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THYROID FUNCTION TEST IN DRUG-NAÏVE BIPOLAR DISORDER PATIENTS –A CROSS SECTIONAL STUDY

Clinical Biochemistry

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KEYWORDS

INTRODUCTION

Bipolar disorder (BD) is a chronic and severe psychiatric condition that affects over 1% of the global population, with lifetime prevalence rates estimated between 0.4% and 2.4%. Characterized by alternating episodes of mania, hypomania, and depression, BD significantly impairs social, occupational, and cognitive functioning. Individuals with BD face an increased risk of obesity, cognitive decline, and a suicide rate 10 to 30 times higher than that of the general population.

The underlying pathophysiology of BD remains complex and multifactorial, involving interactions among genetic, neurochemical, hormonal, and environmental factors. Among these, increasing attention has been given to the role of the hypothalamic-pituitary-thyroid (HPT) axis. Thyroid hormones are essential for brain function, and disturbances in thyroid regulation have been linked to mood instability. Notably, hypothyroidism and subclinical thyroid dysfunction have been associated with depressive symptoms in BD, while hyperthyroid states may exacerbate manic symptoms.

Pharmacological treatments for BD, as well as psychological stressors, may influence thyroid function, making it challenging to isolate the effects of the disorder itself on thyroid activity. To address this, examining drug-naive patients—those who have not yet received psychiatric medications—provides a clearer perspective on the intrinsic relationship between thyroid function and mood states in BD.

This study aims to investigate thyroid function in drug-naive individuals with BD across different affective states. By exploring these associations, we seek to contribute to a deeper understanding of the biological underpinnings of BD and to identify potential biomarkers or targets for early intervention and personalized treatment strategies.

MATERIALS AND METHODS

This cross-sectional study was conducted over a period of four months, from April 2024 to July 2024, at a tertiary care teaching hospital in Central India. The study population comprised patients diagnosed with bipolar disorder (BD) based on the International Classification of Diseases, 10th Edition (ICD-10) criteria and/or the Bipolar Spectrum Diagnostic Scale. Only drug-naïve patients—those who had never received psychotropic medications prior to hospitalization or attending the outpatient department (OPD)—were included.

Participants were eligible if they were between 18 and 60 years of age and had a confirmed discharge diagnosis of BD according to ICD-10 or the Bipolar Spectrum Diagnostic Scale. Patients were excluded if they had comorbid psychiatric disorders such as schizophrenia, chronic medical illnesses requiring ongoing treatment, known autoimmune or thyroid disorders, or were pregnant or lactating. Individuals with a history of substance abuse, excluding tobacco use, were also excluded.

After applying the inclusion and exclusion criteria, a total of 140 patients were enrolled in the study. These were further categorized based on their predominant affective state into three groups: the Bipolar Mania group (BD-M) consisting of 66 patients, the Bipolar Depression group (BD-D) with 64 patients, and the Mixed Episode group (BD-MIX) comprising 10 patients.

All collected data were entered into Microsoft Excel for analysis. Numerical variables were summarized using mean and standard deviation, while categorical variables were presented as percentages. Ethical approval for the study was obtained from the Institutional Ethics Committee (IEC) under approval number IGGMC/ pharma/ 3742-2024.)

Distribution of Study Population by Bipolar Subtype and Episode Characteristics

Group	Subtype	Number of Patients (n)
Bipolar Mania Group (BD-M)	Hypomanic Episodes (BD-M I)	8
	Manic Episodes without Psychotic Symptoms (BD-M II)	30
	Manic Episodes with Psychotic Symptoms (BD-M III)	28
	Total	66
Bipolar Depression Group (BD-D)	Mild to Moderate Depressive Episode (BD-D I)	28
	Major Depressive Episode without Psychotic Symptoms (BD-D II)	19
	Major Depressive Episode with Psychotic Symptoms (BD-D III)	17
	Total	64
Mixed Episode Group (BD-MIX)	-	10
	Total	10
Overall Study Population		140

Demographic Characteristics of the Study Population (N = 140)

Variable	Category	Number of Patients (n)	Percentage (%)
Gender	Male	66	47.14%
	Female	74	52.86%
Education	Junior High School or below	61	43.57%
	High School or Junior College	31	22.14%
	Bachelor Degree or above	48	34.29%
Marital Status	Unmarried	63	45.00%
	Married	53	37.86%
	Divorced/Widowed	24	17.14%
Mean Age			28.5 ± 7.5 years
Mean Age of Onset			21.0 ± 5.8 years
Illness Duration			7.2 ± 5.1 years

RESULT

Parameter	Mean ± SD
TSH	6.31 ± 2.49 mcg I.U/mL
TT4	7.20 ± 3.20 mcg/dL
TT3	0.46 ± 0.70 ng/mL

Thyroid Hormone Secretion Abnormalities

Comparison	Finding	p-value
Increased secretion rate (overall)	Significant differences among subgroups	$p = 0.002$
BD-M II vs BD-D II	Higher increase in BD-M II (20.00%) vs BD-D II (1.61%)	$p < 0.005$
BD-M vs BD-D	Higher increase in BD-M (20.59%) vs BD-D (1.56%)	$p < 0.005$
Abnormality rate: BD-M II vs BD-D III	Higher in BD-M II (70.00%) vs BD-D III (30.43%)	$p < 0.005$

Summary of Thyroid Hormone Differences Among Diagnostic Subgroups

Hormone	Findings
TT4	No significant differences among diagnostic subgroups
TSH	Significantly higher in BD-M II compared to BD-MIX, BD-D I, BD-D II, and BD-D III
TT3	Significantly lower in BD-M II compared to BD-MIX, BD-D I, BD-D II, and BD-D III

DISCUSSION

This study involved 140 drug-naïve patients diagnosed with bipolar disorder (BD), divided into three groups based on their current mood state: manic (BD-M), depressive (BD-D), and mixed episodes (BD-MIX). The BD-M group had 66 patients, BD-D had 64 patients, and BD-MIX had 10 patients. Further classification showed different severity levels within the manic and depressive groups. The average age of participants was 28.5 years, with the illness typically starting around age 21. The average duration of illness was about 7.2 years. There were slightly more female patients (52.86%) than male patients (47.14%). No significant age or gender differences were found between the manic and depressive groups.

When comparing thyroid hormone levels, patients in the manic group (especially those with manic episodes without psychotic symptoms) showed higher levels of TSH and TT3 compared to those in the depressive group. There were no significant differences in TT4 levels across the different mood groups. Importantly, the rate of abnormal thyroid hormone secretion was much higher in the manic group than in the depressive group. For example, in the BD-M II subgroup, 20% of patients had increased thyroid hormone secretion, compared to just 1.61% in the BD-D II subgroup. Also, the rate of any thyroid abnormality was significantly higher in BD-M II compared to BD-D III (70% vs. 30.43%). However, no notable differences were found in the rates of decreased thyroid hormone secretion across groups.

These results suggest that thyroid function, particularly the activity of the hypothalamic-pituitary-thyroid (HPT) axis, may be more disrupted during manic episodes than during depressive episodes in BD. Although thyroid abnormalities were more common in mania, a weak correlation was found between hormone levels and symptom severity, indicating that thyroid dysfunction may play a role in mood changes, but is not the only factor involved.

Our findings differ from those of Li et al., who reported no significant differences in thyroid profiles across mood states in BD patients. This contrast may be due to differences in sample selection and study design, as our research focused specifically on drug-naïve individuals, eliminating the potential influence of psychiatric medications on thyroid function.

It is important to note that this was a cross-sectional study, which means it only provides a snapshot in time and cannot determine cause and effect. Therefore, further long-term and prospective studies are needed to better understand how thyroid function relates to mood changes in bipolar disorder. Such research could help determine whether thyroid abnormalities are a temporary state during mood episodes or a consistent feature of the illness, potentially guiding future treatment strategies

CONCLUSION

This study is notable for exclusively including drug-naïve bipolar disorder (BD) patients, which reduces the influence of confounding factors often present in similar studies where patients are already on psychotropic medication. A key finding was that 42.75% of BD-D (bipolar depression) patients showed decreased thyroid hormone secretion, suggesting the need for caution when prescribing medications that might further suppress thyroid function. This highlights the potential role of adjunctive thyroid hormone therapy in treatment-resistant cases, especially in patients with rapid-cycling BD. However, the study measured thyroid hormones at a single time point, not accounting for natural fluctuations in hormone levels throughout the day, which may affect accuracy. Additionally, the small sample size in the mixed episode (BD-MIX) group may introduce statistical variability or error. Despite these limitations, the study clearly shows that thyroid function varies significantly between manic and depressive episodes in BD, which has direct implications for clinical diagnosis and treatment strategies. One limitation was the unavailability of reagents for assessing free thyroid hormones (FT3, FT4), free TSH, and thyroid antibodies, which could have provided a more comprehensive endocrine profile. There were no conflicts of interest declared by the author

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