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Association between bipolar affective disorder and thyroid dysfunction

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ABSTRACT

Background: Bipolar affective disorder may be associated with alterations in thyroid function. A comprehensive thyroid assessment is important for assessing clinical and sub-clinical imbalances linked to a variety of mood disorders like bipolar affective disorder.
Aim: To find out the association between bipolar affective disorder and thyroid dysfunction.
Materials and method: The present cross-sectional study was conducted at Government District Wenlock Hospital, Mangalore (GDWH), India. A total of 50 newly diagnosed bipolar affective disorder patients and 50 age and sex matched controls without bipolar affective disorder as confirmed by the application of Bipolar Spectrum Diagnostic Scale were included in the study. Thyroid function was assessed among the patients and control group to study the association between bipolar affective disorder and thyroid dysfunction. Odds ratio was calculated to find out the strength of association between thyroid gland dysfunction and bipolar affective disorder.
Results: The mean Bipolar Spectrum Diagnostic Scale score among patients diagnosed with bipolar affective disorder was 20.84 and that of the control group was 1.98. The proportion of thyroid dysfunction among bipolar affective disorder patients and among control group was 14% and 6% respectively. The odds ratio was calculated to be 2.55. Mean T3 values were higher in the bipolar affective disorder patients than the control group and this association was found to be statistically significant ($p = 0.031$). Mean T4 and TSH values were higher among the bipolar affective disorder patients but did not show any significant differences when compared with the control group.
Conclusion: The present study concludes that a statistically significant association exists between elevated T3 hormone and bipolar affective disorder and observes that the patients with bipolar affective disorder are 2.55 times more commonly associated with thyroid dysfunction.

1. Introduction

The relationship between thyroid dysfunction and psychiatric illness has interested clinicians since long. In 1888 the Committee of the Clinical society of London reported on the mental changes observed in over 100 cases of Myxoedema and noted the general retardation, sluggishness and slowness of apprehension, which was associated with insanity in the form of melancholia, chronic mania and dementia (Asher, 1949). It is now clearer that the thyroid hormones play a major role in the functioning and regulation of the neural tissue activity. Hence, it follows that any derangement in the synthesis, secretion, action and peripheral metabolism of thyroid hormones affects the normal functioning of neural tissue, the symptoms of which may manifest as psychiatric syndromes (Bauer and Whybrow, 2001). Thyroid hormones have profound effects on mood and behavior, and seem to be able to modulate the phenotypic expression of major affective illness (Bauer and Whybrow, 2001). Disturbances of affect and mood, such as major depression and bipolar affective disorder, are associated with disturbances of peripheral thyroid hormone metabolism (Müller-Oerlinghausen et al., 2002). This is supported by the fact that administration of adjunctive supraphysiological doses of levothyroxine have been found to be an effective

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treatment option for refractory bipolar affective disorder (Bauer et al., 1998; Baumgartner et al., 1994). Sub-clinical hypothyroidism has also been suspected of being a risk factor for depression (Haggerty et al., 1993; Kraus et al., 1997; Oomen et al., 1996). A number of studies have investigated the association between thyroid dysfunction and mood disorders. The investigators in these studies had observed an altered thyroid function in mood disorder (Baumgartner et al., 1988; Kraus et al., 1997; Maes et al., 1993; Poirier et al., 1995). It is evident from earlier studies that there exists an association between thyroid gland dysfunction and psychiatric disorders. To the best of our knowledge no previous study had investigated such an association in the bipolar disorder psychiatric group.

The manifestations in patients with bipolar affective disorder are exceptionally diverse ranging from mild hypomania or mild depression to severe forms of mania or depression accompanied by profound psychosis. The lifetime prevalence of bipolar affective disorder is 1.3–1.6% with mortality rates being 2–3 times higher than that of the general population. Equally prevalent among both sexes (except rapid cycling bipolar disorder which is more common in females), nearly one third of the affected patients admit to at least one suicide attempt (Müller-Oerlinghausen et al., 2002). Bipolar affective disorder has been eating into the vitals of mankind leading to obesity, loss of work efficiency, impairment of mental functions, deteriorating social relationships and finally deliberate self-harm (Elmslie et al., 2001). Lewnsohn et al. (2003) found that the onset of bipolar affective disorder occurred mostly during adolescence and also pointed out that relatives of bipolar affective disorder adolescents have elevated rates of sub threshold bipolar disorder and major depressive disorder. Preventing bipolar affective disorder, thus, becomes a high public health priority. It has been suggested that of all the endocrine systems thought to be linked to the pathophysiology of bipolar affective disorder, the *hypothalamic–pituitary–thyroid axis* is the prime candidate (Müller-Oerlinghausen et al., 2002). Thus, it has been assumed that bipolar affective disorder may be associated with alterations in thyroid function and hence the need for a comprehensive thyroid assessment is important for assessing clinical and sub-clinical imbalances linked to a variety of mood disorders like bipolar affective disorder (Nath and Sagar, 2001).

The present cross-sectional study is intended to test the association between thyroid dysfunction and bipolar disorder spectrum in patients with newly diagnosed bipolar affective disorder (ICD-10). In the present investigation, the strength of association would be defined using odds ratio. The degree of association between the two might help in a better prognosis of patients with bipolar affective disorder as appropriate treatment can be administered to both the problems without undermining the importance of this association.

2. Materials and methods

The present cross-sectional study was conducted at Government District Wenlock Hospital, Mangalore (GDWH) which is a 550 bed tertiary care hospital providing comprehensive health care to the patients of Dakshina Kannada district in Karnataka. GDWH is also a teaching hospital for Kasturba Medical College (KMC), Mangalore. The present research included 50 newly diagnosed bipolar affective disorder patients and 50 age and sex matched controls without bipolar affective disorder. Institutional ethical committee approval was taken prior to the study. Informed consent was obtained from each participant before undertaking the research.

Bipolar affective disorder patients for this study were taken from amongst those who attended the psychiatric outpatient department of GDWH. The clinical diagnosis was reached by the consultant psychiatrist. The diagnosis was confirmed by the application of Bipolar Spectrum Diagnostic Scale (Nassir Ghaemi et al., 2005). The Bipolar Spectrum Diagnostic Scale (BSDS) developed by Dr. Ronald Pies is a self-report questionnaire that is found to be highly sensitive and specific for bipolar spectrum illness (Nassir Ghaemi et al., 2005) in its original format and even when the local versions of the BSDS are used (Zaratiegui et al., 2011). With regards to BSDS score, a total score of 20–25 indicates that bipolar spectrum disorder is highly likely; a score from 13 to 19 indicates moderate probability; a score from 7 to 12 indicates low probability; and a score from 0 to 6 indicates that bipolar disorder is highly unlikely. The severity of symptoms in the present study was measured using Hamilton rating scale for depression (Hamilton, 1967) and Young mania rating scale (Young et al., 1978).

All the newly diagnosed bipolar affective disorder (ICD-10) patients aged between 18 and 50 years without any thyroid dysfunction clinically and without any prior history of lithium or thyroid hormone treatment were included in the study and constituted the bipolar affective disorder group. Control group consisted of participants aged between 18 and 50 years who were employed in various industries and did not suffer from bipolar affective disorder as confirmed by the application of BSDS. While recruiting participants in the control group individual matching was done for age and sex, i.e. once the bipolar affective disorder patients were included in the study, the corresponding age and sex matched participants were included in the control group. Thus, a total of 24 males and 26 females were included in each group. Mean age of participants in both groups was 36.9 years. All participants had at least completed their high school education and were able to understand and comprehend English language well. It was ensured that the participants had no thyroid dysfunction clinically or any prior history of lithium or thyroid hormone treatment. Participants who were on steroid treatment, amiodarone and antihypertensive drug therapy or had taken cough medicines within last two weeks, or had any contrast medium during the previous eight months for any investigation were excluded from the study.

For assessment of thyroid function, blood samples were collected from the cases and controls and analyzed for T3, T4 and TSH levels using ''ECLIA'' electrochemiluminescence immunoassay. The normal ranges for thyroid hormones as indicated in the assessment kit was were 0.6–2.02 ng/mL, 5.13–14.06 μg/dL, and 0.27–5.5 μIU/mL for T3, T4 and TSH respectively. Presence of a genuine thyroid dysfunction was in accordance with defined biochemical parameters. Participants having $T3 > 2.02$ ng/mL, $T4 > 14.06$ μg/dL and $TSH < 0.27$ μIU/mL were considered hyperthyroid while participants with $T3 < 0.6$ ng/mL, $T4 < 5.13$ μg/dL and $TSH > 5.5$ μIU/mL were considered hypothyroid.

The details of all participants in both groups were collected using a pretested proforma that was filled by interviewing the participants. The proforma contained patient's individual information, personal history, family history, childhood experiences, investigation reports, BSDS score, Young mania rating scale score and Hamilton rating scale for depression score.

The data collected was analyzed statistically using SPSS (*Statistical Package for Social Sciences*) computer software version 11.0. Student's *t*-test was done to compare mean values of thyroid hormone levels among cases and controls. A *p*-value of <0.05 was considered as significant. Odds ratio was calculated to find out the strength of association between thyroid gland dysfunction and bipolar affective disorder.