

## Levels of Serum Vitamin B6 and GABA In Clinically Depressed Patients: A Study.

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### ABSTRACT

**Background:** Depression is the most common type of mental illness. As per the WHO criterion of prevalence of depression, this disease has a prevalence of 4.4% all over the world and 4.5% in India. Some water-soluble vitamins like vitamin B2, B6, B9, B12; play an important role in mental health. Of these vitamins pyridoxal phosphate, the active form of vitamin B6 plays a pivotal role in a number of transamination reactions, decarboxylation reactions and in the control of plasma homocysteine concentration. PLP is vital for the biosynthesis of GABA, which is being used as the neurotransmitter in at least 40% of the inhibitory synaptic processing in the brain. Therefore, the present study was planned to assay the blood levels of vitamin B6 and GABA in patients with depression. The objective of the study was to help psychiatrists to take appropriate and informed decision about supplementation of vitamin B6 and use of specific antidepressant medication in the treatment of depression cases. **Methods:** Current study was an experimental case control study conducted at Santosh Medical College and Hospitals. A total of 204 (102 controls and 102 patients) both males and females, in the age group between 18-65 years were included in the study. Hamilton Depression Rating Scale (HDRS) 17 items was used to rate the level of depression. **Results:** In the present study, a total of 204 subjects including 97 females and 107 males participated, out of which 102 were clinically diagnosed cases of depression attending psychiatry OPD and included 55 females and 47 males. 47.1% of the cases were of mild depression, 23.5% were of moderate depression, 11.8% of severe depression and the remaining 17.6% belonged to very severe depression category. The mean value of vitamin B6 was found lowest in severe to very severe depressed patients (5.25) than in mild to moderate depressed patients (8.83) and the mean value of GABA was found to be highest in severe to very severe category (5571.73) than in mild to moderate depressed patients (5184.73). **Conclusion:** This study showed that majority of the patients with clinical depression had vitamin B6 deficiency and increase in GABA levels.

**Keywords:** Depression, vitamin B6, GABA

### INTRODUCTION

Depression is the most common type of mental illness. It is the leading cause of global burden of disease worldwide. It negatively affects the feeling, actions and thinking of the individual [1]. As per the WHO criterion of prevalence of depression, the disease has a Global prevalence of 4.4% and about 4.5% in India [2]. Depression may affect both males and females, any socio-economic group, young or old and the burden of disability in females is about 50 % higher (WHO 2008).

An epidemiological study from Uttar Pradesh

showed that people with less education and from socio- economically weaker section are more prone to develop this depression [3]. The sickness starts usually during late teens to mid-20s and at any given time about 16.6 % individuals will be affected by depression sometime in their life [4]. If the present trend continues, then, by the year 2030 depression is estimated to account for 6.2% of the total disability burden and will be the leading cause of this burden of mental disorder [5].

The signs and symptoms of depression includes low mood, difficulty in concentration, irregular dietary habits, feeling worthless, suicidal thoughts etc. The types of depression are unipolar major depression (major depressive disorder), bipolar disorder (manic depressive illness) and dysthymic disorders/dysthymia.

Over the years, research has shown that perhaps, the chemical neurotransmitters used by cells of the

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nervous system for communication go out of balance in depressive patients. Various researches have emphasized that there is a relationship between low levels of dietary B complex vitamins and depression [6]. Some studies have found low levels of pyridoxal phosphate (the active form of vitamin B6) among depressed patients [7]. Vitamin B6 is a cofactor in tryptophan - serotonin pathway, hence its reduced levels may cause depression. B6 vitamin plays an important role to control plasma homocysteine concentration [8&9]. Levels of vitamin B6 decline recognizably in old age and is involved in macronutrient metabolism as well as in synthesizing neurotransmitters [10,11]. GABA is used as neurotransmitter in at least 40 % of the inhibitory synaptic processing in the brain. It works as inhibitory neurotransmitter<sup>12</sup>. In depression, a chemical imbalance arises and the communication becomes out of control / over stimulated at the synapse. When there is too little GABA in the brain the other neurotransmitters such as serotonin, nor-epinephrine are not being controlled and when too much GABA is present in the brain, the individual is overly relaxed and sedated and has impaired normal actions and reactions.

As depression is linked with the deficiency of B complex vitamins, the individuals may show improvement by modifying the diet. Hence, the present study has been planned to assay the levels of vitamin B6 and the neurotransmitter GABA in the depression patients.

## MATERIALS AND METHODS

The current study was an experimental case control study and was conducted at Santosh Medical College and Hospitals, Ghaziabad. Total subjects involved in the study were 204; cases (102 patients) and healthy volunteers (102 controls) including both females and males in the age group between 18-65 years. The patients were those who attended the psychiatry OPD at Santosh Hospitals, Ghaziabad and the controls were healthy volunteers, who accompanied the patients.

### The exclusion criteria for the selection of patients as well as the controls was as follows

- Known cases of depression under treatment
- Cases of substance abuse disorder (except caffeine, nicotine and alcohol)

- Cases of bipolar disorder with manic episodes and with mental retardation.
- Cases on fluid therapy or vitamin supplements

The ethics clearance for the study was obtained from the Institutional ethics committee of Santosh Medical College and Hospitals, Ghaziabad as well as Base Hospital Delhi Cantt, New Delhi. Written informed consent was obtained from all the individuals included in the study, in the language they understood. 5 ml of venous blood was collected from each participant. After separating, the serum was preserved at -80°C at Santosh Hospital laboratory, Ghaziabad, Uttar Pradesh, India. The samples were processed at the Bio Diagnostics laboratory, Rohini, New Delhi, India. The temperature of the laboratory was maintained between 25° C to 28° Celsius. The serum samples were processed for the vitamin B6 and gamma aminobutyric acid (GABA) by ELISA (Enzyme linked immunosorbent assay).

To assess the severity of depression, Hamilton Depression Rating Scale (HDRS) 17-item scale was used. HDRS scores of depression were allotted on the basis of personal interview of the patient and additional input given by the escorting family members. The assessment criteria for the severity of depression was as under:

Normal range : 0-7, mild depression : 8-13, moderate depression : 14-18, severe depression : 19-22 and score from 23 onwards was taken for very severe depression.

## RESULTS

In the present study, a total of 204 subjects including 107 males and 97 females participated. Of which 102 were controls including 60 males and 42 females [Table 1]. A total of 45 participants were in the age group of <25 years, 66 subjects were in the age group of 26-35 years, 56 were between ages 36-49 years and the remaining 37 individuals were in the age group of > 50 years [Table 1]. Out of the 102 depression cases, 47.1% individuals were in mild depression category, 23.5% were of moderate depression, 11.8% belonged to severe depression category and the remaining 17.6% individuals were of most severe depression category [Figure 1]. In the present study, there were two groups, one with 102 depressed cases and the other group with 102 healthy controls.

**Table 1: Comparison of demographic variables between cases and controls.**

Variables	Control		Case		Total		p-value
	n	%	n	%	n	%	
Total patients	102		102		204		
Age group (years)							
<=25	22	21.6	23	22.5	45	22.1	0.282
26-35	39	38.2	27	26.5	66	32.4	
36-49	26	25.5	30	29.4	56	27.5	
>=50	15	14.7	22	21.6	37	18.1	

Mean age ± SD	35.2 ± 11.4		37.2 ± 12.2		36.2 ± 11.8		0.221
Sex							
Female	42	41.2	55	53.9	97	47.5	0.068
Male	60	58.8	47	46.1	107	52.5	
Marital status							
Unmarried	22	21.6	36	35.3	58	28.4	0.030
Married	80	78.4	66	64.7	146	71.6	

Table 2: Comparison of serum biochemical variables between cases and controls

Parameters	Control		Percentiles			Case		Percentiles			p-value
	Mean	SD	25th	50th	75th	Mean	SD	25th	50th	75th	
Vitamin B6 (ng/ml)	28.4	9.6	21.4	28.0	33.9	7.8	5.9	5.1	6.5	9.3	p<0.001
GABA (pg/ml)	1626.6	1394.7	733.0	1250.5	2022.0	5298.7	3214.7	2770.5	4519.0	7968.8	p<0.001
Creatinine (mg/dl)	0.8	0.2	0.6	0.8	1.0	0.9	0.3	0.7	0.8	1.1	0.102
Urea (mg/dl)	27.4	7.6	21.2	28.0	32.4	26.3	15.7	14.6	25.0	36.6	0.038
Total proteins (gm/dl)	6.8	0.9	5.9	6.8	7.6	6.5	1.3	5.8	6.7	7.4	0.230
SGOT (U/L)	31.3	10.7	23.1	28.9	38.6	31.1	17.3	18.5	28.4	34.5	0.203
SGPT (U/L)	30.3	14.2	20.4	27.8	39.5	34.7	24.7	15.8	26.2	53.5	0.996

Table 3: Comparison of HDRS scores with serum biochemical variables

Variables	No depression (n=102)		Mild to moderate (n=72)		Severe to very severe (n=30)		p-value
	Mean	SD	Mean	SD	Mean	SD	
Age (years)	35.18	11.37	35.68	11.97	40.87	12.18	0.073
Vitamin B6 (ng/ml)	28.36	9.60	8.83	6.76	5.25	1.35	p<0.001
GABA (pg/ml)	1626.57	1394.66	5184.96	3105.22	5571.73	3503.48	p<0.001
Creatinine (mg/dl)	0.82	0.23	0.89	0.26	0.91	0.34	0.255
Urea (mg/dl)	27.42	7.62	25.10	13.22	29.18	20.55	0.111
Total proteins (gm/dl)	6.79	0.92	6.58	1.27	6.45	1.23	0.439
SGOT (U/L)	31.27	10.69	31.72	17.16	29.71	17.68	0.297
SGPT (U/L)	30.33	14.16	35.28	25.59	33.38	22.73	0.998

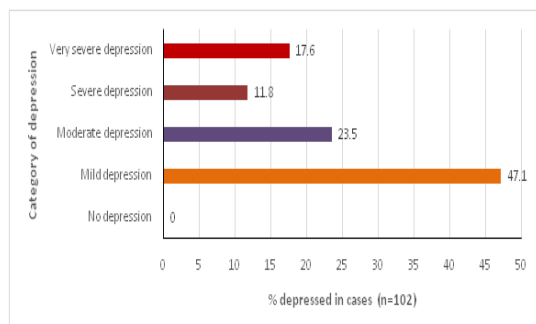


Figure 1: Distribution of depression among cases

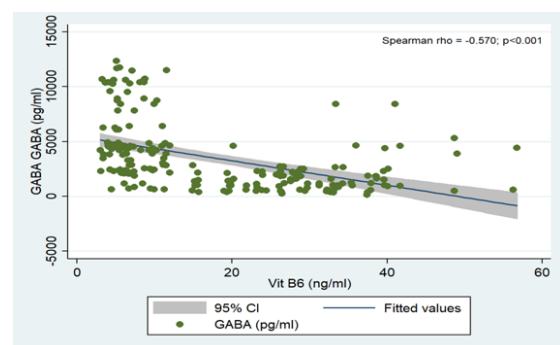


Figure 2: Correlation between GABA and Vitamin B6

As far as the comparison of serum biochemical variables between cases and controls [Table 2], the mean value of vitamin B6 in controls ( $28.4 \pm 9.6$ )

was significantly ( $P < 0.001$ ) higher than the cases ( $7.8 \pm 5.9$ ) and the mean value of GABA in controls ( $1626.6 \pm 1394.7$ ) was statistically significant ( $P < 0.001$ ) lower than the depression cases ( $5298.7 \pm 3214.7$ ). The other biochemical variables were not statistically significantly correlated between cases and the control groups.

The comparison of HDRS categories with biochemical variables [Table 3] revealed that all the three categories of no depression, mild to moderate depression and severe to very severe depression with respect to both, vitamin B6 and GABA variables was significant ( $P < 0.001$ ). Vitamin B6 predicted nearly 20% low risk ( $P < 0.001$ ) of having higher HDRS categories when increased by one unit, whereas one unit increase in GABA predicted higher chances of shift towards higher categories of HDRS. However, it was weakly associated ( $P = 0.012$ ). The correlation between GABA and vitamin B6 variables have been found to be significant ( $P < 0.001$ ) [Figure 2].

## DISCUSSION

Depression affects all age groups and it has been observed that it affects women more than men. A survey conducted on World Mental Health in more than 17 countries, reported that on an average, 1 in 20 individuals had suffered from depression at least once during the previous year.

Amongst the patients attending the psychiatric OPDs at various hospitals, a large percentage (5-26.7%) were found to be suffering from depression.<sup>[13,14]</sup>

An epidemiological study from Uttar Pradesh, showed neurotic depression as most common psychiatric illness. Though the disease can affect anybody at any point of time, the most affected are the people of socially, educationally and economically weaker section.

It has been found that there is an association between pyridoxal phosphate (vitamin B6) and depression and the levels of vitamin B6 decline to a great extent in old age. Similarly, studies show that GABA levels are also correlated with depression. Low levels of GABA are associated with bipolar disorder, mania and if GABA levels below average, the brain is too stimulated. Other studies reveal that, when there is too much GABA, we are too relaxed and sedated often to the extent that the normal reactions are impaired.

Our study aimed to analyse levels of serum vitamin B6 and GABA in clinically depressive patients. The results of our study may be helpful to the psychiatrists to take appropriate and informed decision about supplementation of vitamin B6 and use of specific anti-depressant medications in depression.

Vitamin B6 deficiency seems to be a common problem in elderly people. Heller J in his study on European elderly reported that vitamin B6 is deficient in about 23.3% of the cases.<sup>[15]</sup> Ida K Kjeldby and co-workers in their study showed that vitamin B6 deficiency is common also in the adult population with a prevalence rate of 11-24%.<sup>[16]</sup> The instant study showed that in the control group, individuals had lower values of vitamin B6 even up to 50th percentile, as compared to the mean value and in the depressed cases these values were still lower than the control group.

GABA plays an important role in the biochemical pathophysiology of mood disorders. Petty F<sup>[17]</sup> concluded that GABA may increase, causing symptoms of depression or mania, due to environmental factors such as, excessive alcohol use and stress. In the study conducted by Yonkers et.al<sup>[18]</sup> it was mentioned that during the luteal phase of the menstrual cycle, GABA increase significantly and studies show that depression is found more frequently in women than men. In the current study, the mean levels of GABA in depressed cases (5298.7), which was found to be high as compared to the mean value in the control group (1626.6) with more women (n= 55) as compared to men (n=47) in the cases group.

Williams et.al,<sup>[19]</sup> found consistent evidence of the importance of supplementing vitamin B6 for depression among premenopausal women and found that increase intake of vitamin B6 was seen to be associated with a lower chance of depression in older adults. Kimberly A et. al<sup>[20]</sup>, in their study concluded that if slightly high intake of vitamin B6 is taken over the time, it may have protective action

against depressive symptoms in the older adults residing in a community.

Joseph Carver in his paper mentioned that the high GABA levels actually smothers the communication between brain neurons;<sup>[21]</sup> sometimes even to the point of total loss of communication which is also known as neuronal death. Honig et. al<sup>[22]</sup>, mentioned in their study that on removal of cerebral cortex by psychosurgery, an inverse correlation ( $P < 0.05$ ) is observed between GABA levels and severity of depression. In the instant study the GABA levels were found to be much higher in the depression cases group as compared to the control group.

## CONCLUSION

This study showed that majority of the patients with clinical depression (cases) had low levels of serum vitamin B6 and an increased serum GABA levels, as compared to the control group. However, to conclude that these findings can be important biological indicators for clinical depression, the sample size should be large. However, these findings can provide the starting point for the more detailed studies regarding this phenomenon in future research.

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