

A Study of Depression and Thyroid Levels in Drug Naïve First Episode Depression

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ABSTRACT

Depression is a major public health problem. Thyroid dysfunction is often seen in patients with depression. Thyroid function test can be considered as an integral part of the evaluation of newly diagnosed depressed patients. The present study was planned to assess the thyroid profile in drug naïve first episode depression cases and to find out a correlation between severity of depression and thyroid level. The present study included 25 patients with first episode depression who were drug naïve from Out Patient department of Psychiatry, Govt. Rajaji Hospital, Madurai. It is a cross sectional study and they were evaluated for thyroid profile. The following tools were used to assess the subjects; they were HDRS, PSLES and SES. The present study revealed that serum T3 and T4 level rises significantly with the severity of depression. It is concluded that, in newly diagnosed depressed patients, evaluation of thyroid profile is essential for effective management.

Key Words: Depression, severity, thyroid levels.

INTRODUCTION

Mood disorders are the most common psychiatric disorder and in the most recent surveys, it has been seen that major depression has the highest lifetime prevalence (almost 17 percent) of any psychiatric disorder. [1] The World Health Organization (WHO) estimated that about 100 million individuals develop depression every year. [2] It is seen that India has about 16.6 million new cases of major depression

per year and 10.3 million cases at any time. [3]

Although a relationship between clinical disorders of thyroid gland and depression has been well established the significance of the association between thyroid function and major depression is much less clear. The most common documented abnormalities in depression are elevated T4 levels, low T3, elevated T3, a blunted TSH response to TRH, positive antithyroid antibodies and elevated CSF TRH concentration. A state of brain hypothyroidism in the setting of systemic euthyroidism. [4-6] Patients with thyroid disturbances can present with a variety of neuropsychiatric symptoms including depressed mood, mania, acute psychosis, anxiety and dementia. Hence the possibility of a relationship between thyroid gland and brain and depression has been of interest to both clinicians and researchers for centuries.

According to Joffe et al.,(1990),the reviews on various studies have yielded a conflicting data in thyroid functioning in acute depression, however the most consistent findings have been elevated total thyroxin (T4) or free thyroxin (FT4) within the euthyroid range that decreases with the treatment for depression. [7] In India, very little work has been done in this field Chopra VK et al.,(2001) has done a study on basal thyroid function in depressive illness and concluded that thyroxin(T4) levels were elevated in the drug naïve first episode depressive patients as compared to healthy controls. [8] This is in agreement with most

of the earlier studies. [9-12] Hence this study was conducted to evaluate the basal thyroid functions in drug naïve patients with first episode depression and to establish the relationship between severity of depression and thyroid levels. As it will be beneficial in the management of depression.

AIMS AND OBJECTIVES

Objectives:

1. To assess the level of serum T3, T4, TSH in patients with first episode depression.
2. To correlate the severity of depression and thyroid hormone level.
3. Presumptive stressful life events and its impact on severity of depression and its relationship with thyroid hormone levels.

Inclusion criteria

1. Age: between 25 to 45 years for both male & female
2. Patients diagnosed as Depressive disorder (according to ICD-10 DCR Criteria) who are drug naïve & first episode.
3. Patient who are cooperative and have given consent

Exclusion Criteria

1. Individuals with past history of psychiatric disorder
2. Individuals with Past and Present history of any systemic illness/substance abuse or dependence and Psychiatric illness.
3. Patients on any psychiatric medications.
4. Patients who have been already diagnosed as hypothyroid or hyperthyroid or on any thyroid medication.

METHODOLOGY

Study design

The study is a cross sectional study. The patients who are diagnosed as drug naïve case of first episode depression and who reported to the outpatient department of psychiatry, Government Rajaji hospital, Madurai. The study samples were selected from those who fulfilled the inclusion and exclusion criteria. Informed consent was obtained from the subjects. Institutional ethical committee approval was obtained. The total numbers of 25 patients were included in the study. The tools were

administered in a following order Case history proforma, ICD 10 DCR, HDRS, PSLES and SES to the entire patients. Thyroid hormone level was assessed after 12hrs fasting between 8am and 9am.

Tools Used:

1. Case history Proforma: It includes personal demographic details, personal history, past history, family history, physical and Mental status examination and biochemical investigations.

2. ICD-10 DCR: criteria the diagnostic criteria for research accompanying the ICD-10 (DCR) Diagnostic Criteria for Research are designed for use in research; their content is derived from the Glossary to the chapter on Mental and Behavioural Disorder in the “Clinical Descriptions and Diagnostic Guidelines” (CDDG) that have been produced for general clinical and educational use by psychiatrists and other mental health professionals (WHO 1992).

3. Hamilton rating scale for depression: The Hamilton Rating Scale for Depression (HAM-D) is one of the most popular depression assessment instruments among the clinicians. Max Hamilton originally published the scale in 1960. The original 1960 version contained 17 items (HDRS-17), but four other questions not added to the total score were used to provide additional clinical information. Each item on the questionnaire is scored on a 3 or 5 point scale, depending on the item, and the total score is compared to the corresponding descriptor.

4. Presumptive stressful life event scale: Developed by Gurmeet Singh et al.(1983), it was constructed and standardized for use in the Indian population. It is a standardization of the Social Readjustment Rating Scale (SRRS)

5. SES scale: Kuppuswamy scale is widely used to measure the socio-economic status of an individual in urban community based on three variables namely education, occupation and income. The modification of Kuppuswamy scale meant to determine the socioeconomic status of family based on education and occupation of head of the

family and per capita income per month has also been widely used.

depression with somatic syndrome.

Statistical Design:

Statistical design was formulated using the data collected as above, for each of the scales and sociodemographic variables the central values and dispersion was calculated. In comparison of the data for categorical variables chi-square and for numerical variables student t test were used.

Table 1 shows the severity of depression based on Hamilton rating scale for depression. Based on HAM-D scoring two patients (8%) had mild depression, 13 patients (52%) had moderate depression. Among patients with severe depression, 5 patients were categorized as severe

Table 1
Table showing Severity of depression in cases

Depression severity	Cases	
	No	%
Mild	2	8
Moderate	13	52
Severe	5	20
Severe with somatic syndrome	5	20
Total	25	100

Table 2
Table showing relationship between socio Demographic variables and severity of depression

Sl. No	Variable	Severity of Depression								P value
		Mild		Moderate		Severe		Severe with S.S		
		No.	%	No.	%	No.	%	No.	%	
1	SEX									0.3012
	Male	0	0	2	40	2	40	1	20	
Female	2	10	11	55	3	15	4	20		
2	MARITAL STATUS									0.6543
	Married	2	9.1	11	50	5	22.7	4	18.2	
Unmarried	0	0	2	66.7	0	0	1	3.3		
3	SES									0.0182*
	Lower Middle	1	6.7	11	73.3	2	13.3	1	6.7	
Upper Middle	1	10	2	20	3	30	4	40		
4	RESIDENCE									0.0533
	Rural	2	12.5	10	52.5	2	12.5	2	12.5	
Urban	0	0	3	33.3	3	33.3	3	33.3		

Table 2 shows the relationship between socio demographic variables and severity of depression. Depression severity and age of patients did not have any significant relationship. It shows that among five males with depression two belong to moderate and three belong to severe category. Among twenty females, two had mild, eleven had moderate and seven had severe depression, but the difference was not significant. Among depressive twenty-two were married and three were unmarried and majority of married (44%) had moderate depression, nine patients (36 %) had severe depression. Severity of depression was not affected by the marital status of patients. Regarding socioeconomic status fifteen patients 60% belong to low socioeconomic status and ten patients belong to middle socio-economic status. Among patients with low socio-economic status eleven patients (73.3%) had moderate depression and three patients (20%) had severe depression. Among middle socio-economic status two patients (20%) had moderate depression and seven patients had (70%) had severe depression. The difference is statistically significant. No difference was noted in comparison between residential status and severity of depression.

Table : 3

Table showing Socio demographic characteristics and thyroid profile

Characteristics	Thyroid Profile					
	T3		T4		TSH	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
AGE						
Upto 25	107.7	11.4	9.8	2.18	3.43	3.92
26-30	109.1	13.6	9.99	1.44	2.09	1.65
31-35	101.5	23.9	9.63	2.59	0.98	1.13
36-40	100.7	28.5	8.93	1.19	1.5	0.01
41-45	103.4	12.4	10.36	1.22	3.04	2.26
'p' value	0.736		0.8083		0.2844	
SEX						
Male	103	12.1	9.29	2.06	4.4	3.57
Female	106	16.8	9.97	1.63	1.84	1.66
'p' value	0.5398		0.4751		0.0351 *	
MARITAL STATUS						
Married	106	16.4	10.03	1.62	1.91	1.63
Unmarried	101	11.5	8.4	1.87	5.62	4.31
'p' value	0.476		0.1429		0.0365 *	
RESIDENCE						
Rural	107.4	15.1	9.87	1.7	2.6	2.74
Urban	101.9	17.2	9.77	1.8	1.92	1.31
SOCIAL CLASS						
Lower middle	104.4	18.2	10.17	1.72	1.79	1.077
Upper Middle	106.9	12.0	9.33	1.61	3.2	2.86
'p' value	0.9114		0.2218		0.1341	

P < 0.05 * P < 0.001**

Table3: It shows the relationship between sociodemographic characteristics and thyroid profile. It shows no significant relation existing between age, residence and social class in relation to serum T3, T4 and TSH levels. On comparison of sex and serum TSH levels there is a significantly high TSH in men compared to women but no relationship between serum T3, serum T4 levels and sex. Since the elevation of TSH level is within normal limits, the results do not reflect underlying subclinical hypothyroidism between sex. On comparison of marital status and serum TSH levels there is a significantly high serum TSH in married person, but no correlation seen between T3, T4 and marital status

Table 4

Table showing Severity of depression and thyroid hormone values

S.No.	Variable	Thyroid hormone values					
		T3 (ng/dl)		T4 (µg/dl)		TSH(mIU/ml)	
		Mean	SD	Mean	SD	Mean	SD
1.	Severity of depression						
	Mild	83.5	4.9	7.55	0.64	0.74	0.12
	Moderate	103.5	16	9.68	1.64	2.2	1.81
	Severe	109.2	15.5	10.27	1.36	2.73	1.25
	Severe with somatic syndrome	115.2	9.5	10.7	1.83	3.02	4.33
	'p' value	0.0234*		0.0301*		0.2317	

[P < 0.05 *, P < 0.001**]

Table 4 shows the relationship between severity of depression and thyroid function values. The mean T3 level in mild depression is 83.5 and increases as the

severity of depression increases with mean T3 in patients with severe depression with somatic syndrome was 115.2. As severity of depression increases the mean T3 value also

increases which was statistically significant. The same trend was noted in relation to serum T4 level with significantly high T4 levels in severe depression compared to mild or moderate depression. On comparison of TSH level, even though TSH values vary with severity of depression, the relationship was not statistically significant.

Table 5

Table showing PSLE and Thyroid hormone values in MDD cases

S.No.	Variable	Thyroid hormone values					
		T3		T4		TSH	
		Mean	SD	Mean	SD	Mean	SD
1	PSLE						
	≤ 200	106.7	15.9	9.95	1.66	2.4	2.48
	>200	98.8	15	9.23	2	2.11	1.42
	'p' value	0.2496		0.4143		0.9704	

Table 5 : Shows the relationship between presumptive stressful life events and the thyroid function values in depressives. The mean serum T3 levels in patients with depression with life event score < 200 was 106.7 and more than 200 was 98.8 showing no statistical difference. On comparison of patients with less than 200 and more than 200 in presumptive stressful life event score in relation to serum T4 levels and serum TSH levels also did not show any statistical difference.

Table 6

Table showing Depression severity and PSLE score

Depression severity	PSLE Score		P value
	Mean	SD	
Mild	193.5	26.2	0.0408 *
Moderate	97.9	40.5	
Severe	163	68.8	
Severe with somatic syndrome	100.2	59.2	

[P < 0.05 *, P < 0.001**]

Table 6 shows the relationship between the severity of depression and presumptive stressful life event score. On comparison of life event scoring and severity of

depression, mean score for mild and severe depression was significantly higher than moderate and severe depression with somatic syndrome.

DISCUSSION

The present study is an evaluation of the basal thyroid functions in drug naïve patients having first episode of depressive illness only. Hence the nonspecific effects of chronicity of illness and pharmacological agents on thyroid functions were avoided. In this study, majority of the sample had moderate depression (52%). One fifth (20%) of the sample had severe depression with somatic syndrome and another one fifth (20%) had severe depression without somatic syndrome, remaining (8%) had mild depression. On comparison of socio demographic variables and severity of depression no significant relationship was observed except socioeconomic status. Also, while comparing sociodemographic characteristics and thyroid profile, there has been a significantly higher TSH level in men and those who are unmarried. Since the elevation of TSH was within normal limits, no significant difference was noted between sex and subclinical hypothyroidism.

Thyroid hormones play an important role in brain development, and then in the adulthood, they influence structure, perfusion and function of the central nervous system. The mechanisms of thyroid hormones action in the brain cells are complicated, warranted by availability of free hormone, activity of thyroid hormone transporters and receptors, activity of deiodinase. According to Bauer and Whybrow 1988, [5] in some cases of depression the brain would be thyroid hormone deficient and the relative increase of thyroxine would exert a compensatory role in the maintenance of the 'affective homeostasis' offering more T4 for the brain. The majority of the studies in major depression found a relative increase of serum FT4, Total T4, within the normal range. Neurobiologically, this thyroid activation has been proposed to represent a

compensatory mechanism to a pathological process that is depression or the primary pathology itself. With regard to T3 Kirkegaard and Faber et al.,(1986) have found no alterations in the freeT3 serum levels in depressed patients. [18] It raises the hypothesis that the combination of production of increased T4 with the production of normal T3 suggest a reduction in conversion of T4 into reduced T3 caused by the decrease in the enzymatic activity of deiodination in the brain. Thus a defect in the brain deiodinase can be a pathogenic factor in depression, raising the possibility of central or brain hypothyroidism. In TSH Cleare et al.,(1996) found a positive relation between depressive scores and the increase in TSH levels confirming the previous findings of this same group. [19] A probable hypothesis for the increase in serum TSH in depression stems from the observation that the plasma level of this hormone is influenced by somatostatin, which inhibits TSH release from the hypophysis. In some studies (Rubinow DR et al., 1983 and Bissette G et al., 1986) they found a reduction in somatostatin in the CSF of depressed subjects, which may contribute for the increase in serum TSH in depressive conditions. [20,21]

Regarding the relationship between severity of depression and thyroid dysfunction the present study showed that the mean T3&T4 levels increased significantly as the severity of the depression increased. Even though the TSH levels also increased with the severity of the depression it was not statistically significant. Joffe et al. (1992) did not find any difference between patients with melancholic and non-melancholic depression with respect to total thyroxin (T4), total triiodothyronine (T3) and thyroid stimulating hormone (TSH). [13] In a study by Chopra VK et al, (2001) he did not find any difference with respect to any of the thyroid parameters between the depressive patients with and without the presence of somatic syndrome. [8] In addition, Saxena J et al., (2000) mildly depressed patients had

significantly lower TSH and severely depressed had higher TSH suggesting direct relationship between severity of depression and TSH levels. [14] Fountaulakis, et al., (2004) concluded that no significant differences can be traced concerning the thyroid function between clinical subtypes of depression nor any correlation between specific clinical symptoms and thyroid indices. [15] Apart from subtle changes in the thyroid functions, many studies have found overt thyroid abnormalities only in a minority of depressive patients (Goldetal., 1981; Diaz-Cabaletal.,1986; Joffe et al.,1992). [16,17, 13] The present study is consistent with the possible explanation for elevated T4. But the explanation for elevated T3 levels needs further evaluation of deiodinase, rT3 and severity of depression. In this study even though TSH has increased it is not statistically significant.

Considering the impact of Presumptive stressful life events within one year of the onset of depression, this study has found that depressives had significantly more life events suggesting that stressful life events within one year increase the onset of depression. However, in this study the PSLE score has no significant correlation with rising severity of depression. In consistent with the similar study by Grover et al.,2010 [22] the present study found that even though depressives had significantly more life events it had no relation with the severity of depression. Moreover, in this study there is no significant correlation was evaluated between stressful life events and thyroid hormone values. This study emphasizes the need for the importance of evaluating the basal thyroid functions in patients with first episode depression.

CONCLUSION

This study concluded that there are subtle but significant abnormalities in the basal level of thyroid hormones in acute depressive illness. There is a need to continue the research efforts in this field to further clarify the aetiological significance

of altered thyroid functioning in depressive illness and the possible role of thyroid hormone level as a biological marker for treatment response.

Further follow up studies will help in understanding the possible association of thyroid abnormalities in depressive disorder, their possible relationship with prognosis, treatment implications and treatment resistant depression. The present study suggests that in patients with major depressive disorder, routine assessment of FT3, FT4 and TSH on admission should be disseminated into routine practice settings, first to exclude overt or subclinical thyroid disorder and second, in case of normal TSH to exclude disturbances in free thyroid hormones, which may influence the clinical outcome. This study has limitations of being a cross sectional study with small sample size.

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Conflicts Of Interest

There is no conflict of interest.

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