



## Study of Thyroid Abnormalities in Psychiatric Out Patients with Depression At A Tertiary Care Centre in Central India

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### Abstract

**Introduction** *Thyroid hormones have a profound influence on the human brain and behaviour, and the interrelationship between thyroid dysfunction and psychiatric disturbances has been well documented. Up to one-third of psychiatric patients may demonstrate thyroid function test abnormalities that do not always reflect true thyroid disease, but rather are a manifestation of secondary effects on one or more levels of the hypothalamic-pituitary-thyroid (HPT) axis.*

**Materials And Methods** *Samples collected from 69 O.P.D. patients who are newly diagnosed cases of depression, not on medication and more than 18 yrs of age. Patient having thyroid disorder or on medication affecting thyroid function are excluded from study. Serological test Thyroid Stimulating Hormone (TSH) Test, Total T4/ Total Thyroxine, Total T3 / Total Triiodothyronine are done for identifying thyroid function abnormality in psychiatric patients.*

**Results-** *Out of 69 psychiatric out patients with clinical diagnosis of depression investigated for thyroid abnormalities, Males were 37 & Female were 32. The mean age of the study subjects was 35.23 yr. Abnormal thyroid function test was observed in 26 out of 69 (37.6%) patients.*

**Conclusion-** *As psychiatric disturbances may be a manifestation of thyroid disease, clinical assessment of physical signs and symptoms of thyroid disease should be a routine element of psychiatric evaluation. If there is suspicion for thyroid disease, measurement of TSH with a sensitive method should be the first test obtained.*

**Key Words-** *Brain, HPT-axis, T3, T4, TSH, interrelationship.*

### Introduction

Thyroid hormones have a profound influence on the human brain and behavior, and the interrelationship between thyroid dysfunction and psychiatric disturbances has been well documented. Up to one-third of psychiatric patients may demonstrate thyroid function test abnormalities that do not always reflect true

thyroid disease, but rather are a manifestation of secondary effects on one or more levels of the hypothalamic-pituitary-thyroid (HPT) axis. Originally termed the euthyroid sick syndrome, this phenomenon is now more commonly referred to as “non-thyroidal illness.”<sup>1</sup>

Nonthyroidal illness is characterized by the presence of altered thyroid function parameters

that are not considered indicative of actual thyroid disease but rather occur as a response to underlying systemic or acute psychiatric illness. This syndrome may be seen in a variety of systemic illnesses and stress states, as well as in psychiatric illness.<sup>3</sup>

The prevalence of mood and anxiety disorders is higher in patients with thyroid dysfunction<sup>6</sup>, thyroid status predicts treatment response in major depression and bipolar disorder<sup>7</sup>, augmentation with thyroid hormone has therapeutic efficacy in treatment-resistant depression<sup>8</sup>, and additionally, thyroid hormone receptors are localized to limbic structures implicated in regulation of mood<sup>9</sup>. There is limited literature on the rates of thyroid dysfunction among patients with major psychiatric disorders in the Indian population.

The term “thyroid dysfunction” refers to abnormalities in laboratory test parameters of thyroid hormonal status, namely serum TSH (thyroid stimulating hormone), T3 (triiodothyroxine), & T4 (L-thyroxine).<sup>5</sup>

### Materials and methods

The prospective study is conducted at M.G.M. Medical College and M.Y. Hospital, Indore, a tertiary-care, Government Hospital in Psychiatric O.P.D. in year 2013-2014. The study protocol is approved by the M.G.M. Medical College Institutional Ethics Review Board (IERB). The patients are assigned an ICD-10<sup>37</sup> diagnosis based on a clinical interview and diagnostic consensus between two consultant psychiatrists. The focus of the analysis is to examine thyroid status in patients with depression disorders.

Samples are collected from Psychiatric O.P.D. patients-

#### Inclusion criteria are-

1. Newly diagnosed cases not on medication.
2. Patient should be more than 18 yrs of age.

#### Exclusion criteria are-

1. Patient having thyroid disorder.
2. Patient on medication affecting thyroid function.

Sample collection consent is taken from the patients or first degree relative of the mentally ill patients.

### Specimen collection and preparation

1. Serum is the recommended sample type for this assay.
2. Samples were collected observing universal precautions for venipuncture.
3. Samples were allowed to clot for 1 hour before centrifugation.
4. Grossly hemolytic, lipemic or turbid samples were avoided.
5. Prior to use, specimens were capped and stored at 2-8°C (upto 48 hrs)

The assays of TSH, T3, and T4 are done by the Chemiluminescence (CLIA) method using Autobio LUMO microplate luminometer. Reagents were obtained from Autobio. The sensitivity and range for the assays were as follows:

T3=0.1 ng/ml (range=0.1-8 ng/ml); T4=0.5 µg/dl (range=0.5-30 µg/dl); TSH=0.003 µIU/ml (range=0.01-100 µIU/ml)

Following serological test are done for identifying thyroid function abnormality in psychiatric patients:

1. Thyroid Stimulating Hormone (TSH) Test  
**Reference Range - 0.5-5.0 µIU/ml**
2. Total T4/ Total Thyroxine **Reference Range- 5.5-12.5 µg/dl**
3. Total T3 / Total Triiodothyronine  
**Reference Range 0.8-2.0 ng/ml**

### RESULTS

Results of 69 patients tested for thyroid function test were recorded. Male=37 & Female=32. The mean age of the study subjects was 35.23 yr. Hypothyroidism was diagnosed when the TSH levels are more than normal reference range (>5.0µIU/ml). Hyperthyroidism was diagnosed when the TSH values are less than normal reference range (<0.5µIU/ml).

### Thyroid dysfunction in patients with depression

The study revealed a significant association of the endocrinopathy with the diagnostic group of Depression. There were 69 patients with depression. (Table No. 1) 26 out of the 69(37.68%) patients with depression had abnormality in one or more parameter of thyroid function test. Hypothyroidism was observed in 8 out of 26 (30.76%) patients and Hyperthyroidism was observed in 4 out of 26 (15.3%) patients of depression with abnormal thyroid function test. Non specific alterations in the TFT are much more common in patients with depression and are seen in 14 out of 26 patients with abnormal TFT. As these patients are clinically euthyroid these patients represent Nonthyroidal illness or Euthyroid Sick Syndrome.

**Gender effect-** Abnormal thyroid hormonal levels are more common in females than male patients with depression. 12 out of 37 males (32.4%) were having abnormal thyroid hormone levels while 14 out of 32 (43.7%) females having abnormal thyroid function test. (Table No. 2)

### Age distribution of abnormal TFT in patients suffering from depression-

Most of the patients in the study group belonged to the age group of 26-35yrs followed by 18-25yrs i.e. young adults. However thyroid function test abnormalities were more common in older age group of 46-55yrs in which 5 out of 8 (62.5%) patients show abnormal thyroid function test. While age group of 26-35 yrs in which 8 out of 22 (36%) patients with second highest number of abnormal thyroid function test were observed. (Table No.3)

**Table No. 1 Diagnosis wise distribution of Abnormal TFT**

Diagnosis	No. of Patients	Abnormal TFT	Hypo-thyroidism	Hyper-thyroidism	Nonspecific findings
Depression	69	26	8	4	14

**Table No. 2 Sex distribution of abnormal TFT**

Sex	No. Of Patients	Abnormal TFT
Male	37	12
Female	32	14

**Table No. 3 -Age distribution of abnormal TFT in Psychiatric patients**

Age interval	Depression	
	Total	Abnormal TFT
18-25	17	7
26-35	22	8
36-45	19	5
46-55	8	5
56-65	3	1

### Discussion

Our results indicated that thyroid abnormalities were present in patients with depression disorders in psychiatric O.P.D. population of a tertiary-care hospital. Thyroid dysfunction in Depression disorder seen in our study was (37.68%) which was higher than that shown by Rajiv Radhakrishnan et al (25.41%)<sup>5</sup> Bartalena et al<sup>11</sup> (32%) and that of Cassidy et al<sup>12</sup> (11.51%).

Among the general population in India, the rates of thyroid dysfunction are, clinical hypothyroidism=3.9 per cent, subclinical hypothyroidism= 9.4 per cent<sup>10</sup>. Hypothyroidism was seen 8 out of 69 (11.5%) psychiatric patients of the study group population. Abnormal thyroid hormonal levels are more common in females (43.7%) than male (32.4%) patients with depression.

Another significant finding is that thyroid hormone abnormalities may represent nonthyroidal illness such as “euthyroid sick syndrome” and “euthyroid hyperthyroxinemia” which are a response to chronic systemic illness. The prevalence of euthyroid sick syndrome ranges from 7 to 33 per cent in psychiatric inpatients<sup>1,13</sup> while euthyroid hyperthyroxinemia is thought to be more common in mood disorders<sup>14</sup>. Although it is difficult to distinguish nonthyroidal illness from true thyroid dysfunction in euthyroid subjects, the TSH level in euthyroid sick syndrome is upto 15-20 $\mu$ IU/ml<sup>15</sup>. Severe thyroid dysfunction may mimic almost any psychiatric symptom profile.<sup>16,17</sup>

It has been assumed that specific psychiatric disorders may be associated with alterations in thyroid functioning, and subclinical hypothyroidism has been suspected of being a risk factor for depression.<sup>18,19</sup> This hypothesis is supported by the fact that, in selected cases, thyroid hormone therapy has proved useful in the management of refractory depression.<sup>20</sup> The close relationship of thyroid economy and cognitive function has interested clinicians and researchers since the possible association between thyroid functioning and behavior was first described by Parry<sup>21</sup> and Graves.<sup>22</sup> Asher's findings show that thyroid hormone deficiency may lead to depression and psychosis and may be reversed by desiccated thyroid administration.<sup>16</sup> Many studies on hypothalamic-pituitary-thyroid (HPT) system have suggested that thyroid hormones play an important role in the pathophysiology of mood disorders.<sup>23,24</sup> Thyroid hormones may interact with neurotransmitter systems and intracellular mechanisms and are capable of modulating the phenotypic expression of major affective illnesses,<sup>23,24</sup> depressive and bipolar disorders in particular. Studying the HPT axis, investigators have found abnormal TSH response to TRH stimulation in depressed patients.<sup>27,29-31</sup> The peak response was blunted in 25% to 30% of patients<sup>32</sup> and exaggerated in 10%.<sup>33</sup> Elevated levels of cerebrospinal fluid (CSF) TSH have also been

reported in depressed patients.<sup>34</sup> Most depressed patients are euthyroid, although subclinical hypothyroidism can be seen in approximately 15% of depressed patients.<sup>25 26</sup> Subclinical hypothyroidism may be a risk factor for depression in women.<sup>67</sup> The time to recurrence of depressive episodes was found to be inversely correlated with serum T<sub>3</sub> but not T<sub>4</sub> levels in patients with unipolar depression.<sup>28</sup> In this study raised serum triiodothyronine (T<sub>3</sub>) level were significantly associated with depressive disorder group of patients with p value < .002. Thyroid measures in the low-normal or below-normal range seem to be relevant for the pathophysiology of bipolar disorders and may result in a less than optimal outcome<sup>37</sup>. Frye and colleagues<sup>35</sup> reported an association of low levels of T<sub>4</sub>, within the normal range, with greater mood instability and depression severity during prophylactic lithium treatment in bipolar patients. Cole and colleagues<sup>36</sup> found poorer treatment response in bipolar patients with lower free T<sub>4</sub> index values and higher TSH values within the normal range. Potential pathophysiologic factors contributing to hyperthyroxinemia in psychiatric patients include redistribution of T<sub>4</sub> out of the tissues (particularly the liver), temporary pituitary thyrotroph resistance to T<sub>4</sub>, or impairment of T<sub>4</sub> clearance<sup>38</sup>. There is some evidence suggesting that centrally mediated hypersecretion of TSH is present in these patients<sup>39</sup> In the case of hypothyroxinemic nonthyroidal illness seen in acute psychiatric patients, inhibition of TSH secretion and impairment of normal feedback responses may be due to production of cytokines and other humoral or local factors.<sup>40,41</sup>

**Conclusion-** In the present study-

- 26 out of 69 psychiatric patients with depressive disorder show thyroid dysfunction, among which 30.7% patients show hypothyroidism, 15.3% patients show hyperthyroidism and 53.8% patients show non-specific alterations in concentration of iodothyronines (T<sub>3</sub> or T<sub>4</sub>).

- Patients with non-specific alterations in concentration of T3 or T4 belonged to the group of Nonthyroidal illness or Euthyroid Sick Syndrome. Nonspecific alterations of T3 and T4 were commonly seen in patients with Depression.
- Raised serum triiodothyronine (T<sub>3</sub>) levels were significantly associated with depressive patients with p value < 0.002. (T- Test)
- Abnormal thyroid hormonal levels are more common in females (43.7%) than male (32.4%) patients with depression.
- Hyperthyroidism was seen more commonly in male patients with depression than females.

Both excess and inadequate thyroid hormones can induce disturbances of behaviour that mimic depression, mania, and dementia. The neuro-cognitive impairments accompanying these dysfunctions are generally reversible following return to euthyroid status. Because psychiatric disturbances may be a manifestation of thyroid disease, clinical assessment of physical signs and symptoms of thyroid disease should be a routine element of psychiatric evaluation. As in the medical inpatient population, the decision to order thyroid screening should be made on an individual basis, and results should be interpreted with caution.

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