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Original Article

Thyroid Dysfunction Associated with Depressive Disorder: A Descriptive Cross-Sectional Study Done in a Tertiary Care Center of Eastern Nepal

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Abstract

Background
Depression is one of the most common psychiatric disorders with substantial morbidity and mortality. It is known to be associated with changes in the hypothalamic-pituitary-thyroid axis, thus may be accompanied by subtle thyroid dysfunction. Thus, our study aims to determine the prevalence and characteristics of thyroid dysfunction in newly diagnosed depressive patients.

Materials and Methods
A prospective descriptive cross sectional study was conducted among 130 patient diagnosed as depression from December 2020 to June 2022 after taking the ethical approval. The patients in the symptomatic phase and above 18 years was recruited in our study. Thyroid profile consisting of free tri-iodothyronine (FT3), free thyroxine (FT4) and thyroid-stimulating hormone (TSH) was estimated by chemiluminescence immunoassay in the central laboratory of Nobel Medical College Teaching Hospital.

Results
Out of 130 depressive patients recruited in our study, 44 patients had abnormal thyroid function test showing a prevalence of 33.84%. The most common form was moderate depression which was 39.99% of our study population. The commonest thyroid abnormality was subclinical hypothyroidism (15.38%) followed by overt hypothyroidism (14.61%). Thyroid abnormality was more common among the severe form of depression (46.66%). The comparison of means of fT3, fT4 and TSH between different grades of depression was statistically significant for fT3 (p=0.048) and TSH (p=0.001).

Conclusion
Thus, the most common thyroid function abnormalities in our study include subclinical and overt hypothyroidism, with associated lower level of fT4 and higher level of TSH.

Keywords: *Depression, Hyperthyroidism, Hypothyroidism, Prevalence*

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Introduction

WHO defines depression as the common and serious medical illness that negatively affects how you feel, the way you think and how you act. WHO has ranked depression as the 4th leading cause of disability worldwide [1] and is characterized by subtle neuro endocrinological disorders [2]. Prevalence of thyroid dysfunction was found to be 26.2% in a study done by Kafle et.al and 21% in another study done by Ojha et.al in Nepal [3, 4]. Thyroid dysfunction is closely associated with neuropsychological function including the mental state and cognitive function [5], as thyroid hormones are widely distributed in the central nervous system and functions to regulate neuronal growth and forms synapse between neurons [6].

Despite the unclear pathophysiological role of thyroid hormones in depressive patients, the relationship between thyroid hormones and the brain serotoninergic (5-HT) system has been suggested as a potential underlying mechanism of action [7]. Thyroid hormones influence serotoninergic neurotransmission which play a key role in the pathogenesis of depression [8]. Depression remains the most common among the various neuropsychiatric manifestations of thyroid disorders [9].

Thus, our study aims to determine the prevalence and characteristics of thyroid dysfunction in newly diagnosed depressive patients. Our study also aims to find the most common thyroid dysfunction prevalent in our population and find the association between depression and thyroid dysfunction.

Materials and Methods

A Descriptive cross-sectional study was conducted prospectively on patients diagnosed with depressive disorders who presented to outpatient and inpatient setting in the psychiatry department of Nobel Medical College Teaching Hospital. The study was conducted from December 2020 to June 2022 after obtaining ethical clearance from the Institutional review committee (IRC proposal approval no: 402/2020). A total of 130 patients clinically diagnosed as depression by the psychiatrist were included in the study. Sample size was calculated taking the prevalence of thyroid dysfunction in depression as 21% according to a study done in Nepal by Ojha et.al [4]. Convenience sampling was done which included all the patients in symptomatic phase of depression and age above 18 years. The exclusion criteria were known case of thyroid disease before the onset of depressive symptoms, known cases of other metabolic conditions like hypertension, diabetes mellitus, pregnant females and patients on substance abuse. A self designed semi-structured pro-forma was used for collecting data. Informed consent was taken from all the patients and their accompanying person. The patients details and laboratory investigations were recorded on the proforma.

Five milliliters of blood sample was collected under aseptic conditions from the ante-cubital vein, centrifuged and analyzed on the same day. All the samples were tested for quantification of serum fT3, fT4 and TSH by Siemens ADVIA Centaur XPT Immunoassay System based on the principle of glow based chemiluminescence immunoassay. According to our laboratory reference ranges, the normal values of fT3 ranges between 2.0-4.4 pg/ml, fT4 ranges between 0.89-1.76 ng/dl and TSH ranges between 0.39-6.6$\mathcal{M}$ IU/L. Serum TSH levels, participants were classified as having hypothyroidism (>6.6 $\mathcal{M}$IU/L), euthyroid status (0.39-6.6 $\mathcal{M}$IU/L) and hyperthyroidism (<0.39 $\mathcal{M}$IU/L). Subclinical hypothyroidism was defined as high TSH and normal fT3 and fT4 levels and subclinical hyperthyroidism was defined for low TSH and normal fT3 and fT4 levels. Overt hypothyroidism was defined as decreased free T3, decreased free T4, and elevated TSH, and overt hyperthyroidism was defined as elevated free T3, elevated free T4, and low TSH [10]. The diagnosis of depression and its grading as mild, moderate and severe was done on the basis of ICD-10, DCR as developed by the division of Mental Health of the World Health Organization (WHO, 1992), the most widely used version for the research purpose by the attending clinician.

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 16. Descriptive analysis was performed, and the data were explained as mean ± standard deviation (SD) wherever suitable. One way analysis of variance (ANOVA) was used among three groups of data show the relationship between the dependent and independent variables. Two sample t- test was done to compare the means of two groups. p value <0.05 was considered statistically significant.

Results

This study was conducted among 130 patients diagnosed as depressive disorder. Out of the total study population 61 patients (46.92%) were males and 69 patients (53.07%) were females. The mean age of the male patients was 34.95 ± 15.83 years whereas it was 34 ± 13.24 years in females. Out of the total study population, 86 patients (66.15%) had normal thyroid function test, of which 52.32% was male whereas 47.67%

was female. Similarly, 33.84% had abnormal thyroid function test, of which 36.36% was male whereas 63.63% was female. Our study showed that, abnormal thyroid function was more common in depressed women. (Table 1). Out of our total study population, 48 patients (36.9%) had mild depression, of which 20% were males and 16.9% were females. The number of study population having moderate depression was 52, which is 39.99% of the total population, out of which 17.69% were males and 22.30% were females. Similarly, 30 patients had severe depression which was 23.04% of our study population, where 9.2% were males and 13.84% were females. Mild depression was common among male patients whereas moderate depression was common in female patients (Table 2)

Table 1: Socio-demographic characteristics of study population

Variables	Number (%)	Age (Years) Mean ±SD	Normal thyroid function test Number (%)	Abnormal thyroid function test Number (%)
Gender : Male	61(46.92%)	34.95 ± 15.83	45 (52.32%)	16 (36.36%)
Female	69(53.07%)	34 ± 13.24	41 (47.67%)	28 (63.63%)
Total	130		86	44

Table 2: Distribution of patient on the basis of severity of depression

Depression severity	Male Number (%)	Female Number (%)	Total Number (%)
Mild	26 (20%)	22 (16.9%)	48 (36.9%)
Moderate	23 (17.69%)	29 (22.30%)	52 (39.99%)
Severe	12 (9.2%)	18 (13.84%)	30 (23.04%)
Total	61 (46.92%)	69 (53.07%)	130 (100%)

Table 3: Distribution of patient on the basis of thyroid status

Thyroid status	N =130, (%)
Euthyroid	86 (66.15%)
Overt hypothyroidism	19 (14.61%)
Overt hyperthyroidism	4 (3.07%)
Subclinical hypothyroidism	20 (15.38 %)
Subclinical hyperthyroidism	1 (0.76%)

The most common thyroid abnormality in our study was subclinical hypothyroidism (15.38%), then overt hypothyroidism (14.61%). Hyperthyroidism was less common in our study population which was 3.07% for overt hyperthyroidism and 0.76% for subclinical hyperthyroidism. 66. 15% of our patients were euthyroid (Table 3). Out of the total patient (N=48) having mild depression, the number of patient having normal thyroid function test was 33 (68.75%), whereas 15 patients (31,25%) had abnormal thyroid function. Among the patients with moderate depression, 37 patient (71.15%) had normal thyroid function test whereas 15 patient (28.84%) had abnormal thyroid function test. Similarly, among the severe depression patients, 16 patient (53.33%) had normal thyroid function whereas 14 patient (46.66%) had abnormal thyroid function test.(Table 4)

Table 4: Distribution of depression patients on the basis of thyroid function test

Depression severity	Normal thyroid function N(%)	Abnormal thyroid function N(%)	Total (N)
Mild	33 (68.75%)	15 (31.25%)	48
Moderate	37 (71.15%)	15 (28.84%)	52
Severe	16 (53.33%)	14 (46.66%)	30
Total (N)	86	44	130

The mean fT3 level was 2.94 ± 1.31 pg/ml in mild depressive patients, 2.44 ± 0.859 pg/ml in moderate depressive patients and 2. 51 ± 0.891 pg/ml among the patients with severe depression. The mean fT3 level was statistically significant among the three groups with p value of 0.048. The mean fT4 level was 1.33 ± 1.21 ng/dl in mild depressive patients,1.15± 1.11 ng/dl in moderate depressive patients and 0.947 ± 0.829 ng/dl among the patients with severe depression. Mean fT4 level was not statistically significant among the three groups. The mean TSH levels was 1.33 ± 2.98M $\mathcal{M}$IU/L among the patient with mild depression and 3.44 ± 4.23 $\mathcal{M}$IU/L among the moderate depression group and 4.63 ± 5.11$\mathcal{M}$IU/L among the patients with severe depression. The mean TSH level was statistically highly significant among the three groups with p value of 0.001. (Table 5). When we compared the means of fT3, fT4 and TSH between the depressive patients with normal thyroid function and abnormal thyroid function test fT3 and TSH, by unpaired t-test, fT3 and TSH levels were statistically significant at 95% confidence interval with p value of 0.001 and 0.0001 respectively. (Table 6)

Table 5: Thyroid function test in different grades of depression (n=130)

Thyroid function tests	Mild Depression	Moderate Depression	Severe Depression	p value ANOVA
fT3 (pg/ml) Mean ±SD	2.94 ± 1.31	2.44 ± 0.859	2. 51 ± 0.891	0.048
fT4 (ng/dl) Mean ±SD	1.33 ± 1.21	1.15 ± 1.11	0.947 ± 0.829	0.320
TSH (M IU/L) Mean ±SD	1.33 ± 2.98	3.44 ± 4.23	4.63 ± 5.11	0.001

Table 6: Comparison of means of thyroid function test parameters between depressive patients with normal and abnormal thyroid function test

Thyroid function test parameters	Normal TFT Mean ± SD	Abnormal TFT Hypothyroidism Mean ± SD	Abnormal TFT Hyperthyroidism Mean ± SD	p value
fT3 (pg/ml) Mean ± SD	1.93 ± 0.93	2.20 ± 1.39	5.07 ± 1.04	0.001
fT4 (ng/dl) Mean ± SD	1.20 ± 1.08	1.002 ± 1.12	3.12 ± 2.16	0.07
TSH (M IU/L) Mean ± SD	2.1 ± 1.56	5.31 ± 5.10	0.16 ± 0.12	0.0001

Discussion

Depression is the most common psychiatric disorder associated with high prevalence rate, chronic course, and increase economic burden [10]. Thyroid function tests are the most frequently performed endocrine tests for a depression work-up [7]. Our study was conducted among 130 patients diagnosed with depression. The prevalence of thyroid dysfunction was 33.84% in our study which was consistent with the findings of the study by Hazarika et.al [11]. A study in Nepal by Kafle et.al showed prevalenceof thyroid dysfunction to be 26.2% [3]. Our study showed that 36.16% of males and 63.63% of females had thyroid dysfunction. Among the depressive patients, females had higher prevalence of thyroid dysfunction in our study population. This finding was consistent with the study done by Hong et.al [7] and Farikappa et.al [10] where female had higher prevalence of thyroid dysfunction. When we analyzed our study population based on the severity of depression, the most common was moderate depression which is 39.99%. Similarly, 36.9% of our study population had mild depression and 23.04% had severe depression. Our findings was consistent with the study done by Kafle et.al in Nepal where moderate depression was the commonest type, but the prevalence of moderate depression was higher (78.3%) in their population as compared to our study [3]. The reason for moderate depression being more common in our setting is because they are the common type that usually come seeking for medical advise, mild depression mostly do not land for medical consultation or sometimes may be undiagnosed [3].

The percentage of euthyroid patients in our study was 66.15%. Out of the total of 44 patients having thyroid dysfunction, the most common thyroid abnormality was subclinical hypothyroidism (15.36%), followed by overt hypothyroidism (14.61%). The findings were similar to the study by Dermatini et.al in Italian population and Almeida et.al where it showed a significant association between depression and subclinical hypothyroidism [12,13]. Many studies have reported that the prevalence of subclinical hypothyroidism to be 15-20% [14]. The patients with subclinical and overt hyperthyroidism were very less in our study. In contrast to our study, Hong et.al showed a correlation between depressive patient and hyperthyroidism [7]. Because depressive symptoms are affected by various conditions, including cultural and socioeconomic factors, the association between subclinical dysfunction and depression could differ according to the characteristics of the study population, including age, socioeconomic status, and ethnicity.

A study done by Radhakrishnan et.al showed that, 19.02% of the patients had hypothyroidism which was almost similar to the findings of our study [15]. Thyroid hormones are believed to have an important role in neurodevelopment, specifically in neurogenesis, myelination, dendrite proliferation and formation of synapses. Many studies have hypothesized potential causes for low thyroid hormone levels and high TSH levels in depressive patients [16]. However, 15% or more of depressed patients have minimal thyroid insufficiency with evidence of an autoimmune thyroid disease, suggesting a 'brain hypothyroidism' without the presence of systemic hypothyroidism. This might be because of inhibition of type II deiodinase required for conversion of T4 to T3, caused by an increase of cortisol and/or a decrease in the T4 transporter through the blood-brain barrier [17]. The drugs used in depression blocks dopaminergic transmission and cause elevation in TSH level. Similarly, lithium concentrates in the thyroid gland and can result in inhibition of iodine uptake into follicular cells, results in alteration of the structure of thyroglobulin by interfering with the coupling of iodotyrosine residues to form iodothyronines, and inhibition of thyroid hormone secretion [15]. We observed that the alterations in the hypothalamic pituitary axis are proposed as an etiology for both the high and low thyroid alterations found in cases of depression [17].

When we analyzed the abnormal thyroid function test among three severity of depression, the thyroid abnormality was more common among the severe form of depression which was 44.66%. The mean fT3 level was statistically significant among the three group of depressive patients with p = 0.048 when we compared using ANOVA. Similarly, the mean TSH level was highest among the severe depressive patients, which was 4.63 ± 5.11 $\mathcal{M}$IU/L and the mean TSH level was statistically significant among the three groups of depression with p=0.001. In accordance with our findings, Ojha et.al found a posi-

tive correlation between severity of depression and thyroid dysfunction i.e, the more severe the form of depression, higher is the prevalence of thyroid dysfunction [4]. However, a study done by Fakirappa et.al found no significant statistical association between the severity of depressive episode and characteristic thyroid dysfunction [10]. This discrepancy may be because of the differences in diagnostic criteria and differences in severity of depressive episodes included in the studies.

The mean fT3 level and mean TSH level was statistically highly significant when we compared the means of fT3, fT4 and TSH levels among the depressive patients with normal and abnormal thyroid function tests. Our findings was consistent with the findings of the study done by Zhou et.al in China, where mean FT3, and FT4 were low and mean TSH levels was high in depressive disorders and were statistically significant [18]. Thus, there is a general consensus that small changes, even with normal ranges of thyroid hormones among depressed patient have significant effect in brain functioning and can be important in understanding the biological basis of depression [17]. Thus, finings of our study suggest the need for inclusion of thyroid function test along with TSH level monitoring in depressive patients for their proper diagnosis and treatment.

The limitation of our study is that it is a single centered study, so our findings cannot be generalized in all the population.

Conclusion

Thus, the most common thyroid function abnormalities in our study include subclinical or overt hypothyroidism, with associated lower level of fT4 and higher level of TSH. Abnormality in thyroid function was quite common in depressed patient in our study population.

Recommendation

Screening patients with depression for thyroid dysfunction seems reasonable for better health outcome of the patients. Thus, the results of our study might potentially influence the clinical practice and improve the quality of life of patients.

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Conflict of interest: None

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