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RESEARCH ARTICLE

Assessment of anxiety depression and executive function in cases of subclinical hypothyroidism attending in a tertiary care centre

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ABSTRACT

Background: Thyroid hormone has important actions in adult brain, and it is well accepted that hypothyroidism is associated with neuropsychiatric symptoms which refer to a spectrum of emotional and cognitive problems and also mood changes. More severe hypothyroidism can mimic melancholic depression and dementia. Subclinical hypothyroidism (SCH) is a condition in which thyroid-stimulating hormone (TSH) value is raised, but FT3 and FT4 values are within normal limit. The prevalence of SCH is 3–7% in general population and as high as 17% in elderly women. A recent study shows people with SCH have impaired working memory. **Aims and Objectives:** The present study attempted to find the correlation between anxiety, depression, and executive function with SCH. **Materials and Methods:** In this study, anxiety, depression, and level of executive function are being assessed in cases of SCH within a period of 1 year (July 2014–June 2015). Cases were collected from patients attending the Department of Biochemistry for thyroid function tests in North Bengal Medical College and Hospital in that period. Patients of 20–50 years of age group having TSH value 5.5–10 mU/L with FT4 and FT3 within normal reference range (FT4 = 0.8–2.7 ng/dl, FT3-1.4–4.5 pg/ml) were included in the study. Patients already on thyroxin supplementation, with pre-existing psychological illness and substance abuse, with chronic diseases and neurological diseases are excluded from the study. **Results:** The extent of anxiety was mild ($P < 0.001$), whereas depression was moderate ($P < 0.07$) among the cases of SCH. The executive function was normal in most of the cases. Correlation between anxiety and SCH was found to be statistically significant ($P = 0.000$), also between depression and SCH ($P = 0.027$). **Conclusion**: It is seen from the study that the extent of anxiety was mild among the SCH in North Bengal Medical College, whereas the extent of depression was moderate among the cases and the executive function was normal in most of the cases. There is a significant correlation between anxiety and SCH and depression and SCH. Anxiety and depression were not significantly correlated with age, sex, and body mass index among the cases of SCH.

KEY WORDS: Subclinical Hypothyroidism; Anxiety; Depression; Executive Function; Thyroid-stimulating Hormone

INTRODUCTION

The thyroid gland is one of the larger endocrine glands in the body. It has two primary functions: One is to secrete thyroid hormones and another is to secrete calcitonin. Thyroid gland produces two related hormones, thyroxine (T4) and triiodothyronine (T3). Thyroid hormone synthesis begins at 11 weeks' gestation. T3 has much greater biological activity than T4 and is specifically generated at its site of action in peripheral tissues by deiodination of T4. These hormones play a critical role in cell differentiation during development and help to maintain thermogenic and metabolic homeostasis in adults. One of the functions of thyroid hormone is to stimulate oxygen consumption by most cells in the body, helps to regulate lipid and

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carbohydrate metabolism and thereby influences body mass and mentation.[1] Thyroid hormones have marked effects on brain development; it is essential for the development of central nervous system (CNS). The parts of CNS most affected are cerebral cortex and basal ganglia. In addition, the cochlea is also affected. Consequently, thyroid hormone deficiency during development causes mental retardation, motor rigidity, and deaf-mutism.[2] Deficiency in fetal life or at birth causes retention of infantile characteristics of the brain, hypoplasia of cortical neurons with poor development of cellular processes, retarded myelination, and reduced vascularity. It is irreversible if the deficiency is not corrected in early life. The absence or hypofunction of thyroid hormone in fetal life or neonatal life also results in mental retardation and dwarfism. Whereas, its deficiency in adult life causes less severe manifestations that usually respond to treatment with hormone.[3] All intellectual functions including slowness of speech and loss of initiatives are present. Slow wittedness and memory defects are common. Lethargy, somnolence is prominent. Dementia in elderly subjects may be mistaken for senile dementia. Psychiatric disorders are common, usually of paranoid type. Sometimes, it may induce agitation. Headaches are also frequent.[4] Subclinical hypothyroidism (SCH) is a special condition in which an asymptomatic patient has a low-normal free T4 but a slightly elevated serum thyroid-stimulating hormone (TSH) level; a value typically between 5 and 15 mU/L. The other terms for this condition are mild hypothyroidism, preclinical hypothyroidism, biochemically hypothyroidism, and decreased thyroid reserve.[5] Recently, it is also termed as minimal symptomatic hypothyroidism.[6] It has been seen from various studies that if the level of TSH rises more than 10 mU/L, there are more chances of overt hypothyroidism with hypercholesterolemia and atherosclerosis. Hence, the value of TSH is considered up to 10 mU/L in case of SCH.[7,8] Thyroid function has important actions in adult brain, and it is well accepted that hypothyroidism is associated with neuropsychiatric complaints and symptoms. Hypothyroidism impacts aspects of cognitive functioning and mood. More severe hypothyroidism can mimic melancholic depression and dementia. The degree to which mild hypothyroidism or SCH impacts mood and cognitive functions and whether these symptoms respond to treatment remain controversial.[9] Cognitive function can be defined as the person's capacity to acquire and use information to adapt to environmental demands and the process involves many skills including attention, creativity, memory, perception, problem solving, thinking, and use of language.[10] It can be studied by various test types such as application of standard mini-mental status examination test and comparative performance in previous annual examination in languages and mathematics can be an indicator of their mental ability.[11] Anxiety is a normal phenomenon which is characterized by a state of apprehension or unease arising out of clinical practice, and anxiety disorders are one of the psychiatric disorders.[7] Mood, which is a sustained and pervasive response which colors the whole psychic life. According to definitions, depression and mania are mood disorders. SCH is a common condition with prevalence of 3–7% in general population. It increases with age and it may be as high as 17% in elderly, especially in women.[12-14] A recent study shows that SCH subjects often found to have impaired working memory.[15] In this study, anxiety, depression, and level of executive function will be assessed in SCH cases in young adults and middle-aged population (20–50 years) of age. Definite scales will be used to evaluate these neuropsychiatric changes.

MATERIALS AND METHODS

This is a cross-sectional and observational study. It was done with the patients attending the Department of Biochemistry for thyroid function test in North Bengal Medical College and Hospital within a period of 1 year (July 2014–June 2015). Patients of 20–50 years of age group having TSH value 5.5–10 mU/L with free T4 and free T3 within normal reference range (FT4 = 0.8–2.7 ng/dl, FT3 = 1.4–4.5 pg/ml) were included in the study. Patients excluded from the study were - patients already on thyroxin supplementation, with pre-existing psychological illness such as schizophrenia, bipolar disorder, and depression, with chronic diseases such as ischemic heart disease, diabetes mellitus, cerebrovascular diseases, and rheumatoid arthritis, and with neurological diseases such as seizures, subjects known to have substance abuse, patients undergone surgery for thyroid gland previously, and cases of SCH with pregnancy. The sample size calculated was 120 assuming anticipated population proportion 50% and absolute precision 10% in the absence of appropriate data. Cases were collected from the laboratory database from the department of biochemistry after getting clearance from the institutional ethics committee. Cases were evaluated by questionnaire method using preformed and predesigned pro forma of the study. Definite scales were used for the assessment of neuropsychiatric changes - Hamilton anxiety rating scale (HAM-A) for evaluation of anxiety, Hamilton rating scale for depression (HAM-D), and a pro forma for cognitive function (which is being used in Bangur Institute of Neurosciences, Kolkata) was used as a scale for executive function.

HAM-A is a clinician-rated scale to assess the severity of symptoms anxiety in children, adolescents, and adults. The scale consists of 14 items each defined by series of symptoms and measures both psychic anxieties (physical complaints related to anxiety). Each item is scored on a scale of 0 (not present)–4 (severe), with a total score range of 0–56, where <17 indicates mild severity, 18–24 indicates mild to moderate severity, and 25–30 indicates moderate to severe.

Hamilton depression rating scale (HDRS/HAM-D) is also a clinician-rated scale to assess the severity of and change in depressive symptoms in adult population. The scale consists

of 17 items and a score of 0–7 generally accepted in normal range while a score of 20 or higher indicates moderate severity.

The scale which was used for the evaluation of executive function consists of total 7 items with a maximum score of various items which are different in various items. The subject was asked to draw diagrams which were shown to them, to follow commands and symptoms of frontal lobe were also tested. Failing to obtain the maximum score was considered as dysfunction of executive function.

RESULTS

The study was conducted over a period of 1 year (July 2014–June 2015) involving 120 subjects among them 14 were male (11.7%) and 106 were female (88.3%). The age of the study population was between 20 and 50 years of age, mean 41.78 with standard deviation of 7.53. The sample was divided into three age groups: Group I - 20–29 years, Group II - 30–39 years, and Group III - 40–50 years for convenience of analysis. Group I consists of 10 cases (8.3%), Group II of 38 cases (31.7%), and Group III of 72 cases (60%). The mean value of TSH was 8.16 with standard deviation of 1.5. Mean value of FT4 was 1.75 with standard deviation of 0.69, whereas mean value of FT3 was 2.169 with standard deviation of 0.88. Anxiety was evaluated by HAM A. Minimum score of HAM-A was 7 and maximum score was 27; mean score of HAM-A was 16.35 with standard deviation of 4.71. ANOVA tests were done among the cases of SCH to subdivide the cases into three groups: Mild anxiety, moderate anxiety, and severe anxiety. 77 cases were found to have mild anxiety (64.2%), 32 cases were of moderate anxiety (26.7%), and 11 cases were found to have severe anxiety (9.2%). Score of HAM-A was found to be significantly correlated with the level of TSH only ($P = 0.000$) but not with the level of T4 ($P = 0.61$) and T3 ($P = 0.923$). Score of HAM-A was found to be not statistically significant with age ($P = 0.574$) and body mass index (BMI) ($P = 0.346$). It was seen that score of HAM-A was affected by the level of TSH. Moreover, the level of TSH was significantly correlated with the score of HAM-A (Pearson's correlation test was applied). Mean score of HAM-D was 9.37 with standard deviation of 3.26. It was

Table 1: Correlation of HAM-A with TSH, age, and BMI

Parameters of the study	HAM-A	HAM-D
TSH	0.000	0.027
T4	0.611	0.760
T3	0.869	0.923
Age	0.574	0.475
BMI	0.346	0.642

HAM-A: Hamilton anxiety rating scale, HAM-D: Hamilton rating scale for depression

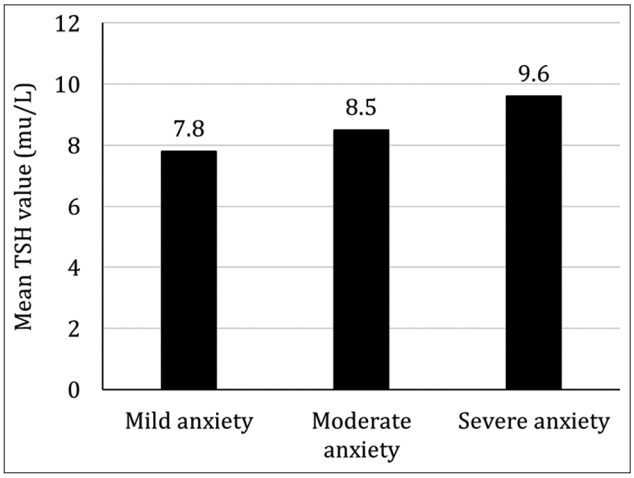

Figure 1: Level of anxiety by the mean value of thyroid-stimulating hormone

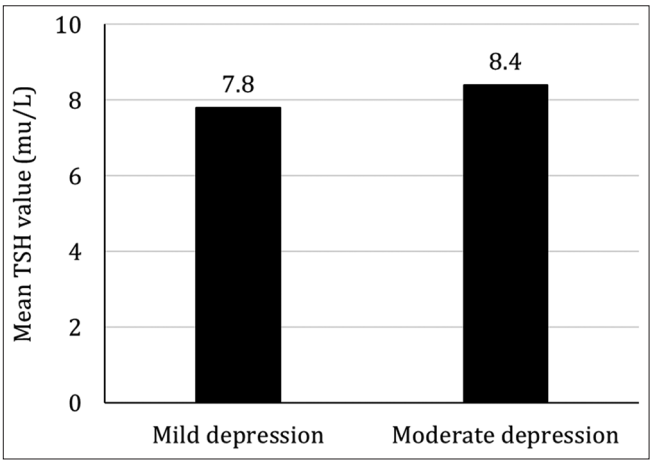

Figure 2: Level of depression by the mean value of thyroid-stimulating hormone

Table 2: Overall prevalence of anxiety and depression

Parameters	*P* (prevalence) value	SE	Z	*P*	95% CI	99% CI
Mild anxiety	0.014	0.0016	8.75	<0.001*	0.014	0.0016
Moderate anxiety	0.0058	0.00032	1.813	<0.07	0.0058	0.00032
Severe anxiety	0.002	0.00019	10.526	<0.001*	0.0016–0.0024	0.0015–0.0025
No depression (normal)		0.0078	0.0012	6.5	*P*<0.08	0.0054–0.102
Depression	0.014	0.0016	8.75	<0.001*	0.011–0.017	0.0099–0.0181

SE: Standard error, CI: Confidence interval

found that cases of mild depressions were 43 (35.8%) and of moderate depression were 77 (64.2%). Cases of depression were divided into mild and moderate by applying ANOVA test. Score of HAM-D was significantly correlated with the value of TSH (P = 0.027). No significant correlation was found between HAM-D and age as well as with FT3. There was no statistically significant correlation of HAM-D with age (P = 0.475) and BMI (P = 0.642). The level of depression was found to be significantly affected by the level of TSH (Pearson's correlation test was applied). Figure 2 showing the relation between depression and mean TSH level – between (P=0.642). and the level of depression. In this study, only 14 persons (11.7%) were found to have impaired cognitive function and rest of the population have normal cognitive function. Executive function was found not to be correlated with the level of TSH in this study. It was found to be not dependent on other parameters of the study such as age, sex, BMI, and locality. Figure 1 showing the relation between the level of anxiety and the TSH level.

Overall, the prevalence of mild anxiety of the study population was 1.4% and it was statistically significant (P < 0.001), the prevalence of moderate anxiety was 0.58% and it was not statistically significant (P < 0.07), the prevalence of severe anxiety was 2.2% and it was statistically significant (P < 0.001), and the prevalence of depression was 1.4% and it was statistically significant (P < 0.001). Overall, the prevalence of anxiety and depression presented in Table 2 suggested that was 2.2%.

DISCUSSIONS

Our study was a cross-sectional study with 14 male and 106 female subjects from the department of biochemistry. They were examined thoroughly of different systems after taking history of the subjects. Baseline height and weight was measured and by this BMI of the subjects was measured. Pulse rate, respiratory rate, and blood pressure of the cases were within normal limits. Lymph nodes and thyroid gland of none of the cases were palpable. The value of TSH of the sample population was 5.5–10 mU/L (mean 8.16 ± 1.5). In terms of pathophysiological consequences, experts typically classify subjects with SCH into two groups: Those with mildly elevated TSH (4.5–10 mU/L) and those with more marked TSH value (>10 mU/L). Risks of cardiovascular complications increase in cases of SCH as TSH level increases beyond 10 mU/L, particularly in elderly people. Age of the study subjects was 20–50 years (mean 41.78 ± 7.53). 10 of them were within 20–29 years of age, 38 were within 30–39 years of age, and 72 of them found within 40–50 years of age. Our study showed that a number of cases of SCH increases with age as maximum number of cases (60%) of SCH were found in the age group of 40–50 years.

A study conducted by Senthilkumaran *et al*. from the Department of Biochemistry, Chennai Medical College Hospital and Research Centre, Tamil Nadu, on prevalence and distribution of SCH in rural women showed that number of cases of SCH increases as the age advances from 15 to 67 years.[16] In a study conducted by Jailkhani *et al*. also found that 17.8% were men (44) and 81.2% were women (203).[17] In our study, 88.3% cases were female, whereas only 11.7% cases were male. Hence, it shows that cases of SCH are more in case of females. Similar finding was obtained by Franklyn; they did a study on 1210 subjects aged over 60 years, who were recruited from primary care, revealed of SCH of 11.6% in women and 2.9% in men.[18] Deshmukh *et al*. from Mumbai did a study that found that the prevalence of SCH was 11.3% (M: F ratio 1:3.7). They found that SCH increases with age.[19] BMI of the study subjects was 2.39 ± 3.09. Majority of the population were obese (67.1%). BMI is found to be not correlated with TSH level (P = 0.126, not significant), with T4 (P = 0.204) not even with T43 (P = 0.138). None of the values were statistically significant (as P value is not less than 0.05). Anxiety was evaluated by HAM-A among the subjects. Score of HAM-A was 16.35 ± 4.72. The severity of anxiety was evaluated by applying homogeneous *post hoc* tests. Number of subjects having mild anxiety was 77, mean 41.78; people with moderate anxiety were 32, mean 40.84; and people with severe anxiety were 11, mean 40.82. Statistically significant correlation was found with TSH and HAM-A (P = 0.000). Similar finding was obtained by a study conducted by Sait Gönen *et al*. from the department of internal medicine, Division of Endocrinology Meram Faculty in collaboration with the department of psychiatry.[20] They divided the patients into three groups: Subclinical hyperthyroidism (TSH <4.5 mU/L), SCH (TSH >4.5 mU/L), and a thyroid group. Beck's anxiety inventory was administered to all patients. One-way ANOVA showed that both the groups subclinical hyper- and hypothyroidism had a significantly higher anxiety scores than euthyroid groups. Depression was evaluated by HAM-D/HDRS among the subjects. Score of HAM-D was 9.37 ± 3.26. Significant correlation was found with TSH and HAM-D. Among the study population, 43 subjects were having mild depression and 77 with moderate depression. Statistically significant correlation was found with TSH and HAM-D (P = 0.027). Similar finding was obtained by Almeida *et al*.[21] They did a study named SCH: Psychiatric disorders and symptoms. They evaluated 94 SCH patients and 43 euthyroid outpatients. Both the groups were evaluated of psychiatric diagnosis based on Structured Clinical Interview Diagnostic for the DSM-IV axis I (SCI-I/DSM-IV) the pathophysiological symptoms on Hamilton anxiety and depression scales and the Beck's inventory. Their data showed an increased prevalence of psychiatric disorders in SCH patients when compared with thyroid group (45.7% vs. 25.6%; P = 0.025), mood disorders being the most frequent. Executive function was evaluated by scale for executive function: A pro forma for examination of cognitive function being used in Bangur Institute of Neurosciences, Kolkata. 14 subjects were found to have impaired cognitive function and the rest 106 found to have normal cognitive function.

No significant correlation was found with TSH and cognitive function. A study conducted by Bajaj *et al*. on cognitive function in elderly SCH concluded that the prevalence of cognitive function was significantly higher in SCH as compared to controls and the cognitive impairment was correlated with the level of TSH.[22] Whereas, in an another study named Birmingham Elderly Thyroid study published in endocrinology and metabolism in the year 2013 showed no significant correlation was present between SCH and cognitive function. Overall, the prevalence of anxiety in SCH population was 2.2% and overall prevalence of depression in SCH was 2.2%. Among the study population, only 1.4% people were suffering from mild anxiety and only 0.2% of population were having severe anxiety, whereas in case of depression 1.4% of the population were having moderate depression.

This study has limitation. The sample size was too small to make a generalization of the conclusion derived from this study. Studies involving larger population should be employed with consideration of the prevalence of anxiety, prevalence of depression and executive function, and their correlation with the SCH.

CONCLUSION

It is seen from the study that the extent of anxiety was mild among the SCH in North Bengal Medical College, whereas the extent of depression was moderate among the cases and the executive function was normal in most of the cases. There is a significant correlation between anxiety and SCH and depression and SCH. Anxiety and depression were not significantly correlated with age, sex, and BMI among the cases of SCH.

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