

# Levels of Serum Folate and Cobalamine in Clinically Depressed Patients in North Indian Population

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## ABSTRACT

**Background:** Depression, the most common type of mental illness is the second leading cause of disability worldwide next to CAD. Vitamin B6, folate and vitamin B12 are involved in a series of methylation reaction that produce monoamine neurotransmitters, phospholipids and nucleotide. Therefore the present study was planned to assay the blood levels of vitamin B12 and folate in patients with depression. The objective of this was to study if metabolites are affected by diet and may be helpful in the prevention of depression. **Methods:** Current study was an experimental case control study, was conducted at Santosh Medical College. A total of 88 cases (44 patients and 44 controls) both males and females in the age between 18 - 65 years were included in the study. Hamilton depression rating scale (HDRS) -17 items scale was used to rate the level of depression. **Results:** In the present study a total of 88 subjects including 45 females and 43 males participated, out of which 44 were control, 24 males and rest 20 were females. Majority 55 patients were of no depression category, 11 were of mild depression category, 10 were of severe depression and rest 9, were of moderate depression category. Mean value of B12 were found lowest in 'moderate' depressed patients (115), than in 'most severe depressed' (137), followed by 'severe' and 'mild' depressed patients category. Value of HDRS increases with severity of depression, it was found lowest in the 'mild' (10.64), then it steadily increases with severity, moderate (15.11), severe (21.20) and most severe (27.55). **Conclusion:** This study showed that majority of the patients with clinical depression had vitamin B12 deficiency.

**Keywords:** Depression, Folic Acid, Vitamin B12

## INTRODUCTION

Depression is a serious mental health concern that affects people lives either directly or through someone close they know. Depression, the most common type of mental illness is the second leading cause of disability worldwide next to CAD. It is the most prevalent mental disorder in the US population and women report more depressive symptoms than men.<sup>[1]</sup> Depression is a medical condition characterized by a wide variety of psychological and physical symptoms. It is an illness that affects people of all ages from all walks of life in all countries. Most of the studies evaluated depression as a unidimensional/single concept diagnosis or a total

score on a questionnaire, whereas depression most likely is a heterogeneous condition.<sup>[2-4]</sup>

Symptoms of depression are drooping mood, feeling of guilt, suicide ideation, insomnia, agitation, anxiety, weight loss etc.

Types of depression include unipolar, bipolar and dysthymic disorder. Diagnosis of major depressive disorder (or unipolar major depression) is made if an individual has five (or) more of these symptoms. Bipolar disorder (or manic-depressive illness) is characterized by episode of major depression as well as episodes of mania-period of abnormally and persistently elevated mood (or) irritability accompanied by at least 3 of the following symptoms : overly – inflated self-esteem, decreased need for sleep, increased talkativeness, racing thoughts, distractibility, increased goal directed activity or physical agitation and excessive involvement in pleasurable activities that have a high potential for painful consequences. Dysthymic disorders (or dysthymia), a less severe, yet typically

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more chronic form of depression is diagnosed when depressed mood persists for two years in adults (one year in children or adolescents) and is accompanied by two other depressive symptoms. Unipolar major depression and dysthymia are the primary forms of depression.

Few studies were conducted with the aim to establish the possible role of dietary factors in depressive symptoms, studies also indicated that the relationship between eating and mood is complex, situation specific, heavily influenced by history, psychological state and measurement dependent.<sup>[5]</sup>

Vitamins like folic acid and vitamin B12 appear to facilitate monoamine neurotransmitter synthesis and thus these vitamins are also suggested to play a role in developing depression. Depression has been associated with deficiency of serotonin or the catecholamines.<sup>[6]</sup>

Vitamin B6, folate and vitamin B12 are involved in a series of methylation reaction that produce monoamine neurotransmitters, phospholipids and nucleotide.

Therefore the present study was planned to assay the blood levels of vitamin B12 and folate in patients with depression. The objective of this was to study if metabolites are affected by diet and may be helpful in the prevention of depression.

## MATERIALS AND METHODS

Current study was an experimental case control study, was conducted at Santosh Medical College. A total of 88 cases (44 patients and 44 controls) both males and females in the age between 18 - 65 years were included in the study.

### Subjects were excluded if they had the following conditions

- Patients with bipolar disorder presenting with manic episodes
- Known cases of depression or any other psychiatric illness under treatment
- Patients on vitamin supplements or fluid therapy were not included in the study.
- Patients with mental retardation, substance abuse disorder (except nicotine and caffeine).

Age and education matched healthy consenting volunteers were recruited. The same exclusion criteria were used as was used for the patients. After getting clearance from Institutional ethics committee, written informed consent was obtained from all the participants. 5 ml of venous blood was collected from the controls and the patients attending psychiatry OPD with the provisional diagnosis of depression at Santosh Hospitals, Ghaziabad, NCR, Delhi. The serum was separated and preserved at – 80°C at Santosh Hospital laboratory. Experiments were performed in the Biochemistry laboratory at Army college of Medical Sciences, Delhi Cantt,

New Delhi and Bio Diagnostics laboratory, Rohini, New Delhi. The temperature of the laboratory was kept between 25 degree C – 28 degree C. All samples were appropriately coded.

### Basic parameters

- Serum total proteins by Biuret method
- Serum aspartate transaminase (AST) by IFCC kinetic method
- Serum alanine transaminase (ALT) by IFCC kinetic method

### Specific Parameters

- Serum folate (vitamin B9) by Chemiluminescence
- Serum cobalamine (vitamin B12) by Chemiluminescence

Hamilton depression rating scale (HDRS) -17 items scale was used to rate the level of depression. Ratings were made on the basis of the clinical interview plus additional information provided by nursing staff and family members. The questionnaire was designed for adults and is used to rate the severity of their depression by probing mood, feeling of guilt, suicide ideation, insomnia, agitation, anxiety, weight loss etc. A total Score of 52 in which Score of 0-7 was generally accepted to be within the normal range. Score of 8-13 was mild depression, score of 14-18 was for moderate depression, score of 19-22 was severe depression and score above 23 was given for very severe depression. Alpha reliability coefficients used were range from 0.766-0.810.<sup>[7,8]</sup>

## RESULTS

In the present study a total of 88 subjects including 45 females and 43 males [Table 2] participated, out of which 44 were control, 24 males and rest 20 were females [Table 2]. Maximum participants 36 were in the age group of 18- 32 years, 32 were in age group of 33-47 years and rest 20 were in more than 48 years old [Table 1]. Majority 55 patients were of no depression category, 11 were of mild depression category, 10 were of severe depression and rest 9, were of moderate depression category [Table 3, Figure 1].

In the instant study, patients were randomized through computer generated software to divide into 2 groups 'depressed patients' and 'controls' of forty four subjects patients in each group.

Serum total proteins and albumin were found to be decreased in patients as compared to the controls. The levels of serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) were also found to be reduced in depression patients as compared to controls. Depressed patients exhibited lower values of vitamin B12 and vitamin B9. HDRS was found to be increased for depression patients in comparison to controls [Table 4].

Mean value of B 9 was found lowest in ‘most severe’ depressed patients (2.6200), than in ‘moderate depressed’ (3.4784), followed by ‘mild’ and ‘severe’ depressed patients category [Table 5].

**Table 1: Distribution of age group versus type of patients**

Age Group	Statistics	Type of Patient		Total
		Controls	Depression Patients	
18 to 32 Years	Count	20	16	36
	% within Type of Patient	45.5%	36.4%	40.9%
33 to 47 Years	Count	16	16	32
	% within Type of Patient	36.4%	36.4%	36.4%
>= 48 Years	Count	8	12	20
	% within Type of Patient	18.2%	27.3%	22.7%
Total	Count	44	44	88
	% within Type of Patient	100.0%	100.0%	100.0%

Chi Square=1.24, P value=0.537

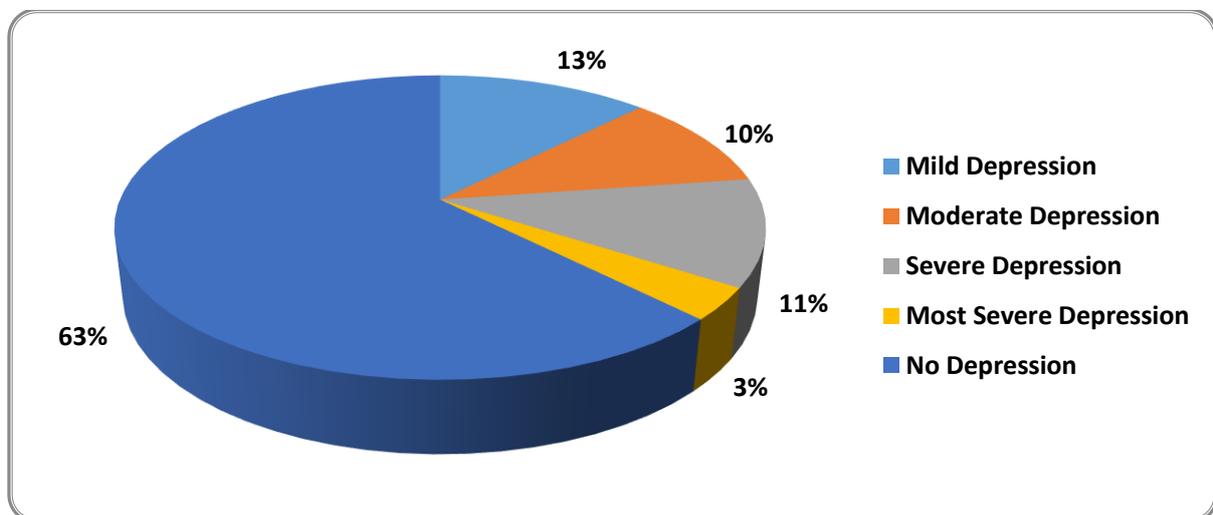
**Table 2: Distribution of sex versus type of patients**

Sex	Statistics	Type of Patient		Total
		Controls	Depression Patients	
Male	Count	24	19	43
	% within Type of Patient	54.5%	43.2%	48.9%
Female	Count	20	25	45
	% within Type of Patient	45.5%	56.8%	51.1%
Total	Count	44	44	88
	% within Type of Patient	100.0%	100.0%	100.0%

Chi Square=1.13, P value=0.624

**Table 3: Distribution of depression grading versus type of patients**

Grades of Depression	Frequency	Percent
Mild	11	12.5%
Moderate	9	10.2%
Severe	10	11.4%
Most Severe	3	3.4%
No Depression	55	62.5%
Total	88	100.0%



**Figure 1: Distribution of depression grading versus type of patients**

**Table 4: Haematological and Biochemistry parameters of depression patients**

	N	Range	Minimum	Maximum	Mean	Std. Deviation
Age	88	45	15	60	33.09	10.00
Glucose	88	484.59	4.58	489.17	117.85	89.25
Total Proteins	88	12.64	1.73	14.37	6.58	1.71
Albumin	88	5.35	1.39	6.74	4.063	0.81
SGPT	88	743.79	0.48	744.27	41.28	80.00
SGOT	88	302	3	305	35.48	33.85
TSH	88	14.97	0.21	15.18	2.71	2.42
B 9	88	19.40	.60	20.00	4.91	4.82
B12	88	1192	12	1204	162.15	199.75
HDRS	88	30	0	30	7.97	7.70

**Table 5: Mean value of haematological and Biochemistry parameters of cases and controls**

	Type of Patient	N	Mean	Std. Deviation	Std. Error Mean	P Value
Age	Controls	44	33.91	10.13	1.53	0.182
	Depression Patients	44	37.05	11.69	1.76	
Glucose	Controls	44	136.48	107.56	16.21	.050
	Depression Patients	44	99.22	61.94	9.34	
Total Proteins	Controls	44	6.92	0.73	0.11	.047
	Depression Patients	44	6.40	1.55	0.23	
Albumin	Controls	44	4.36	0.44	0.06	.003
	Depression Patients	44	3.94	0.78	0.12	
SGPT	Controls	44	50.1341	110.72	16.69	.302
	Depression Patients	44	32.4318	23.01	3.47	
SGOT	Controls	44	39.3657	44.18	6.66	.284
	Depression Patients	44	31.5982	18.33	2.76	
TSH	Controls	44	2.9350	2.31	0.35	.392
	Depression Patients	44	2.4914	2.47	0.37	
B 9	Controls	44	5.942	1.34	0.20	.995
	Depression Patients	44	5.936	5.92	0.89	
B 12	Controls	44	388.14	198.07	29.86	.000
	Depression Patients	44	204.05	255.26	38.48	
HDRS	Controls	44	3.05	2.023	.305	.000
	Depression Patients	44	14.93	6.009	.906	

Similarly, mean value of B12 were found lowest in 'moderate' depressed patients (115), than in 'most severe depressed' (137), followed by 'severe' and 'mild' depressed patients category.

Value of HDRS increases with severity of depression, it was found lowest in the 'mild' (10.64), then it steadily increases with severity, moderate (15.11), severe (21.20) and most severe (27.55).

## DISCUSSION

Depression is an extremely common illness affecting people of all ages, genders, different socioeconomic groups and religions in India and all over the world. Globally estimated about 322 million people were affected by depression in 2015. Depression contributes to significant disease burden at national and global levels. At the individual and family level, depression leads to poor quality of life, causing huge social and economic impact.

India is home to an estimated 57 million people (18% of the global estimate) affected by depression. With India witnessing significant changes (including globalization, urbanization, migration and modernization) that is coupled with rapid socio demographic transition, depression is likely to increase in the coming years.

Both low folate and low vitamin B12 status have been found in studies of depressive patients and an association between depression and low levels of the two vitamins is found in studies of the general population. A link between depression and low folate has similarly been found in patients with alcoholism.

Our study aimed to analyse level of serum folate and cobalamine in clinically depressive patients. The results of this study will help psychiatrist to take more appropriate and informed decision about supplementation of folic acid and cobalamine in depressive patients.

Morris and co-workers reported that depressed subjects in the U.S. population,<sup>[9]</sup> especially those who had recently had an episode of depression, had lower folate concentrations in serum and RBC. In the instant study, B9 level was almost equal in both test and control cases, whereas B12 levels were found decreased in depressive patients.

Lindeman et al.<sup>[10]</sup> found significant associations between serum folate concentrations and measures of cognitive function, and not seen with B12 or C, nor between any of the vitamins and affective function. Similarly in our study serum folate was found to be slightly towards the lower side in the depressive patients which may impair their cognitive functions.

Penninx et al.<sup>[11]</sup> concluded that the depressed subjects, especially those with severe depression, had a significantly higher serum methyl malonic acid level and a no significantly lower serum vitamin B 12 level than the nondepressed subjects. Metabolically significant vitamin B12 deficiency was present in 14.9% of the 478 non depressed subjects.

Gulash Kaner et.al (2015) studied that vitamin B6, folate, vitamin B12 were lower in depression group their findings are consistent with results of our study.<sup>[12]</sup>

Depressive and anxiety disorders show a common comorbidity pattern, they are also found to be strongly associated with obsessive-compulsive disorder (OCD). A study was conducted by Nuray Türksoy and his associates to measure vitamin B12, folate and homocysteine levels in OCD patients. A total of 57 subjects were included in the study 35 controls and 22 patients. They found that compared to the control group, the level of vitamin B12 was significantly lower in the patient group (245.4±84.6 versus 291.4±80.9 pg/mL, respectively; P=0.036). The rate of vitamin B12 deficiency (<200 pg/mL) was 31.4% in the patient group, while there was no

vitamin B12 deficiency in the control group. The difference between the groups was statistically significant ( $P=0.004$ ). Although there was no folate deficiency in either of the groups. Similarly in our study vitamin B12 was found lower in concentration, 208.14 ( $P=0.004$ ) in cases of 44 patients (test group) as compared to control group.<sup>[13]</sup>

There are few cases available in literature in which vitamin B12 deficiency has been directly found associated with clinical depression. In one such case reported by Durand C of a patient with vitamin B12 deficiency, who presented severe depression with delusion and Capgras' syndrome, delusion with lability of mood and hypomania successively, during a period of two Months. Blood investigations confirmed anemia (hemoglobin=11,4 g/dl) and revealed vitamin B12 deficiency (52 pmol/l) and normal folate level. Vitamin B12 replacement therapy was started with hydroxycobalamin 1000 ng/day i/m for 10 days and iron replacement therapy. Her mental state improved dramatically within a few days.<sup>[14]</sup>

Similarly Verbank et al. described the case of a patient with vitamin B12 deficiency in whom hypomania, paranoia and depression had been successively presented during a period of 5 years before anemia have been developed. The case of Mme V. is similar in the succession of severe depression with delusion of persecution and Capgras' syndrome, delusion with lability of mood and hypomania, during a period of two Months.<sup>[15]</sup>

The clinical implications of thyroid hormones in depression have been studied extensively and still remain disputable. Supplementation of thyroid hormones is considered to augment and accelerate antidepressant treatment. Studies on the role of thyroid hormones in depression deliver contradictory results. A study conducted by Berent D and his associates on 44 patients found that the TSH serum level in patients with depression were within normal range.<sup>[16]</sup> In the instant study, TSH level was found decreased in the patients group (2.4914) as compared to control group (2.9350).<sup>[16]</sup>

Association between depression and glycemic control in patients with type 2 diabetes mellitus was studied by José María De la Roca-Chiapas and his associates in 68 patients. They found that fasting glucose level was higher (175+-63.5) and their glycaemic control was also poor. Similarly in our study glucose level was found higher in the patients group (99.2159) as compared to control group (1.36482).<sup>[17]</sup>

Voican CS and his colleagues did a review on the liver function in 321 clinically depressed patient in the year 2016. They found that the liver dysfunction was present in the one fifth of the total patients. In those patients cause of LFT abnormalities was unknown in 32% of patients due to the absence of etiological investigations. In our study SGOT and

SGPT were elevated in the control group of patients as compared to patient group.<sup>[18]</sup>

## CONCLUSION

This study showed that majority of the patients with clinical depression had vitamin B12 deficiency. However, the sample was too small to conclude that this finding is an important biological indicator for clinical depression. Although more detailed studies regarding this phenomenon are to be carried out, these findings can provide a starting point for future research.

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