

## Research article

**Study of thyroid profile among patients with major depressive disorder and generalized anxiety disorder in a tertiary care center**

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(Received: March 2022

Revised: December 2022

Accepted: February 2023)

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**ABSTRACT**

**Introduction and Aim:** Depressive disorder is a prevalent psychiatric disorder worldwide. Thyroid disorders have symptoms like major depressive disorder (MDD). Anxiety disorders are the most prevalent psychiatric disorders. Thyroid dysfunction is associated with increasing anxiety in generalized anxiety disorder (GAD). This study aimed to evaluate thyroid status in major depressive disorder and generalized anxiety disorder.

**Materials and Methods:** This cross-sectional study was conducted in a 17-months period. Diagnosis was made using DSM 5 (The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition Criteria). Estimation of serum free thyroxine (FT4), free triiodothyronine (FT3) and ultrasensitive thyroid stimulating hormone (U-TSH) was done by ELISA. The study included 126 patients, 66 GAD and 60 MDD patients.

**Results:** In both GAD and MDD, females outnumbered males. Age-group and disorder-type had significant association. In GAD and MDD, the mean values of FT3, FT4 and U-TSH were all within normal range. Among GAD patients, maximum were euthyroids followed by hyperthyroids and hypothyroids. In MDD patients, maximum were euthyroids followed by hypothyroids and hyperthyroids. The percentage of abnormal thyroid status in GAD and MDD were 21.2% and 23.3 % respectively.

**Conclusion:** Abnormal thyroid status is prevalent in both GAD and MDD patients with differences in thyroid response. Thyroid profile may play an important role in proper management of the diseases.

**Keywords:** Depression; anxiety; thyroid hormone.

**INTRODUCTION**

Depressive disorder is a prevalent psychiatric disorder worldwide with high disease burden (1). Depression is also one of the major cause of Disability Adjusted Life Years (DALYs) and ranked 4th among most urgent health problems in the world according to World Health Organization (2). Major depressive episode generally occurs for a minimum 2 weeks and have minimum four symptoms which include alteration in weight and appetite, altered sleep, less energy, guilt feelings, thinking and decision-making problems and recurring death or suicidal thoughts. Major depressive disorder (MDD) or unipolar depression refers to patients with only major depressive episodes (3). In depressive patients, 21% prevalence of thyroid dysfunction was seen (4). Patho-physiology of MDD is yet not established clearly (5). Thyroid disorder patients are prone to show depressive symptoms and depressive patients also may show thyroid abnormalities and thyroid hormone supplements have shown to improve the clinical response to antidepressant medications (6). In depression, clinical features of subclinical or overt hypothyroidism, associated with lower levels of thyroxine or Tetra-iodothyronine (T4) and elevated thyroid stimulating hormone (TSH) are most seen. Many overt hyperthyroid patients were known to show psychiatric disorders like depression, anxiety, and mania (1). Anxiety disorders, being the most prevalent psychiatric disorders, affects one-third of population

in their lifetime mainly in women as compared to men. Stressors and stress sensitivity in young age has shown to increase susceptibility to this disorder (7,8).

Generalized anxiety disorder (GAD) is the most common type of anxiety disorder with excess worrying and anxiety regarding some activities or incidents for many days within a period of 6 months (9). Increased prevalence of anxiety and mood disorders are associated with thyroid dysfunction. Among males, depressed mood was the most common anxiety symptom whereas in females, it was anxious mood (10). Subclinical thyroid dysfunction is also associated with increasing the anxiety of patients whether it may be hyperthyroid or hypothyroid (11). Symptoms of anxiety also interfere with cognitive performance in hypothyroid patients (12). Hyperthyroidism is an etiologic factor particularly for anxiety. Clinical features of hyperthyroidism and anxiety patients show some similarities. Association of generalized anxiety disorder and major depressive disorder with Graves' disease is found. Depression and anxiety were observed in almost one third of recently diagnosed untreated hyperthyroidism patients (13). Thyroid gland, after being stimulated by thyroid stimulating hormone, produces hormones like T3 (Triiodothyronine) and T4 which stimulate metabolism of almost every tissue in our body. The synthesis of TSH is controlled by hypothalamus using thyroid releasing hormone (TRH) which causes

anterior pituitary stimulation. Inhibition of TSH production is carried out by somatostatin via a negative feedback loop by T3 and T4 (1). The present study is taken up to evaluate levels of the following thyroid hormones *i.e.*, ultrasensitive thyroid stimulating hormone (U-TSH), free triiodothyronine (FT3) and free tetraiodothyronine (FT4) or thyroxine in serum among patients with MDD and GAD as well as to determine the prevalence of thyroid status and lastly compare thyroid status between the two disorders.

## MATERIALS AND METHODS

### Study design and setting

The following study is a cross-sectional study conducted from May 2019 to September 2021 at Biochemistry Department in collaboration with Psychiatry Department of Jawaharlal Nehru Institute of Medical Sciences in Imphal, Manipur. Sixty (60) cases of major depressive disorder and sixty-six (66) cases of generalized anxiety disorder were included in the study. Clearance and approval from the Institutional Ethical Committee, JNIMS, Imphal was taken.

### Inclusion criteria

Study population comprises newly diagnosed cases of major depressive disorder (MDD) and generalized anxiety disorder (GAD). Patients without medication for at least 1 month prior to the onset of the current episode were taken.

### Exclusion criteria

Patients with comorbid medical illness, pregnancy or any other psychiatric disorder were excluded.

### Study tools

Patients in the age group 18-65 years who were diagnosed with MDD or GAD and had attended Psychiatry OPD or admitted in the psychiatry ward of J.N. Institute of Medical Sciences, Imphal, Manipur, were selected. Diagnosis for both disorders was made by using DSM 5 (The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition Criteria. Detailed history and clinical examination including BMI (Asian Criteria) were taken for each patient.

### Thyroid function test

About 5 ml of blood, drawn from the cubital vein of each patient, was collected into a sterile plain vial. Serum was separated by centrifugation. Grossly hemolytic, lipemic & turbid samples were discarded. Laboratory estimation of serum FT3 (BeneSphera), FT4 (BeneSphera) and U-TSH (Erba) was done using Enzyme Linked Immunosorbent Assay (ELISA) Method using Alere's Microplate Reader and Washer. Interpretations of the results were as per the laboratory optimized reference range of serum FT3 (1.4 to 4.2

pg/ml), FT4 (0.8 to 2.0 ng/dl) and TSH (0.54 to 4.72  $\mu$ IU/mL).

### Definition of thyroid status

For patients with normal levels of U-TSH, FT4 and FT3, thyroid status was considered as normal *i.e.*, Euthyroid. Abnormal thyroid status was grouped as hyperthyroid, increased level in any one or combination of FT3 and FT4 with decreased U-TSH, and hypothyroid, having decrease in FT4 with high U-TSH. Subclinical hypothyroids had normal FT4 level with elevated serum TSH level and subclinical hyperthyroids had decreased U-TSH and normal FT4 level.

### Statistical analysis

Analysis was done using descriptive statistics like standard deviation, median, mean, percentage, range etc. Appropriate inferential or analytical statistics were applied. The software that was used for statistical analysis is the SPSS 20.0 version. *p* value <0.05 was considered significant.

## RESULTS

The study included 126 patients where 66 were diagnosed with GAD and another 60 with MDD.

Among GAD patients, females outnumbered males (53% vs 47%) and in MDD, same trend was observed (60% vs 40%). Among GAD patients, maximum was in 31-40 age group (39.4%), followed by 21-30 age group (22.7%) whereas in MDD patients, maximum was in both 21-30 and 41-50 age groups (40% each). Significant association observed between age group and disorder type (*p*-value 0.001). In GAD, maximum patients had normal BMI (78.8%), followed by overweight (12.1%). Same trend observed in MDD patients with normal BMI (76.7%) and overweight (16.7%). No underweight was seen in MDD patients as seen in Table 1.

As seen in Table 2, among GAD patients, mean values regarding FT3, FT4 and U-TSH were 2.94 pg/ml ( $SD \pm 0.80$ ), 1.4 ng/dl ( $SD \pm 0.55$ ) and 1.34  $\mu$ IU/mL ( $SD \pm 1.24$ ) respectively. The mean age was 37.92 years ( $SD \pm 11.84$ ). Minimum age recorded was 18 years whereas maximum was 65 years of age.

In MDD, mean values of FT3, FT4 and U-TSH were 2.99 pg/ml ( $SD \pm 1.03$ ), 1.37 ng/dl ( $SD \pm 0.37$ ) and 1.38  $\mu$ IU/mL ( $SD \pm 1.39$ ) respectively. The mean age was 37.36 years ( $SD \pm 13.6$ ) as shown in Table 3.

### Thyroid status

Of the total patients, 98 (77.8%) were euthyroid. Hypothyroid and subclinical hypothyroid constituted 9 (7.1%) and 5 (4%) respectively. Hyperthyroid and subclinical hyperthyroid also constituted 9 (7.1%) and 5 (4%) respectively. Thus, overall abnormal thyroid status constituted 22.2% (Table 4).

Among euthyroids, 53 (54.1%) were female and 45 (45.9%) were male. Females outnumbered males in all thyroid status except in subclinical hypothyroidism. Among euthyroids, 33 (33.8%) patients were in the 21-30 age group. 4 (44.4%) hypothyroids and 3 (33.3%) hyperthyroids were in 31-40 and 41-50 age

groups respectively. 60% of subclinical hyperthyroids were in the 41-50 age group. Among euthyroids, maximum patients had normal BMI (84.7%). In hypothyroids, all patients were evenly distributed among normal BMI, overweight and obese (33.3% each; Fig. 1).

**Table 1:** Distribution according to general characteristics and disorder type

		Disorder		Total	Chi-square p-value
		GAD	MDD		
Gender	Male	31 (47%)	24 (40%)	55(43.6%)	0.43
	Female	35 (53%)	36 (60%)	71(56.4%)	
Age Group (in Years)	<20	4 (6.1%)	2 (3.3%)	6 (4.7%)	0.001
	21-30	15 (22.7%)	24 (40%)	39 (31%)	
	31-40	26 (39.4%)	6 (10%)	32 (25.4%)	
	41-50	12 (18.2%)	24 (40%)	36 (28.6%)	
	51-60	4 (6.1%)	2 (3.3%)	6 (4.7%)	
	>60	5 (7.6%)	2 (3.3%)	7 (5.6%)	
BMI	Underweight	3 (4.5%)	0	3 (2.4%)	0.32
	Normal	52 (78.8%)	46 (76.7%)	98 (77.8%)	
	Overweight	8 (12.1%)	10 (16.7%)	18 (14.3%)	
	Obese	3 (4.5%)	4 (6.6%)	7 (5.6%)	

MDD=Major Depressive Disorder, GAD=Generalized Anxiety Disorder, BMI=Body mass Index

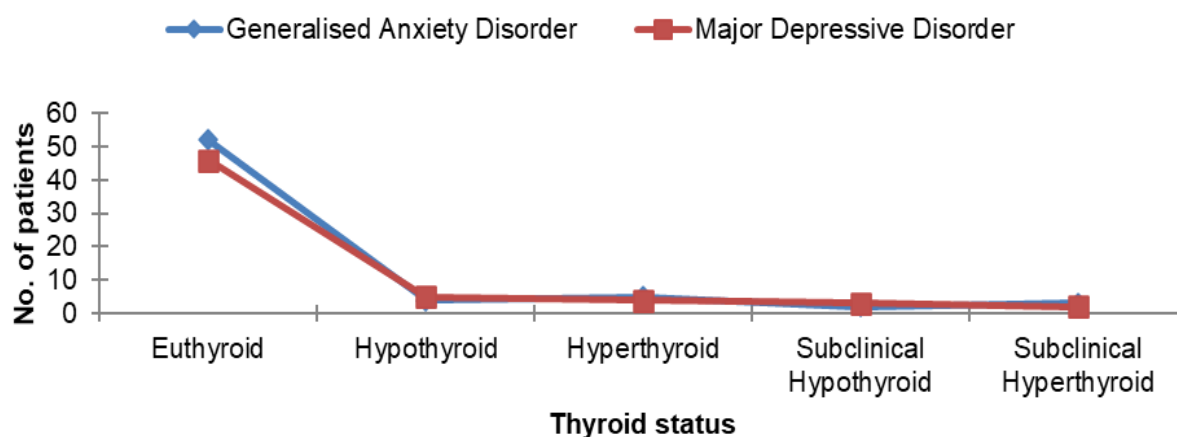
**Table 2:** Descriptive Statistics For GAD

	No. of Patients (N)	Range	Minimum	Maximum	Mean	Standard Deviation
AGE	66	47.00	18.00	65.00	37.92	11.84
FT3	66	3.90	1.20	5.10	2.94	0.80
FT4	66	2.50	0.60	3.10	1.40	0.55
U-TSH	66	4.80	0.20	5.00	1.34	1.24
BMI	66	8.60	18.00	26.60	21.99	1.61
Valid N (listwise)	66					

FT3=Free Triiodothyronine, U-TSH=Ultrasensitive Thyroid Stimulating Hormone, FT4=Free Tetra-iodothyronine

**Table 3:** Descriptive statistics for major depressive disorder

	No. of Patients (N)	Range	Minimum	Maximum	Mean	Standard Deviation
AGE	60	63.00	20.00	83.00	37.36	13.61
FT3	60	5.30	1.20	6.50	2.99	1.03
FT4	60	1.70	0.60	2.30	1.37	0.37
U-TSH	60	4.70	0.20	4.90	1.38	1.39
BMI	60	8.00	19.00	27.00	22.20	1.78
Valid N (listwise)	60					



**Fig. 1:** Line chart for patient distribution according to disorder type and thyroid status

**Table 4:** Population distribution according to general characteristics and thyroid status

		Thyroid Status					Total	Chi-Square p-value
		Euthy.	Hypo	Hyper	Sub C Hypo	Sub C Hyper		
Gender	Male	45 81.9%	3 5.4%	4 7.3%	3 5.4%	0	55 100%	0.28
	Female	53 74.6%	6 8.4%	5 7.1%	2 2.8%	5 7.1%	71 100%	
Age group (in years)	<20	3 50%	1 16.7%	1 16.7%	1 16.7%	0	6 100%	0.77
	21-30	33 84.8%	1 2.5%	2 5.1%	2 5.1%	1 2.5%	39 100%	
	31-40	25 78.1%	4 12.6%	2 6.2%	0	1 3.1%	32 100%	
	41-50	26 72.2%	2 5.6%	3 8.3%	2 5.6%	3 8.3%	36 100%	
	51-60	6 100%	0	0	0	0	6 100%	
	>60	5 71.4%	1 14.3%	1 14.3%	0	0	7 100%	
BMI	Under-weight	0	0	3 100%	0	0	3 100%	<0.0001
	Normal	83 84.6%	3 3.1%	5 5.1%	3 3.1%	4 4.1%	98 100%	
	Over-weight	12 66.6%	3 16.6%	1 5.6%	1 5.6%	1 5.6%	18 100%	
	Obese	3 42.8%	3 42.8%	0	1 14.4%	0	7 100%	
Disorder	GAD	52 78.8%	4 6.1%	5 7.6%	2 3%	3 4.5%	66 100%	0.95
	MDD	46 76.7%	5 8.3%	4 6.7%	3 5%	2 3.3%	60 100%	

p value of <0.05 was considered significant. Euthy=euthyroid / normal, Hypo= hypothyroid, Hyper= hyperthyroid, Sub C Hypo= subclinical hypothyroid, Sub C Hyper= subclinical hypothyroid, GAD=Generalized Anxiety Disorder, MDD=Major Depressive Disorder

Among hyperthyroids, maximum patients were having normal BMI (55.5%). 60% subclinical hypothyroids and 80% subclinical hyperthyroids had normal BMI. Among euthyroids, 53.1% had GAD while 46.9% had MDD. In hypothyroids, more patients had MDD (55.6%). But in hyperthyroids, more patients had GAD (55.6%). More subclinical hypothyroids seen in MDD (60%) while more subclinical hyperthyroids seen in GAD (60%).

Thyroid status distribution among patients as shown in fig. 1 and table 4:

**1. Gender:** Among male patients, 81.9% were euthyroids, followed by hyperthyroids (7.3%) with equal numbers among hypothyroid and subclinical hypothyroid (5.4%). In females, 74.6% were euthyroids, followed by hypothyroids (8.4%) with the same number among hyperthyroid and subclinical hyperthyroid (5.4%) and lastly subclinical hypothyroid (2.8%). Abnormal thyroid status in males and females were 18.1% and 25.4% respectively.

**2. Age group:** Among 21-30 years age group, Table 4 shows 84.33% were euthyroids, followed by both hyperthyroids and subclinical hypothyroid (5.1% each). In 31-41 years, 78.1% were euthyroids, followed by hypothyroids (8.4%). In 41-50 years,

72.2% were euthyroids, followed by both hyperthyroid and subclinical hyperthyroid (8.3% each). Only euthyroid were in the 51–60-year group. The abnormal thyroid status in the age group of 21 to 30 years, 31 to 40 years, and 41 to 50 years (productive age group) were 15.2%, 21.9% and 27.8% respectively.

**3. BMI:** Among normal BMI, 84.6% were euthyroid followed by hyperthyroids (5.1%). In overweight, 66.6% euthyroid followed by hypothyroids (16.6%). In obese, euthyroids and hypothyroids were equal in number (42.8% each). Only hyperthyroid was seen in underweight. Significant association observed between BMI and thyroid status (p value <0.0001). The abnormal thyroid status among Normal, overweight, and obese BMI were 15.4 % 33.4 %, 57.2% respectively.

**4. Disorders:** Among GAD patients, 78.8% were euthyroid followed by hyperthyroid (7.6%), hypothyroid (6.1%), subclinical hyperthyroid (4.3%) and subclinical hypothyroid (3%). In MDD patients, 76.7% were euthyroid followed by hypothyroid (8.3%), hyperthyroid (6.7%), subclinical hypothyroid (5%) and subclinical hyperthyroid (3.3%). The percentage of abnormal thyroid status in GAD and MDD were 21.2% and 23.3 % respectively.

## DISCUSSION

The study population includes both GAD and MDD, females outnumbered males in our study which indicate more prevalence of these psychiatric disorders in the female population. Both GAD and MDD seemed more prevalent among the productive age group (20-50 years) of the society.

### Generalized Anxiety Disorder (GAD) and Major depressive Disorder (MDD)

Both GAD as well as MDD were more associated with females compared to males in our study. Similar finding was observed in previous studies related to MDD by Charnsil *et al.*, (4) Mahendra *et al.*, (14) and Hazarika *et al.*, and Gupta *et al.*, (5) Zhicheng *et al.*, also reported higher prevalence of MDD as well as GAD in females suggesting that female's patients need additional attention and their results showed that women who were unmarried, had low education, low per capita income and menopausal transition had significant association with more risk of GAD as well as MDD (15).

Maximum number of patients fell in the age group of 31 - 40 years, followed by 21 - 30 age group among GAD patients whereas in MDD, maximum patients were in both 21 - 30 and 41 - 50 age groups. Among GAD patients, the mean age was  $37.92 \pm 11.84$  years where as the mean age among MDD patients was  $37.36 \pm 13.6$  years in our study. Hazarika *et al.*, also observed more prevalence of depressive disorder in the productive age group 20 - 50 years in their study (1). As most of the MDD and GAD patients fall in the productive age group category, both diseases may be commonly affecting the working force of society. Maximum GAD patients had normal BMI, followed by overweight. Same trend was also observed among MDD patients. The similar finding was also observed among MMD patients by Dreimuller *et al.*, (16).

In our study among GAD, the mean values of FT3, FT4 and U-TSH were within the normal range on average showing no significant changes. Habib *et al.*, also reported similar findings in TSH in his study regarding anxiety patients (17). In case of MDD, the mean values of FT3, FT4 and U-TSH were within the normal values signifying that these thyroid function parameters are not much affected by the disease. Wysokinski *et al.*, also found TSH level within normal range in unipolar depression (18). Both Shaikh *et al.*, and Saxena *et al.*, reported that normal mean T4 & TSH level but lower mean T3 in their respective studies (2,19).

### Thyroid status and general characteristics

Females outnumbered males in all thyroid status except in subclinical hypothyroidism. Maximum patients both in male and female were having euthyroid status while more abnormal thyroid status was seen in females (25.4%) than males (18.1%). It is

seen in this study that hypothyroidism was more common in the age-group of 21 to 40 years while hyperthyroidism was seemed more in 41-50 years. The abnormal thyroid status in the age-group of 21 to 30, 31 to 40 and 41 to 50 years (productive age group) were 15.2%, 21.9% and 27.8% respectively. Hyperthyroidism is seen more in normal BMI patients while hypothyroidism was seen in overweight and obese patients comparatively. Statistically significant association between BMI and thyroid status ( $p < 0.0001$ ) was seen. The abnormal thyroid statuses among normal, overweight, and obese categories were 15.4 %, 33.4 %, 57.2% respectively. Higher numbers of patients with abnormal thyroid status were observed in abnormal BMI categories (underweight, overweight, and obese) compared to normal BMI groups.

### Thyroid status in MDD and GAD

In GAD, maximum patients were euthyroids followed by hyperthyroids. And in case of MDD patients, maximum were euthyroids followed by hypothyroids. The percentage of abnormal thyroid status in GAD and MDD were 21.2% and 23.3 % respectively where MDD was slightly more. Most patients both in GAD and MDD were euthyroids. While comparing the abnormal thyroid status between GAD and MDD, our study suggested that hypothyroidism and subclinical hypothyroidism may be more associated with MDD whereas hyperthyroidism and subclinical hyperthyroidism may be more associated with GAD. Similar findings were observed Sheikh *et al.*, where depressive patients showed higher prevalence of hypothyroidism and subclinical hypothyroidism (2). Yazmin *et al.*, reported 4% prevalence of subclinical hypothyroidism in depression like our finding (20).

## CONCLUSION

The study showed that abnormal thyroid status is quite prevalent in both GAD and MDD patients. One of the important and significant findings was that there were prominent differences regarding thyroid response in these two psychiatric disorders. Thus, thyroid profile is helpful and recommended for patients with these major psychiatric disorders due to its important role and implications regarding proper management and treatment of the diseases.

## CONFLICT OF INTEREST

There is no conflict of interest.

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