

Thyroid Function and Mental Disorders: An Insight into the Complex Interaction

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ABSTRACT

Objective: To assess the serum levels of Thyroxine (T4), Triiodothyronine (T3) and the thyroid stimulating hormone (TSH) in patients with depression.

Methods: Sixty clinically diagnosed and drug naive depressed patients and an equal number of healthy, age and sex matched control subjects were included in this study. The Ham-D scale was used to classify the degree of depression into the mild, moderate and the severe grades. The biochemical parameters (T3, T4 and TSH) were estimated by using commercially available kits. The data were analyzed by using the SPSS-10 software, one way ANOVA and the χ^2 test.

Result: The female depressive (n = 48) cases outnumbered the male depressive cases. The distributions of the patients in

the mild, moderate and the severe categories were similar. A significant decline in the T3 level and an elevation in the T4 level were found in the depressive cases as compared to those in the healthy controls. ANOVA with multiple comparisons testing among the patient group showed no significant difference in the TSH level when the depressive cases with various degrees of depression were compared. A total of twelve depressive patients were found to have thyroid abnormalities.

Conclusion: This study therefore observed the presence of thyroid dysfunction among the depressive cases, which is most often characterized as the "Lower Thyroid Syndrome". Thus, the inclusion of the thyroid screening test among the depressive patients may be helpful in the proper management of the cases.

Key Words: Total T3, Total T4, TSH, Depression

INTRODUCTION

The coexistence of thyroid insufficiency with mental disorders was recognized over a century ago [1], and it is supported by a good amount of evidence. Mental disorders accounted for 6 of the 20 leading causes of disability worldwide for the most productive section of the population. Unipolar depressive disorders were ranked as the fourth leading cause of disability after lower respiratory infections, perinatal conditions and HIV/AIDs. The point prevalence rate (%) of unipolar depression is 1.9 (for men) and 3.2 (for women) [2].

Thyroid hormones play a key role in the development, metabolism and the functioning of many organs. Numerous multidisciplinary studies documented a high prevalence of mood disorders, particularly depression, among the patients with thyroid dysfunction. Although the role which is played by the thyroid hormones in the pathophysiology of mental disorders is not clear, it has been suggested that small changes in the thyroid hormone levels, even within the normal range, may be related to the altered brain function in depression. The literature data on the plasma hormone values in patients with depression are controversial. In view of this, the present study was conceived in order to contribute to a better understanding of the relationship between the thyroid activity and depression, for which we assessed the thyroid function by measuring the serum total T3, total T4 and the TSH levels in patients with major depression, who had no prior history of thyroid-related illnesses and in healthy controls.

MATERIAL AND METHOD

The present case-control study was carried out in the Department of Biochemistry, Government Medical College and Hospital, Nagpur, India, from July 2008 to June 2010. The cases included 60 diagnosed patients of depression who presented to the OPD in the Psychiatry Department at Government Medical College and Hospital, Nagpur. These depressive cases were in the age range of 20 to 60 years and they were free from any medication for at least 2 weeks. The depressive patients were rated on the Hamilton's depressive rating scale to assess the severity of the depression into mild, moderate and severe.

The patients with a prior clinical and / or laboratory evidence of hypo or hyperthyroidism, alcohol or nicotine dependence, somatic illnesses (diabetes and renal or hepatic disorders), infections, or autoimmune diseases, a recent surgical treatment or a significantly changed body weight and with other axis-I and axis II diagnoses were excluded from the study.

Pregnant or lactating female subjects or those who were on an oestrogen therapy and contraceptives were also excluded.

60 age and sex matched healthy controls who belonged to similar socio-cultural and geographical backgrounds as the patients group, were included in this study.

An ethical clearance was obtained from the institutional ethical committee. After obtaining written and informed consents from the subjects in the study and the control groups, two ml of blood was collected from each participant and the sera were separated.

The serum levels of total T3 (TT3), total T4 (TT4) and TSH, were estimated by using commercially available competitive immunoassay kits (TECO, USA) and a microplate reader in both the groups.

STATISTICAL ANALYSIS

The statistical analysis was done by using the Chi-Square (χ^2) test, the Student's t-test and ANOVA, with multiple comparison testing. For all the tests, a p value < 0.05 was considered to reflect statistical significance.

RESULTS

The mean age (41.03 ± 10.26 yrs), height (167.68 ± 4.06 cm) and weight (57.78 ± 3.57 kg) of the depressive patients were similar to that of the controls [age (40.23 ± 10.29 yrs), height (168.6 ± 3.40 cm) and weight (57.95 ± 2.38 Kg) respectively]. There was no significant difference between the two groups with respect to sex, marital status, religion, education, dietary habits and the socioeconomic status [Table/Fig-1]. Thus, [Table/Fig-1] confirms the matching of the cases and the controls. Out of the 60 patients, 20 patients had mild, 20 had moderate and 20 had severe grades of depression [Table/Fig-2]. There were more depressive patients ($n = 24$) in the 31-40 yrs age group. 20 % ($n=4$) of the mild depressive cases were seen in the 21-30 years age group and 30 % ($n=6$) were seen in the 31-40 years age group. 25 % ($n=5$) of the mild depressive cases were seen in the both the 41-50 years and the 51-60 years age groups.

15 % ($n=3$) of the moderate depressive cases were seen in the 21-30 years and the 41-50 years age groups. 40 % ($n=8$) of the moderate depressive cases were seen in the 31-40 years age group and 30 % ($n=6$) were seen in the 51-60 years age group.

The 31-40 years age group included most the severe cases, amounting to 50 % of the cases ($n=10$). 10 % ($n=2$) of the severe depressive cases were seen in the 21-30 years age group. The 41-50 years age group showed 15 % ($n=3$) of the severe depressive cases and 25 % ($n=5$) of the severe depressive cases were seen in the 51-60 years age group.

[Table/Fig-3] shows the comparison of the thyroid profile between the controls and the mild to moderate and the severe depressive cases.

The mean value of TT3 was 1.50 ± 0.14 ng / mL in the controls. It was evident that the mean levels of TT3 were at a lower range in the mild (1.37 ± 0.10 ng / mL), moderate (1.31 ± 0.17 ng / mL) and the severe depressives (0.97 ± 0.16 ng / mL) as compared to the controls and that the difference was statistically significant ($p < 0.01$).

The mean value of TT4 was 6.94 ± 1.96 μ g / dL in the controls. It was observed that the mean levels of TT4 were elevated in the mild (8.39 ± 0.80 μ g / dL), moderate (8.86 ± 1.31 μ g / dL) and the severe depressives (8.88 ± 1.97 μ g / dL) as compared to the controls and that the difference was statistically significant ($p < 0.01$).

The mean value of TSH was 3.10 ± 0.52 mIU / L in the controls. There was no statistically significant difference between the mean value of TSH in the control and the depressive groups.

DISCUSSION

Previous studies which were done in this field revealed inconsistent data. These inconsistencies which are seen in the literature may

Variable	Controls Mean \pm SD	Cases Mean \pm SD	p value
Age (years)	40.23 \pm 10.29	41.03 \pm 10.26	0.67
Height (cm)	168.66 \pm 3.40	167.68 \pm 4.06	0.15
Weight (kg)	57.95 \pm 2.38	57.78 \pm 3.57	0.76
Sex - Male	12	12	1.0
Female	48	48	1.0

Variable	Controls	Cases	p Value	
Marital status	Married	48	48	NS
	Unmarried	12	12	NS
Religion	Hindu	56	54	NS
	Non Hindu	04	06	
Education	Up to 5 th class	14	14	NS
	6 th to 12 th class	32	36	
	Graduation	14	10	
Dietary habit	Vegetarian	10	14	NS
	Non - vegetarian	50	46	
Socioeconomic status	Lower	12	14	NS
	Lower middle	02	04	
	Middle	28	28	
	Upper middle	08	10	
	Higher	10	04	

[Table/Fig-1]: Anthropometric and socio-demographical profiles of healthy controls and depressive cases

Age Group (Years)	Mild depressives (%)	Moderate depressives (%)	Severe depressives (%)	Total (%)
21-30	4 (20 %)	3 (15 %)	2 (10 %)	9 (15%)
31- 40	6 (30 %)	8 (40 %)	10 (50 %)	24 (40 %)
41-50	5 (25 %)	3 (15 %)	3 (15 %)	11 (18.33%)
51-60	5 (25 %)	6 (30 %)	5 (25 %)	16 (26.67%)
Total	20 (100 %)	20 (100 %)	20 (100%)	60 (100 %)

[Table/Fig-2]: Age wise distribution of depressive cases according to grades of depression

Variable	Control Mean \pm SD (n= 60)	Depressive cases		
		Mild Depressives (n=20)	Moderate Depressives (n=20)	Severe Depressives (n=20)
TT3 (ng /mL)	1.50 \pm 0.14	1.37 \pm 0.10**	1.31 \pm 0.17***	0.97 \pm 0.16***
TT4 (μ g / mL)	6.94 \pm 1.96	8.39 \pm 0.80**	8.86 \pm 1.31***	8.88 \pm 1.97***
TSH (mIU / L)	3.10 \pm 0.52	3.13 \pm 0.39 ^{NS}	3.83 \pm 3.12 ^{NS}	3.00 \pm 2.54 ^{NS}

[Table/Fig-3]: Comparison of Thyroid Profile between Controls and Mild, Moderate and Severe Depressive Cases

* = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.001$; NS = Not significant

be attributed to the in/outpatients status which was included in this study, the inclusion of the depressive cases who were on an antidepressant medication and the heterogeneity of the depression. We tried to take care of these confoundable factors by recruiting only the freshly diagnosed and the drug naive depressive cases.

The anthropometric and the demographic profiles of both the cases and the healthy controls confirmed the match between them with respect to age, sex, education, marital status, dietary pattern, etc The age wise distribution of the patients showed that there were more depressive patients in the 31-40 years age group [Table/Fig-2]. This was in agreement with the findings

of most of the earlier studies [3]. The female depressive cases outnumbered the male depressive cases in our study. In a study which was done by Munoz Cruzado PM et al., [4] they found a similar female preponderance among the major depressive disorder patients.

In our study, we found that the mean value of total triiodothyronine (T3) was significantly lower in the depressive patients as compared to that in the controls. This was in agreement with the findings of many previous studies which were done. We also found elevated levels of total T4 in the depressive cases. A similar observation was reported by Kirkegaard C and Faber J. [5] and by Muller and Boning [6].

The mean value of the Thyroid Stimulating Hormone (TSH) in our study did not show a significant difference between the depressive cases and the control group.

Similar findings were seen in most of the previous studies (Takahashi et al., [7] Gold et al., [8] and Loosen and Prange [9]).

The exact significance of these findings is not clear. However, along with the elevated levels of total thyroxine (T4), the decreased total triiodothyronines (T3) in the depressive patients indicated that the conversion of thyroxine (T4) to triiodothyronine (T3) may be defective in the depressive illness.

This can further be explained as in major depression. The bioavailability of the biologically active thyroid hormone, T3 in the CNS is decreased, in context of the systemic euthyroidism [10]. This might be explained by the role of Type 2 Deiodinase (D2), that causes the deiodination of T4 to T3 in the brain. A decreased activity of D2 in the patients with major depression contributes to a decreased bioavailability of T3 in the brain. But then, what might be the cause of this decreased D2 activity in depression? This can possibly be explained by the hypercortisolism which is seen in the patients with depression, together with the contribution of the elevated T4 levels. The hypercortisolism of depression probably occurs due to an impaired functioning of the hippocampus, which is the negative feedback site of glucocorticoids along the hypothalamic-hypophyseal-adrenal axis [11]. Therefore, the existence of a functional disconnection between the hypothalamus and other brain areas can remove the inhibitory influence of the hippocampus in some depressive pictures, thus favouring hypercortisolism and consequently, the increase of T4.

In the present study, a total of twelve depressive patients were found to have thyroid abnormalities in the form of sub-clinical hypothyroidism (n=12). A number of previous studies have suggested that the thyroid function of depressed patients was within the normal range, while in overt thyroid dysfunction, it was extremely uncommon [12-14]. It has been reported that most of the patients with depression may have alterations in their thyroid functions, which include a slight elevation in the serum T4 level, a blunted TSH response to the TRH stimulation and loss of the nocturnal TSH rise. These may reflect brain hypothyroidism [15].

In conclusion, the present study observed the presence of thyroid dysfunction among the depressives, which is most often characterized as the "Lower Thyroid Syndrome." There is a strong possibility that the aetiology and the treatment outcome of depression could be related to the thyroid status. Thus, the inclusion of a thyroid screening test among the depressive patients may be helpful in the proper management of the cases. However, there is a need to continue the research efforts in this field, to further clarify the aetiopathological significance of the altered thyroid function in the depressive illness in a larger population.

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