence of Clinical Symptoms and Depression

The clinical symptoms related to serum vitamin B12 status, are depicted in Table 2. The severity of symptoms was found more prominent in the deficient group, in comparison to the insufficient group. Among all, a large number (98.3%) of participants from the deficient group were suffering from indigestibility-related symptoms and the Odds (CI) of having indigestibility among the vitamin B12 deficient group was 5.57 (1.96-15.76) in reference to the insufficient group. Furthermore, significant associations were found for fatigue (chi sq=4.24, d.f= 1, and p=0.03), dizziness (chi sq=8.6, d.f= 1, and p=0.003), pale skin (chi sq=6.78, d.f= 1, and p=0.009), heartburn (chi sq=9.85, d.f= 1, and p=0.001), indigestibility (chi sq=9.177, d.f= 1, and p=0.002) with deficient and insufficient participants, respectively.

Significant depressive symptoms were found to be associated with participants with vitamin B12 deficiency in comparison to the insufficiency group (Table 3). Among all participants, 8.5% had a BDI score>20, out of which, 47.1% were from the deficient group and 52.9% were from the insufficient group. A higher incidence of depression was found in females (68.5%) compared to males (31.5%) (p=0.004), between the age of 46-60 years (p=0.001), those belonging to Hinduism (p=0.02) and vegetarians.

Table 2. Odds of presence of clinical symptoms among Vitamin B12 deficient participants

Symptoms	OR	CI (95%)	p value
Hyperpigmentation	0.43	0.23-1.05	0.34
Fatigue	2.01	1.01 -3.96	0.03*
Dizziness	2.36	1.31-4.24	0.0033*
Pale Skin	2.32	1.21-4.44	0.009*
Gastric Problem	3.66	1.75- 7.67	<0.001*
Heartburn	1.73	1.43-5.21	0.0016*
Breathlessness	0.63	0.37-1.09	0.1
Indigestibility	5.57	1.96-15.76	0.002*

OR: Odd ratio, CI: Confidence interval, *p<0.05: values are statistically significant

Table 3. Prevalence of depression according to baseline characteristics

Parameters	Total N[a] (%)	BDI Score>20	BDI score<20	p value
Gender	N=400	N=34	N=366	
Female	274 (68.5)	16 (47%)	258 (70%)	0.00489*
Male	126 (31.5)	18 (14.3%)	108 (85.3%)	
Religion				
Hindu	294 (73.5)	26 (76.47)	268 (73.22)	0.0229*
Muslim	90 (22.5)	4 (11.76)	86 (23.48)	
Others	16 (4)	4 (11.75)	12 (3.27)	
Locality				
(Locality) Rural	250 (62.5)	9 (26.47)	256 (69.94)	< .00001*
Urban	150 (37.5)	25 (73.52)	110 (30.05)	
BMI(kg/mt2)				
Normal	164 (41)	11 (32.35)	152 (41.53)	0.0047*

Parameters	Total N[a] (%)	BDI Score>20	BDI score<20	*p* value
Obese	36 (9)	8 (23.52)	28 (7.65)	
Overweight	144 (36)	14 (41.17)	130 (35.51)	
Underweight	56 (14)	1 (2.94)	56 (15.30)	
Age Group				
18-30years	106 (26.5)	0.00 (0)	106 (28.96)	0.001*
31-45years	150 (37.5)	4 (11.76)	146 (39.89)	
46-60 years	144 (36)	30 (88.23)	114 (31.14)	
Alcohol intake				
No	300 (75)	24 (70.58)	276 (75.40)	0 .534
Yes	100 (25)	10 (29.41)	90 (24.59)	
Education				
Intermediate and above	333 (83.25)	29 (85.29)	304 (83.06)	0.54789
Primary and secondary school	67 (16.75)	5 (14.70)	62 (16.93)	
Family Income				
HIG (>5L)	92 (23)	6 (17.64)	86 (23.49)	0.74037
LIG (Less than 2L)	66 (16.5)	6 (17.64)	60 (16.39)	
MIG (2-5L)	242 (60.5)	22 (64.70)	220 (60.10)	
Food Preference				
Eggetarian	52 (13)	2 (5.88)	50 (13.66)	.000077*
Non vegetarian	92 (23)	18 (52.94)	74 (20.21)	
vegetarian	256 (64)	14 (41.18)	242 (66.12)	
Marital Status				
Married	292 (73)	14 (41.17)	278 (75.95)	
other	22 (5.5)	10 (29.4)	12 (3.27)	<0.00001*
Unmarried	86 (21.5)	10 (29.41)	76 (20.76)	
Metformin Usage				
0 (No metformin)	150 (37.5)	6 (17.64)	144 (39.34)	0.01561
>1000	170 (42.5)	22 (64.71)	148 (40.43)	
500-1000	80 (20)	6 (17.65)	74 (20.21)	

[a]Sociodemographic characteristics are represented in numbers with percentage [n(%)]. Significance was calculated using X^2 test, with 95% CI. *Values are significant.

Serum Vitamin B12 and risk factors as predictors of Depression

As demonstrated in Table 4, baseline serum vitamin B12 levels of participants were significantly and inversely associated with the likelihood of depressive symptoms. After adjusting for factors such as sex, BMI, and age, the odds of having depressive symptoms for the participants with the lowest vitamin B12 levels (<150pg/ml) and insufficient vitamin B12 levels (150pg/ml -200pg/ml) were found to be 1.18 (95%CI, Model 1), and 0.59 (95%CL, Model 1) respectively (p<0.05). In Model 2, when additionally adjusted for religion, smoking, and metformin usage, the odds of having depressive symptoms for deficient and insufficient participants were 1.74 (95%CI, Model 2) and 0.59 (95%CI, Model 2), respectively. After further adjustment for income, food preference, sleep duration, profession, family type, marital status and clinical symptoms, a significant association (p<0.05) with odds of 2.66 (95% CI, Model 3) and 1.10 (95% CI, Model 3) were found for both deficient and insufficient participants, respectively. In logistic regression, the odds of having clinically significant depression with serum vitamin B12 deficient category was 5.23 (unadjusted, 95% CI) in comparison to insufficient category.

Table 4. Odd ratio for the presence of clinically significant depression according to vitaminB12 status

	Serum Vitamin B12 status (pg/ml)	
	<150	**151-200**
Median	124.5	172.6
Range	90.4-150	151-200
Unadjusted odds[a] (95% CI)	5.88 (2.81-12.32)	Reference
p value	<0.001*	
Model 1: OR (95% CI)[b]	1.18 (0.52-2.37)	0.59 (0.57-1.54)
p value	0.04*	0.53
Model 2: OR (95% CI)[c]	1.74 (0.92-5.37)	0.78 (0.57-2.64)
p value	0.02*	0.24
Model 3: OR (95% CI)[d]	2.66 (1.52-7.23)	1.10 (0.57- 5.56)
p value	0.004*	0.03*

[a]Based on logistic regression, odds of depression among deficient group with reference to insufficient group
[b]Adjusted for age, gender and BMI
[c]Adjusted with Model 1+ religion, metformin usage and smoking
[d]Adjusted with Model 2+Income group, food preferences, profession, family type, marital status and clinical symptoms

DISCUSSION

This cross-sectional study was conducted to examine the association of the presence of depression with serum vitamin B12 status. Serum vitamin B12 was determined by electron chemiluminescence immunoassay method and depression was measured by previously validated BDI II scale.[15] In the present investigation, a significant (p<0.05) association between depression and serum vitamin B12 levels was observed (Table 3). Among all participants, 8.4% of vitamin B12 deficient participants had clinically significant depression. Vitamin B12 is linked with one carbon metabolic reaction, which chiefly contributes to the methylation reaction of neurotransmitters and membrane formulation. Furthermore, vitamin B12 is also required for DNA synthesis. The deficiency of Vitamin B12 leads to hindered methylation and reduced neurotransmitters and leads to depressive symptoms.[16,17] Laird et al.[2] also highlighted the significant association of depression with serum vitamin B12 in a 4-year longitudinal study conducted on the older population. Similarly, the data from multiple observational studies by Markun et al.[18] revealed a significant relation between low serum vitamin B12 and cognitive decline in elderly people.

The present finding agrees with meta-analysis and cross-sectional studies conducted worldwide.[17-19] The majority of previous research investigations were carried out on older adults in other locations differing in terms of sociocultural elements, temperature, evaluation, and cut-off scores for serum vitamin B12 as well as the seasons of obtaining samples. The present investigation establishes the incidence of depression in vitamin B12 deficiency. The majority of participants were non-alcoholic (75%), however, among the deficient group, 21.9% were consuming alcohol once a week. Beulens et al.[20] reported that the intake of beer reduced serum vitamin B12 levels, which was associated with a moderate increase in homocysteine. Other workers have also reported that the low levels of vitamin B12 are inversely correlated with total homocysteine (tHcy) and strongly

associated with symptoms of liver damage caused by alcohol.[21,22]

The administration of metformin has previously been identified as a key risk factor for inadequate vitamin B12 levels in patients.[23,24] The results of the current study revealed similar conclusions. Noticeably, 59.4% and 39.3% of vitamin B12 deficient and insufficient participants were taking metformin above 1000mg/day, respectively. Similarly, in a systematic review, Fituri et al.[24] found that individuals on long term metformin therapy had a higher risk of developing vitamin B12 deficiency. The present study also found a significantly higher prevalence of vitamin B12 deficiency among vegetarians and obese individuals in comparison to non-vegetarians and Vitamin B12 insufficient participants. Similar findings were also reported by other workers.[25,26]

We found a higher prevalence of depression in the 45-60 years age group and those who were overweight (12.3%). The majority of participants were residing in nuclear families in urban areas. Participants with marital squabble or separation from partners showed significant clinical depressive symptoms. The findings are similar to those reported by previous studies stating that marital discords can be risk factors for depression.[26-28]

A significantly higher clinical sign of depression was found among the participants who were on metformin doses. Several cross-sectional studies[29,30] also support the present findings, showing that the prevalence of vitamin B12 deficiency was observed in 17%-30% of the population that was using metformin. Additionally, a systematic review found that more than 50% of people on metformin had a prevalence of vitamin B12 insufficiency.[31,32] Metformin is used as a first-line drug for the treatment of Type II diabetes, and also various endocrine disorders like thyroid problems, polycystic ovarian disease, metabolic syndrome, and weight reduction. It increases insulin sensitivity, reduces glycolysis, increases glucose utilization by muscles, and reduces lipolysis in adipose tissues. The side effects of metformin administration are altered gastrointestinal tract, nutrient malabsorption, and abdominal distention. Metformin reduces vitamin B12 levels by inhibiting its absorption due to ilium impairment, reducing intrinsic factors, and stimulating bacterial overgrowth.[31]

The odds of developing clinically significant depression among vitamin B12 deficient participants were higher in comparison to serum vitamin B12 insufficiency. The depressive symptoms were noted to reduce inversely with an increase in vitamin B12 serum levels in a step-wise manner. After adjusting for several confounding variables, this association remained the same. Although studies from throughout the world have also demonstrated a strong link between depression and vitamin D deficiency,[32-34] vitamin B12 deficiency also negatively affects cognitive function and can cause depression. The strength of the study was the involvement of a large population with wide age groups from both urban and rural localities and the inclusion of a wide range of confounding variables. Several previous studies highlighted the prevalence of vitamin B12 among depressive patients, however, the present study highlighted the presence of significant depression among vitamin B12 deficiency.

RECOMMENDATIONS

The present population based cross-sectional study highlights the association between vitamin B12 deficiency and increased likelihood of depressive symptoms. The odds of having depression were found 5.88 times higher among the deficient population in reference to vitamin B12 insufficiency. Thus, the early supplementation of vitamin B12 may be a successful strategy to combat depression among adults**.** However, a longitudinal

study could further be conducted to track the development of depression over time in relation to vitamin B12 levels. People should be encouraged to eat more vitamin B12-rich foods like eggs, fish, and dairy products; while for vegetarians and vegans, such B12 fortified plant-based foods could be an alternative. In addition to this, regular monitoring of high-risk populations, such as older people or individuals on certain medications, should be conducted periodically to prevent B12 deficiency.

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AUTHORS CONTRIBUTION

Conception and study design: M.R., S.S., M.K.G., B.S., A.S.; Data Collection: M.R. and M.K.G.; Data analysis and interpretation: M.R., A.S.; Drafting the article: M.R.; S.S.; Critical revision of article: M.R., S.S., M.K.G., B.S., A.S.; Final approval of article: S.S., and A.S.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

The study was ethically approved (Ref. No. SU/SMS&R/76-A/2021/124) by Sharda School of Medical Sciences, Sharda University, Medical Council of India, Greater Noida, India and written informed consent was obtained from the participants. All the data was kept confidential and one copy of the data and result analysis was submitted to the ethical committee.

CONFLICT OF INTEREST

There is no conflict of interest between the authors.

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