

Study on Thyroid Dysfunction in Patients with Major Depressive Disorder

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ABSTRACT

BACKGROUND

We wanted to evaluate serum levels of thyroid hormones (FT3, FT4 and TSH) among the patients with major depressive disorder (MDD) and determine the prevalence of hypothyroidism among MDD patients.

METHODS

This cross-sectional study was conducted in the Department of Psychiatry, JNIMS for a period of one year from Nov. 2017 to Oct. 2018. After obtaining informed consent, confirmed cases of MDD who attended JNIMS psychiatry OPD were selected for study.

RESULTS

Prevalence of hypothyroidism among MDD patients was found to be 24 % and more in females, patients from low-socio-economic status and in older age group.

CONCLUSIONS

Considering the higher prevalence of hypothyroidism in females and low socio-economic status among the major depressive disorder patients, attention has to be paid to screening thyroid hormone testing in all major depressive disorders and early treatment of hypothyroidism.

KEYWORDS

Euthyroid, Hypothyroidism, Major Depressive Disorder

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BACKGROUND

Depression is a common psychiatric disorder with an estimated global burden of about 350 million people.¹ It was shown that depressive disorders often start at younger age, reducing peoples' functioning and often recurring.² The largest endocrine glands in the body is thyroid gland and it secretes important hormones like triiodothyronine (T3), thyroxine (T4) and calcitonin. At 11 weeks' of gestation, synthesis of thyroid hormone begins in the fetus. T3 has much greater biological activity as compared to T4 and is specifically generated at its site of action in peripheral tissues by deiodination of T4. These hormones, in fact, act a very critical and important role in brain development and in later parts specially in adults, they help to maintain thermogenic and metabolic homeostasis.

One of the functions of thyroid hormone is to stimulate oxygen consumption in cells of the body, thus helping in the regulation of carbohydrate and lipid metabolism and thereby influences body mass. Thyroid hormones have marked effects on brain development; it is essential for the development of central nervous system (CNS). Hypothyroidism is diagnosed when there is a decrease in the production of thyroid hormone with an increased in the level of thyroid stimulating hormone (TSH). It has recently increased and is considered as one of the most common endocrine diseases. The causes can be classified into primary ones that are dysfunction in the thyroid gland itself and secondary causes related to a defect in the pituitary or hypothalamus. The thyroid gland secretes three hormones thyroxin (T4), triiodothyronine (T3) and calcitonin. T4 and T3 are necessary for normal brain development and function. It has a greater effect on metabolism.

Oral Thyroxin is used in the treatment of hypothyroidism and dose varies from patient to patient. Hypothyroidism has a significant impact on physical and mental health. One of the psychiatric disorders associated with hypothyroidism is depression. Depression is a mental illness, which is considered by the World Health Organization appears as the second largest killing disease just after cardio-vascular disease by 2020. Many studies show that there is a significant relationship between hypothyroidism and depression like, there is an overlap between their symptoms such as loss of interest, lethargy, loss of appetite, sleeping too much, poor memory, loss of concentration and decreased libido. These psychological symptoms can severely affect quality of life. Many researchers have revealed that there is a significant link between hypothyroidism and depressive symptoms. In Brazil, they studied the association between hypothyroidism and depressive symptoms among middle age women, the prevalence of depression was reported at about 45.7 % and 12.3 % were presented with hypothyroidism. In Spain, the overall prevalence of hypothyroidism in major psychiatric disorders was 10.5 %, 11.1 % was in depressive disorder.

In Delhi (2013), it was revealed that the prevalence of hypothyroidism in depressed patient was 20 % and depression in hypothyroidism was 36.67 %. The prevalence, in India, of depressive illness among hypothyroid patients

was found to be 60 %. In Nepal, 21 % of patients with depression had thyroid dysfunction.

So, the relationship and association between depression and hypothyroidism was accepted throughout the globe and it had been taught in the medical fraternity since long time back, however the association, relationship and factors which determined it was not been convincingly proven till date. On the other hand, the relationship and association regarding the similarity of symptoms in hypothyroid patients and major depressive disorder, the therapeutic indication of thyroid hormones in the treatment and management of major depressive disorder and the apparent dysfunction in the hypothalamic-pituitary-adrenal (HPA) axis of patients with major depressive disorder. On the contrary, there were many conflicting findings in the relationship and association between major depressive disorder and hypothyroidism. So, keeping this in mind, a further research work is required in the near future. But our knowledge in this area has increased significantly with many research works and studies in the recent years.

WHO projected that major depressive disorder ranks 4th position among the leading causes of Disability Adjusted Life Years (DALY) and major depressive disorder will rank 2nd position among the different causes of DALYs by 2020.³ An episode of depressive disorder usually lasts for a period of minimum two weeks and also experiencing minimum of four symptoms from the list which include changes in vegetative signs (changes in appetite and sleep), changes in weight and activity, lack of energy, guilty feelings, problems and abnormalities in thought and difficulty in decision making, and recurrent ideas and thoughts of suicide or death. Patients with depressive episodes are often found to have a major depressive disorder (MDD) or unipolar depression.⁴ In a previous study, the prevalence of thyroid dysfunction in depressive patients was found to be 21 %.⁵ MDD, though is a leading cause of disability along with an alarmingly increased global prevalence, its patho-physiology is yet not established clearly.⁶

It has been recognized for long time back that there is association and relationship between major depressive disorder and hypothyroidism. It was observed that hypothyroid patients are riskier and more prone to develop major depressive disorder specially in the female and vice versa major depressive disorder are likely to have subclinical hypothyroidism or clinical hypothyroidism. So, supplementation of thyroid hormone appears to enhance the clinical response and effect to anti-depressant drugs. But the mechanism underlying interaction and relationship between hypothyroidism and major depressive disorder needs to be further clarify and many researches will be needed in the near future. Overt thyroid disease is rare in depression, 1 to 4 % found to be hypothyroid, while 4 % to 40 % of depressive patients have subclinical hypothyroidism.⁷

Talaei A et al conducted a study in 2017 to find out the TSH cut off point based on depression on 174 hypothyroid patients and concluded that TSH cut off value of 2.5 MIU / L is optimal.⁸

Mani K et al conducted a study in 2018 to find the correlation between anxiety, depression, and executive function with subclinical hypothyroidism (SCH), and it was

reported that the extent of anxiety was mild among the SCH whereas the extent of depression was moderate among the cases. There is a significant correlation between anxiety and SCH and depression and SCH.⁹

Hong JW et al conducted a study in 2018 about relationship between subclinical hypothyroidism and major depressive disorder among the adult population of Korea and observed and found that subclinical hyperthyroidism was associated independently with major depressive disorder in the general adult population of Korea by using cross-sectional data of the nation.¹⁰

Loh HH et al did a study by using meta-analysis in 2019 to assess: 1) the relationship and association between sub-clinical hypothyroidism (SCH) and major depressive disorder 2) the therapeutic use and effect of thyroid hormone like levothyroxine among patients with SCH and coexistent depression. It was found that there is a SCH has an adverse impact on the major depressive disorder. So, routine and early screening of major depressive disorder is recommended especially in the elderly and female patients to avert morbidity and mortality however, the therapeutic indications and uses of thyroid hormones like levothyroxine in patients with SCH and co-morbid depression requires to be customized individually.¹¹ The aim and objectives of the study are to determine the serum levels of thyroid hormones (FT3, FT4 and TSH) among the patients with major depressive disorder and to find out the prevalence of hypothyroidism among MDD patients.

METHODS

This was a cross-sectional, hospital-based study. Participants were the patients who were attending psychiatry OPD on every working day with diagnosis of major depressive disorder. We used DSM IV-TR criteria for the diagnosis of MDD. The study was conducted over a period of one year from Nov. 2017 to Oct. 2018. We had included any patient presenting in psychiatry dept. with MDD irrespective of their age status. We had excluded those patients who were not willing to participate in the study. We also explained them that at any point of time if they wished, they could withdraw from the study. We collected data from those serious patients after improvement of their symptoms or from patient's attendant. Those with concurrent medical illness / es and / or any other psychiatry illness other than MDD were also excluded from the study. After obtaining informed consent, confirmed cases of MDD who attended JNIMS psychiatry OPD were selected for study. For data collection, the assessment tools used were a semi-structured proforma for collection of information on socio-demographic characteristics. Blood samples were collected from the participants for assessment of their thyroid status. Data was entered and analysed using SPSS 20 version. Statistical analysis was done by applying chi-square test and p-value below 0.05 is considered to be statistically significant.

RESULTS

There were 53 hypothyroid patients among 220 major depressive disorder participants.

Economic Status Income Group (Rupees per annum)	Number of Depressed Subjects (%)	
	Euthyroid Patients	Hypothyroid Patients
Low (≤ 20,000)	18 (50)	18 (50)
Lower middle (20,000 - 40,000)	88 (87)	13 (13)
Upper middle (40,000 - 62,000)	35 (72.9)	13 (26.1)
High (≥ 62,000)	26 (78.8)	9 (21.2)
Total	167 (100)	53 (100)

Table 1. Cross-Tabulation of Thyroid Status among MDD Patients against Their Economic Status

$\chi^2 = 20.453, df = 3, p\text{-value} = 0.0001$

Among the income levels of the participants, it was found to be more prevalent among low socio-economic groups (50 %) as compared to lower middle (13 %) and high (21 %) income level. However, the relationship is found to be highly significant ($p = 0.0001$).

Age in Years	Number of Depressed Subjects (%)	
	Euthyroid Patients	Hypothyroid Patients
30 - 49	53 (80.3)	13 (19.7)
50 - 69	70 (79.5)	18 (20.5)
70 - 80	44 (66.67)	22 (33.33)
Total	167 (100)	53 (100)

Table 2. Cross-Tabulation of Thyroid Status among MDD Patients against Their Age

$\chi^2 = 4.418, df = 2, p\text{-value} = 0.1099$

Table 2 reflects the increased prevalence of hypothyroidism among higher age group i.e., 33.33 % in 70 - 80 years of age as compared to lower age group i.e. 20.5 %, in the remaining age groups the relationship is found to be insignificant ($p = 0.1099$).

Sex	Number of Depressed Subjects (%)		Total
	Hypothyroidism	Euthyroid	
Male	9 (8.5)	97 (91.5)	106
Female	44 (38.6)	70 (61.4)	114
Total	53 (100)	167 (100)	220

Table 3. Cross-Tabulation of Thyroid Status among MDD Patients against Their Sex

Corrected $\chi^2 = 27.224, df = 1, p = 0.0000$

In Table 3, the prevalence of hypothyroidism among the major depressive disorders was found to be higher among females (38.6 %) compared to males (8.5 %) and it was found to be highly significant ($p = 0.0000$).

DISCUSSION

This study shows the prevalence of hypothyroidism among the major depressive disorder to be 24 % which conformed to the global trend i.e. 20 - 25 %. The prevalence of hypothyroidism was more in female when compared to males i.e. 3 : 1 ratio ; it was also found to be more prevalent among older age group and low-socio economic groups.

It is well known fact that thyroid dysfunctions are associated with psychiatric co-morbidities including anxiety and depressive disorders. In a study regarding prevalence of anxiety in hypothyroidism, the most common anxiety symptom among males was found to be depressed mood and among females was anxious mood.¹² In 2004, Bahls SC et al observed that dysfunction in hypothalamus-pituitary-thyroid (HPT) axis abnormalities in major depressive patients and those abnormalities were: increased serum T4 level, abnormal or aberrant TSH responses to TRH; presence of anti-thyroid antibodies and raised CSF-TRH levels in serum. The relation of these dysfunction of HPT and monoamines neuro-transmitters and different subtypes of major depressive disorder is found to be complex and doesn't support the linear relationship.¹³ In 2005, Constant EL et al conducted a study "Anxiety and depression, attention, and executive functions in hypothyroidism" and found that hypothyroid patients were depressed and anxious as compared to the controls and found to be disturbed in cognitive and executive functions in the areas of attention, concentration and abstract. Further, it was reported that the cognitive performance in patients of hypothyroidism was interfered by the clinical features of anxiety but, not by the clinical features of major depressive disorder.¹⁴

In 2013, Lokesh J et al showed in their study that the prevalence of hypothyroidism in depressed subjects was 20 % and depression in hypothyroid subjects was 36.67 %. Sub clinical hypothyroidism were found to be more prevalent than clinical hypothyroidism. Thus, correlation between major depression and hypothyroidism was found to be significant.¹⁵ In an article published in 2013, Feldman AZ et al mentioned that major depressive manifestations triggered by hypothyroidism are likely responding well to the return of the euthyroid state, but some of the major depressive patients found to have persistent signs and symptoms. So, restoration of the truly euthyroid state from the hypothyroid among the major depressive patients play a key and important role in the treatment and management of residual signs and symptoms of major depressive disorder co-morbid with hypothyroid patients.¹⁶

Wysokiński A and Kłoszewska I et al conducted a study in 2014 to investigate the differences in the serum levels of thyroid-stimulating hormone (TSH) in patients with unipolar depression, bipolar depression and bipolar mania and the results confirmed the higher prevalence of hypothyroidism (increased serum TSH level in patients with mood disorders both unipolar and bipolar).¹⁷ In a study conducted in 2014, Berent D et al reported that hypothyroidism patients are associated with severity of the major depressive disorder and found to have an impact on the prognosis of the final clinical outcome of the patients with major depressive disorder co-morbid with hypothyroidism.

So, it is recommended to treat the hypothyroidism with thyroid hormone along with ant depressive drugs for the major depressive disorder together for the rapid recovery and good clinical outcome of the patients.¹⁸ Blum MR et al conducted a large prospective study in 2015 on the relationship and association between persistent subclinical hypothyroidism and major depressive disorder and found that major depressive symptoms were not found in patients

of sub-clinical hypothyroidism among the older adults.¹⁹ In a study conducted in 2015, Fam J et al found that major depressive patients are associated with anti-thyroid antibodies and IL-17 found to be associated with the autoimmune thyroid diseases. Their study investigated whether specific thyroid auto antibodies and IL-17 in distinguished persons with depression from non-depressed controls and reported that median TSH receptor antibody concentration was significantly higher in the depressed than control group. It was concluded that TSH receptor antibodies might be a biomarker of immune dysfunction in depression.²⁰ Delitala AP et al conducted in a population-based cohort study in 2017 on depressive symptoms, thyroid hormone and autoimmunity. It was observed that there was no association between symptoms of depression and Thyroid Peroxidase Antibody (TPOAb). No linear association was found between TSH or FT4 levels and depressive symptoms, but a U-shaped relation was found between depressive symptoms and FT4. Both hyper and hypo thyroidism was found to have a strong association with depressive symptoms.²¹

In 2017, de Souza Duarte N et al found that thyroid hormones, cortisol, corticotrophin hormone, female sex hormones (estrogen and progesterone) were found as the main hormones linked to depression and this hormone is essential for the metabolism in the body. It was concluded that the hormonal changes specially in the female have a relationship with the development of depressive symptoms as well as aggravate it.²² Hong JW et al conducted a study in 2018 about association between subclinical thyroid dysfunction and depressive symptoms in the Korean adult population and demonstrated that subclinical hyperthyroidism was independently associated with depressive symptoms in the Korean general population using national cross-sectional data.¹⁰

Loh HH et al conducted a meta-analysis in 2019 to evaluate: 1) the association between sub clinical hypothyroidism (SCH) and depression 2) the effect of levothyroxine therapy among patients with SCH and coexistent depression. It was found that SCH has a negative impact on depression. Early and routine screening of depression is recommended especially the elderly, to prevent morbidity and mortality but the use of levothyroxine among patients with SCH and coexistent depression needs to be individualized.¹¹

CONCLUSIONS

There was a higher prevalence of hypothyroidism in females, patients from low-socio-economic status, among patients with major depressive disorders. Screening thyroid hormone testing in all major depressive disorders and early treatment of hypothyroidism should be done.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

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