



## PLASMA SEROTONIN LEVELS IN BIPOLAR DISORDER

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### Abstract:

Bipolar disorder is a debilitating psychiatric disorder with prevalence of 1-3% in general population. It is a multifactorial disorder which involves environmental, genetic, nutritional and other factors. 5HT widely known as serotonin is synthesized in enterochromaffin cells of intestine, blood platelets and serotonergic neurons of brain. In blood 5HT is stored in platelets. 5HT is an intermediate product of tryptophan metabolism and is a monoamine neurotransmitter in central nervous system. Abnormality in this neurotransmitter is associated with development of bipolar disorder and other psychiatric disorders like depression, anxiety, schizophrenia, mania, aggression. Disturbances in the level of 5HT changes one's mood. Low level of 5HT is associated with violent behaviour in humans. In the present study plasma 5HT levels were estimated in 38 bipolar disorder individuals and 38 age and sex matched controls without a family history of bipolar disorder. All the patients included in the present study belonged to North Coastal Andhra Pradesh. Student *t* test was used to compare the 5HT levels in cases and controls. A decrease in the level of plasma 5HT was observed in bipolar cases.

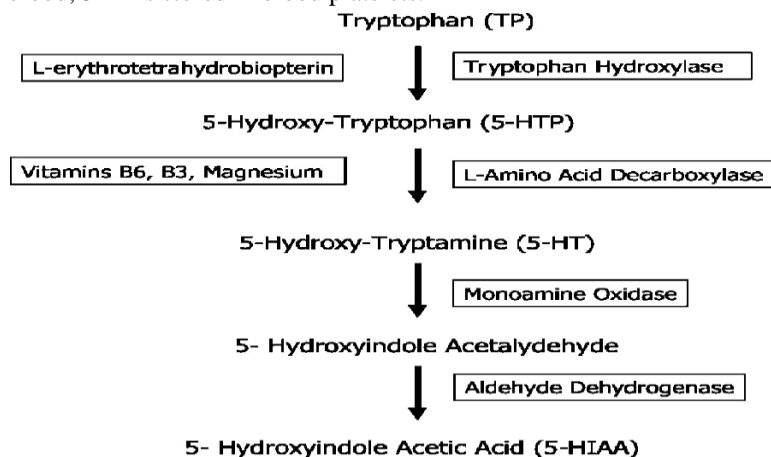
**Key Words:** Bipolar Disorder, Serotonin, Mania, Depression & Aggression

### Introduction:

Bipolar disorder (BD) also known as manic depressive illness is a multifactorial disease categorized under mood disorder in 10<sup>th</sup> version of International Classification of Diseases (Gururaj et al., 2005). It causes shifts in mood which ranges from depression to mania which may last for hours, days, weeks or months. The life time prevalence of BD is 1% (Bebbington & Ramana, 1995) and the average age at onset is 21 years (Kessler et al., 1997).

Serotonin is a monoamine neurotransmitter in the central nervous system. It is synthesized from an essential amino acid tryptophan (Trp) which is obtained from diet. Trp is the sole precursor for peripheral and central 5HT (Richard et al., 2009). After ingestion, Trp is converted to 5HT through a series of reactions. Initially, L-Trp is hydroxylated to 5-hydroxy-L-tryptophan (5-HTP) by non neuronal isoform of tryptophan hydroxylase (TPH) i.e., TPH1 and this is the rate limiting step in 5HT synthesis (Jonnakuty & Gragnoli, 2008). 5HTP is permeable to blood brain barrier and also it does not require carrier protein for its transport unlike Trp to cross blood brain barrier (Jonnakuty & Gragnoli, 2008).

Nearly 90% 5HT is synthesized peripherally in gut neurons and enterochromaffin cells of intestine, and 5% is synthesized centrally (Jenkins et al., 2016) in serotonergic neurons of brain (Brenner et al., 2007). By oxidative deamination, 5HT is metabolized into 5-hydroxy indole acetic acid (5-HIAA) by monoamine oxidase (MAO) enzyme. In blood, 5HT is stored in blood platelets.



Depletion of the sole precursor for 5HT i.e., Trp in diet causes decrease of Trp in plasma and increase in negative mood state in humans (Young et al., 1985). Trp depletion is associated with manic symptoms in BD

(Cappiello et al., 1997). Disturbance in the serotonergic system is associated with alcoholism and negative mood states (Heinz et al., 2001). Depletion of brain 5HT also induces alcohol intake which in turn induces aggressive episode (Badaway, 1998).

While there are several studies which report low level of 5HT in depression phase of BD, inconsistent findings (Mohmood & Silverstone, 2001) are reported by the few studies which examined the association between 5HT and manic phase of the disease. Hence the present study was carried out to find out the level of 5HT in mania patients.

**Materials and Methods:**

The study group includes 38 bipolar manic patients attending Government Hospital for Mental Care, Visakhapatnam during September 2017, the cases were diagnosed according to ICD 10 criteria and severity of manic symptoms was assessed using Young mania rating scale. Control group includes 38 drug free, healthy, age and sex matched unrelated individuals without any family history of psychological disorders. The institutional ethical committee approved the present study. Fasting blood samples were collected after taking prior informed consent. 2ml of blood was drawn into anticoagulant tube. Plasma was separated by centrifuging the collected blood at 3000 rpm for 10 minutes. Collected plasma was kept in deep freezer at -20°C until further analysis. Plasma 5HT level in both patients and controls was determined by serotonin ELISA kit from Enzo Life Sciences. Student *t* test was used for comparison as the variables are continuous.

**Results and Discussion:**

BD cases show decreased concentration of plasma 5HT ( $98.96 \pm 60.31$ ) when compared to controls ( $144 \pm 44.86$ ), with a significant *p* value. ( $p=0.0000001$ ).

Table 1: Plasma serotonin concentrations in cases and controls

	N	Plasma 5 HT ng/ml Mean±SD	P
Cases	38	$98.96 \pm 60.31$	0.0000001
Controls	38	$144 \pm 44.86$	

5HT shows its effect directly on mood and aggression (Young & Leyton, 2002) and also plays an important role in many functions like behavior, depression, anxiety, sleep, appetite (Kato et al., 1999).

Abnormality in this neurotransmitter is associated with development of BD and other psychiatric disorders like depression, aggression, Schizophrenia, (Saldhana et al., 2008).

Disturbances in the level of 5HT changes one's mood (Falishia, 2007). Deficiency of 5HT is associated with depression (Takahashi, 1976; Mohmood & Silverstone, 2001; Cowen & Browning, 2015).

Low level of 5HT is also associated with aggression in humans (Brown et al., 1979, Linnola et al., 1983; Virkkunen et al., 1994). Banki (1978) and Shiah & Yatham (2000) reported reduced level of this neurotransmitter in blood of manic patients. Increased 5HT level may induce mania and a rare serious illness, serotonin syndrome (Wolf, 2017).

The present study reports low level of 5HT in bipolar mania patients with violent behavior when compared to controls which is in accordance with Shiah & Yatham (2000) in BD cases with mania and Falishia (2007) in cases with violent behavior.

**Conclusion:**

Decreased level of 5HT is observed not only in bipolar depression cases but also in cases with mania. However apart from 5HT, other factors like 5HT receptor subtypes and interaction between 5HT and other neurotransmitters should also be considered.

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