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Original Article

Study of Thyroid Hormone Status in Patients with Major Depressive Disorder

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ABSTRACT

Introduction: *Major depressive disorder (MDD) is a severe psychiatric disorder which has both mental and somatic symptomatology. The clinical implications of thyroid hormones in depression have been studied extensively and still remains disputable. Considering the scarcity of study in our country context, this study aimed to find out the thyroid hormone status in patients with MDD compared to healthy subjects.* ***Methods and Material:*** *This cross-sectional comparative study was conducted in the Department of Biochemistry in collaboration with the Department of Psychiatry, Sylhet MAG Osmani Medical College Hospital, from July 2021 to June 2022. Fifty patients with MDD and 50 age- and gender-matched healthy subjects were included in this study. Thyroid hormones [Serum thyrotropin (TSH), free triiodothyronine (FT3), and free thyroxine (FT4)] levels were measured and compared between two groups.* ***Results****: Both MDD patients and healthy control groups had similar sociodemographic characteristics. Serum FT3 level was significantly lower (2.23 ± 1.07 versus 2.60 ± 0.66 pg/mL) and TSH level was significantly higher (4.10±4.23 versus 2.50 ± 1.56 mIU/L) among patients with MDD than the healthy individuals. Overall thyroid dysfunction was significantly higher in MDD Group than the*

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control Group (32% versus 6%, p<0.01). Serum TSH, FT3 and FT4 had no significant association with age and gender (p>0.05) in patients with MDD. ***Conclusion****: This study revealed that thyroid dysfunction is significantly higher in patients with MDD than that of apparently healthy subjects. MDD patients were more prone to have hypothyroidism.*

Keywords: *Major Depressive Disorder, Thyroid Dysfunction, FT3, FT4, TSH.*

INTRODUCTION

Major depressive disorder (MDD) is a form of mood or affective disorder that has both mental and somatic symptomatology. Its chronic courses severely limits psychosocial functioning and diminishes quality of life[1]. The lifetime prevalence of MDD in worldwide is 16.2% and one-year prevalence is 6.6% among the general population[2]. The estimated prevalence of depression in adults in Bangladesh is 6.7%[3].

Now a days usually people lead a stressful life. Stress is an important risk factors for depressive disorders. Stress can influence hypothalamic pituitary adrenal axis that may affects thyroid hormone secretion[4]. MDD is thought to be accompanied by mild neuroendocrine disorders, including thyroid disease[5]. Thyroid hormone increases serotonin release in brain which may act as co-transmitter to norepinephrine, accelerate and enhance the clinical response to antidepressant agents[6,7]. In animal studies, thyroid hormones influence noradrenergic and serotonergic neurotransmission, which is a target for current antidepressant therapies and plays a key role in the pathogenesis of depression[8]. As thyroid function abnormalities in depressive patients can lead to unresponsiveness to antidepressant therapy, so thyroid screening test in depressive patient may help in proper management[9].

There are many studies in this area with varied and often conflicting results. Different studies in abroad are focusing on current understanding of this relationship, although the nature of this relationship and what determines it have not been convincingly proven[10-14]. In this context this study is designed to find out the thyroid hormone status in patients with major depressive disorder in our set up which emphasizes pre-treatment assessment of these patients.

METHODS AND MATERIAL

A comparative cross-sectional study was conducted in Sylhet MAG Osmani Medical College Hospital, Sylhet from July 2021 to June 2022.The study protocol was approved by the Ethical Review Committee of Sylhet MAG Osmani Medical College and informed consent was obtained from the participants.

Fifty patients with a diagnosis of MDD as per DSM-V criteria, aged 18 years and above were included in this study from the outpatient Department of Psychiatry. Equal number of age and gender matched apparently healthy subjects from general population were included as comparison group. Known case of endocrinopathies, severe chronic illness,

malignancy, psychiatric disorders other than MDD, MDD patients taking lithium, and pregnant women and lactating mother were excluded.

For biochemical analysis, 5 ml of fasting venous blood was drawn and carried to the Sylhet MAG Osmani Medical College Biochemistry laboratory. Serum TSH, FT3, and FT4 levels were estimated by using an Enzyme-Linked Immunosorbent assay (ELISA) kit using 'Plate Reader'(Italy). Thyroid dysfunction was defined as decreased or elevated serum FT3 or FT4 levels with abnormal TSH levels rather than abnormal TSH levels alone. Hypothyroidism was defined as an elevated TSH with a decreased FT3 and FT4 concentration. Subclinical Hypothyroidism was defined as increased serum TSH with an average FT3 and FT4 concentration. Hyperthyroidism was a decreased serum TSH with elevated FT3 and FT4 concentration. Subclinical Hyperthyroidism was defined as reduced serum TSH with normal FT3 and FT4 concentrations. The normal thyroid hormone range was FT3: 1.4-4.2 pg/ml, FT4: 0.8-2.0 ng/dl, and TSH: 0.4-4.2 μIU/L.

Data were analyzed by using window-based computer software device with Statistical Package for Social Science (SPSS 25). Qualitative data were expressed as frequency and percentages and comparison was done using Chi-Square test or Fisher's Exact test. Quantitative data were expressed as mean and standard deviation, comparison was done using independent sample *t* test. The probability (p) value of <0.05 was considered as statistically significant.

RESULTS

The mean age of the patients with MDD was 34.96 ± 15.38 years, more than half of the patients (54%) were ≤30 years of aged, and 68% were female. **Table I** shows that MDD patients and healthy control groups were similar regarding age, gender, socioeconomic class, literacy, and marital status.

Table – I: Sociodemographic Characteristics of the Participants

Characteristics	Study group		*p*-value
	MDD patients (*n*=50)	Healthy control (*n*=50)	
Age			
≤30 years	27 (54.0)	22 (44.0)	0.424*
>30 years	23 (46.0)	28 (56.0)	
Mean ±SD, years	34.96±15.38	39.38±14.33	0.140†
Sex			
Male	16 (32.0)	17 (34.0)	0.500*
Female	34 (68.0)	33 (66.0)	
Socioeconomic class (Taka)			
Low (<10,000)	30 (60.0)	25 (50.0)	0.346*

Middle (10,000-20000)	15 (30.0)	15 (30.0)	
High (>20,000)	5 (10.0)	10 (20.0)	
Educational status			
Illiterate	35 (70.0)	30 (60.0)	0.295*
Literate	15 (30.0)	20 (40.0)	
Marital status			
Married	30 (60.0)	25 (50.0)	0.065*
Unmarried	20 (40.0)	25 (50.0)	

MDD: Major depressive disorder **SD:** Standard deviation; Data were expressed as frequency %) or Mean± SD; *Chi-square test; †Independent sample *t* test.

In this study, the mean TSH level was significantly higher in patients with MDD than the healthy control (p=0.021) and opposite trend was observed regarding FT3 level, which was significantly lower in MDD patients than the control group (p=0.040). Though the mean FT4 level was higher in MDD group than the control group, the difference failed to reach statistical significance p=0.176 (**Table II**).

Table – II: Comparison of the Thyroid Hormones Levels between two Groups

Thyroid hormones	Study group		*p*-value
	MDD patients (*n*=50)	Healthy control (*n*=50)	
TSH (mIU/L)	4.10 ± 4.23	2.50 ± 1.56	0.021†
FT3 (pg/ml)	2.23 ± 1.07	2.60 ± 0.66	0.040†
FT4 (ng/dl)	1.33 ± 0.49	1.22 ± 0.30	0.176†

MDD: Major depressive disorder **SD:** Standard deviation; Data were expressed as Mean±SD; †Independent sample *t* test.

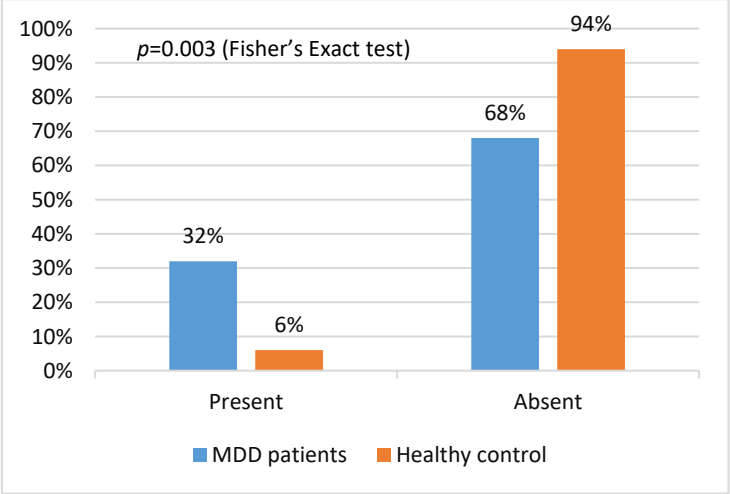

Figure – 1: Comparison of Thyroid Dysfunction between two Groups

In this study, thyroid dysfunction was detected in significantly higher proportion of the participants in MDD group, than the healthy control group (32% vs 6%, *p*=0.003) (**Figure 1**).

The most prevalent thyroid abnormality was overt hypothyroidism, followed by subclinical hypothyroidism in patients with MDD (**Table III**).

Table – III: Comparison of types of Thyroid Abnormalities between two Groups

Types of thyroid abnormality	Study group		*p*-value
	MDD patients *n*=50 (%)	Healthy control *n*=50 (%)	
Hypothyroidism	8 (16.0)	3 (6.0)	0.027*
Hyperthyroidism	1 (2.0)	-	
Subclinical hypothyroidism	6 (12.0)	-	
Subclinical hyperthyroidism	1 (2.0)	-	

MDD: Major depressive disorder; Data were expressed as frequency (%) *Fisher's Exact test.

Table IV shows that thyroid hormone levels were similar between MDD patients with aged ≤30 years and patients aged >30 years. No significant difference found between gender and thyroid hormones level was observed in this study (p>0.05).

Table – IV: Thyroid Hormones Levels According to Age and Gender Group in Patients with MDD (*n*=50)

Characteristics	Values of Thyroid Hormones (Mean±SD)		
	TSH (mIU/L)	FT3 (pg/ml)	FT4 (ng/dl)
Age group			
≤30 years	4.16 ± 5.04	2.26 ± 1.34	1.32 ± 0.51
>30 years	3.80 ± 3.12	2.20 ± 0.67	1.33 ± 0.44
p-value†	0.769	0.840	0.935
Sex			
Male	3.23 ± 2.23	2.16 ± 0.73	1.29 ± 0.36
Female	4.36 ± 4.88	2.27 ± 1.22	1.35 ± 0.53
p-value†	0.385	0.472	0.712

†Independent sample *t* test

DISCUSSION

The present study aimed to determine thyroid dysfunction among patients with MDD compared to apparently healthy individuals. The study demonstrated significantly higher thyroid dysfunction among patients with MDD than the healthy control group. This was an age, gender-matched cross-sectional

comparative analysis, and both the MDD and healthy control group have similar educational, socioeconomic, and marital characteristics. So, the differences in the thyroid hormone levels between the two groups were independent of the sociodemographic factors.

In this study, FT3 level was significantly lower and TSH level was significantly higher among MDD patients compared to healthy subjects. This result was consistent with the some other studies[14,15]. Several studies found that the female gender had lower thyroid hormones level than males[16,17]. But the current study found no significant difference between thyroid hormones level with the age subgroup and gender subgroup of the MDD patients. ***Zhou et al.*** also revealed that compared to the healthy control group[14], the MDD group had a significantly lower serum FT3 level and also found that the level of TSH was significantly higher among females than males, while the levels of FT3 and FT4 were lower among females than males.

The current study found that about one third (32%) of the MDD patients had thyroid dysfunction among them 16% had hypothyroidism, 12% had subclinical hypothyroidism, 2% had hyperthyroidism and 2% had subclinical hyperthyroidism. ***Chueire et al.*** found that the prevalence of MDD was more than four times in subclinical hypothyroidism patients than in the general population[15]. ***Demartini et al.*** found that the level of depression was significantly higher in patients with subclinical hypothyroidism than in healthy controls[18].

Although depression is clearly not caused by the thyroid dysfunction and patients are generally viewed as euthyroid, many patients with depression show subtle alterations in thyroid function as a consequence of altered hypothalamus-pituitary-thyroid axis activity[19]. Among depressed population, slight free thyroid hormones disturbances with concomitant normal TSH were seen and a possible correlation between free thyroid hormone levels and severity and improvement in MDD patients was also observed[20]. It has been suggested that most patients with depression, although generally viewed as chemically euthyroid, have alterations in their thyroid function which are generally reversed following alleviation of the depression[21].

The present study reports that few patients with MDD have significant change in their thyroid function including increase in serum TSH level and decrease in serum T3 level in comparison to healthy subjects. According to this study, it is clear that a subgroup of depressed patients may manifest subtle thyroid abnormalities. There is strong possibility that the presence of a subtle thyroid dysfunction is a negative prognostic factor for MDD and may demand specific therapeutic intervention. So, maintaining thyroid function is mandatory for a healthy life.

Conclusion

In conclusion, current study showed that MDD patients exhibited a higher incidence of abnormal thyroid function, as compared to healthy individuals. Besides, thyroid hormones had no signifi-

cant association with age and gender. The study results indicated that MDD patients are more prone to have hypothyroidism irrespective of age and gender. Monitoring of thyroid function is important for the prevention of thyroid disease as well as MDD.

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Conflict of Interest

The authors declare no conflict of interest.

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