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Original Article

Altered serum levels of thyroxine, triiodothyroinine and thyroid stimulating hormone in patients with depression

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Abstract

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

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

Result: Female depressed (n = 17) cases outnumber the male depressed cases. The distributions of patients in mild, moderate and severe categories were similar. The T3 and T4 level were found to be significantly raised in the moderate depression as compared to the healthy controls. ANOVA with multiple comparisons testing among the patient group showed a significant high TSH level (F> 3.17) at 5% level of significance. A total of six depressive patients were found to have thyroid abnormalities.

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

In the recent years, there has been an increased interest in the hypothalamic pituitary thyroid axis in association to psychiatric problems. Psychiatric syndromes associated with endocrine dysfunction include mood disturbances, anxiety, cognitive dysfunction, dementia, delirium and psychosis[1]. Depression is a wide spread problem. It is estimated that 20 to 26 % of women and 8 to 12 % of men suffer from a major depression during their life times[2]. Report of WHO Global Burden of disease studies, in 1997 indicated the unipolar depression being ranked fifth among other diseases and was projected to rank second by the year 2020[3].

Thyroid function testing is obtained more frequently than any other endocrine screens in the evaluation of mood disorders. There are plenty of evidences that hypothyroidism can produce symptoms and signs that come to the attentions of the psychiatrists as depression, dysthymia or lethargy. However hypothyroidism is not all or none phenomenon[4].

Some studies reported elevated levels of total thyroxine (T4) and free thyroxine (FT4) in acute depressive illness, while other studies found no difference[5]. Some mixed picture with increased T4 with lower level of T3 and TSH, and lower T3 and raised TSH has been reported[6].

There are conflicting data about changes in thyroid functioning during depression. Thyroid hormone parameters are also influenced by climate, genetic and regional factors. No such systematic study has been done in the local population of eastern Nepal. Therefore this study was conceived with the aim of estimating serum thyroid profile parameters and studying their abnormal patterns, if any, in a cross-section of freshly diagnosed depressive patients attending the psychiatric out patients department of B.P. Koirala Institute of Health Sciences, Dharan (BPKIHS), Nepal.

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Material and method

Thirty-one patients (14 male and 17 female) of unipolar depression in the age range 15–60 years and equal numbers of age and sex matched healthy controls belonging to similar socio-cultural and geographical background as the patients group were included in this study. Patients at their first visit to Psychiatric out patient department of (BPKIHS), Dharan and without any prior intake of anti-depressants only were considered eligible for the study.

Informed consent was obtained from the patient's guardian (on behalf of the patients) and all the healthy control subjects prior to their inclusion in this study. This study was approved by the institute Research and Ethical Review Board of (BPKIHS), Dharan, Nepal. A careful history thorough physical examination and relevant laboratory investigations were performed to rule out any evidence of endocrinological, hepatic, renal, cardiac, chronic systemic illness, significant alcoholism and pregnancy or oral contraceptive use (in case of female subjects). The depressive patients were rated on Hamilton's depressive rating scale[7] (Hamilton, 1967) to assess the severity of depression into mild, moderate and severe.

Blood samples were drawn in the fasting state. T3, T4 were estimated by competitive solid phase enzyme linked immunosorbent assay (ELISA) and TSH by sandwich ELISA employing monoclonal antibodies. Data were analyzed using the statistical product and service solution (SPSS-10).

Chi-Square (χ^2) was used to compare qualitative variables. Student t-test and ANOVA with multiple comparison testing were applied to compare quantitative variable. A p value ≤ 0.05 was considered to be statistically significant.

Results

The mean age (34±11.70yrs), height (164±6.7 cm) and weight (56±7.85 Kg) of depressive patients were similar to that of controls age (34±10.4 yrs), height (166±4.8 cm) and weight (57±6.1 Kg) respectively. There was no significant difference between the two groups with respect to sex, marital status, religion, education, dietary habits and socioeconomic status **(Table 1)**. Thus this table confirms the matching of cases and control. Out of 31 patients, 10 patients had mild, 10 had moderate and 11 had severe grade of depression **(Table 2).** There were more depressive patients (n = 12) in the 26-40 yrs age group. Mild and moderate depressive patients were more in the 15-26 yrs age group. The 26-40 yrs age group included most severe cases**.**

The comparison of T3, T4, TSH & T3/T4 ratio values between the grades of depressive patients and controls has been shown in Table 3. The T3 level was elevated in the mild (1.48±0.4 ng/ml) and moderate (1.87±0.33 ng/ml) and decreased in severe (1.26±0.53 ng/ml) as compared to controls (1.41±0.34 ng/ml). The T4 level was also increased in severe grade of depression. The T4 level was also increased in mild (8.50±1.77 µg/ml) and moderate (10.62±3.1 µg/ml) but decreased in severe (7.18±4.53 µg/ml) grade of depression. The TSH level was decreased in mild (3.82±4.60 mIU/L) and moderate (1.74±2.37 mIU/L), and significantly increased in severe (9.59±11.38 mIU/L) depression ($p<0.001$). The ratio of T3/T4 value was found increased only in moderate and severe cases compared to healthy controls. The significant increase of T3 and T4 was found only in moderate grade of depressive patients ($p<0.001$) as compared to controls. ANOVA with multiple comparison testing between these groups of the patients of mild, moderate and severe depression showed significantly high TSH levels ($F<3.17$) at the 5% level of significance

The data was analyzed to find out the frank as well as sub-clinical thyroid abnormalities in cases and controls. The plot of individual T4 values corresponding versus TSH values **(Fig 1)** suggested that the majority of depressed patients and total controls were located in the normal reference area. Five patients (16.12%) showed increased TSH level among which three (9.6%) were located in the hypothyroid region, two (6.45%) in the area of sub clinical hypothyroidism and one (3.22%) in the area of hyperthyroidism.

Table 1: Anthropometric and socio-demographical profiles of the healthy controls and depressive cases

Variable	Control	Cases	P value
Age(yrs)	34 ± 10.43	34.26 ± 11.70	0.93
Height(cm)	166 ± 4.8	164 ± 6.7	0.073
Weight(Kg)	57 ± 6.1	56 ± 7.85	0.18
Sex			
Male	14	14	1.0
Female	17	17	
Marital status			1.0
Married	25	25	
Unmarried	6	6	
Religion			0.06
Hindus	29	27	
Non-Hindus	2	4	
Education			0.25
Up to 5th class	9	9	
6th to 12the class	13	18	
Above intermediate	9	4	
Dietary Habit			
Vegetarian	4	7	0.5
Non-vegetarian	27	24	
Socio-economic status			
Lower	3	7	0.32
Lower middle	4	2	
Middle	14	14	
Upper middle	4	6	
Higher	6	2	

Table 2: Age wise distribution of depressive case (n = 31); (Grading was done using Hamilton Scale)

Age (yrs)	Mild (%)	Moderate (%)	Severe (%)	Total
15-25	4 (40%)	4 (40%)	2 (18%)	10 (32%)
26-40	3 (30%)	4 (40%)	5 (46%)	12 (39%)
41-60	3 (30%)	2 (20%)	4 (36%)	9 (29%)
Total	10 (100%)	10 (100%)	11 (100%)	31 (100%)

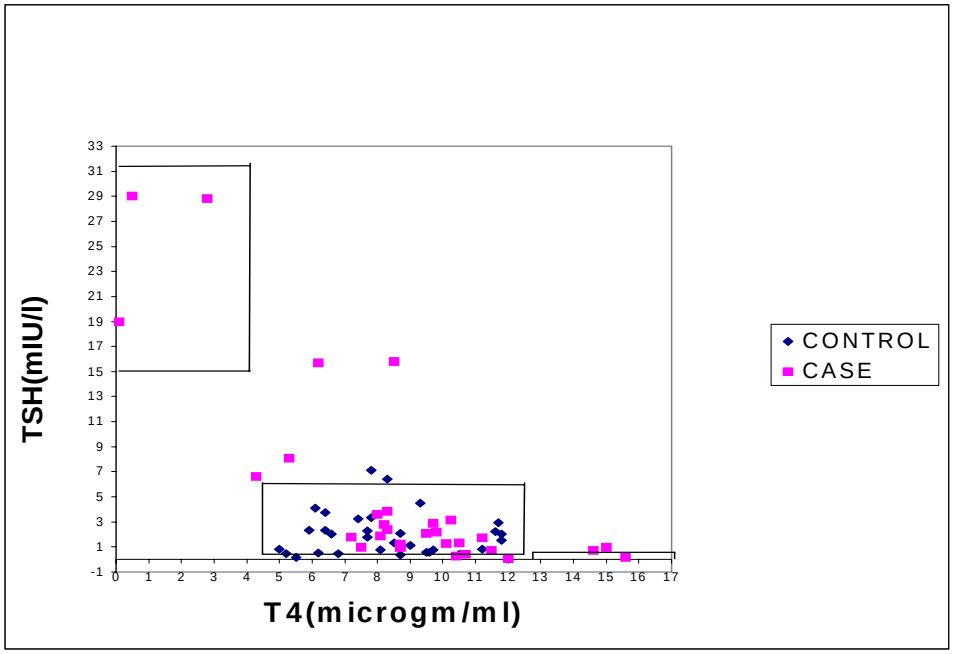
$\chi^2 = 1.86$; df = 4; P = 0.7

Table 3: Comparison of thyroid profile between controls and depressive ranked cases

Variable	Controls (n=31) (Mean±SD)	Depressives (n=31) (Mean±SD)		
		Mild(n=10)	Moderate(n=10)	Severe(n=11)
T3(ng/mL)	1.41±0.34	1.48±0.4	1.87±0.33**	1.26±0.53
T4(µg/mL)	8.27±2.04	8.50±1.77	10.62±3.1**	7.18±4.53
TSH(mIU/L)	2.03±1.73	3.82±4.60	1.74±2.37	9.59±11.38**
T3/T4	0.17±0.03	0.17±0.03	0.19±0.07	0.49±0.74

** *P ≤ 0.01*

Fig 1: Bivariate scatter plot between TSH and T4 levels



Discussion

The possibility of the relationship between thyroid gland, brain and behaviour has been the subject of intense studies in recent years. Many of the previous studies done in this field had various methodological flaws in the case selection such as being on psychotropic medication, chronic illness. The present study includes only Psychotropic drug naïve depressive cases. This way, the non specific effects of pharmacological agents and chronicity of illness on thyroid functions were taken care of.

The anthropometric and demographic profile of both cases and healthy controls confirm the matching with respect to age, sex, education, marital status, dietary pattern etc (Table-1). Female depressed cases outnumber the male depressed cases. The age wise distribution of the patients showed that there were more depressive patients in the 26-40 yrs age group (table 2)**.** This is in agreement with most of the earlier studies[8]. Mild depressive patients were more in the age group 15-25 yrs. Some recent epidemiological data suggest that the incidence of depression may be increasing among people less than 20 years of age which may be related to the increase substance abuse.

Although there were slight but insignificant increase in the levels of T3 & T4 in the patient as compared to the control groups, those levels were still within the range of biochemical euthyroid status (Table 3). Decrease level of T3 in severe grade of depression and significant increase of T4 in moderate grade of depression was also found. It is proposed that elevated total T4 during acute phase of depression is a compensatory phenomenon to help increase the catecholamine neurotransmission for alleviation of depressive affect[9]. It is assumed that the conversion of T4 to T3 may be defective in the depressive illness.

While considering the levels of TSH in depressive patients in comparison to the controls, it was found to be significantly higher in the depressive group. It is in agreement with many previous studies [10]. The alteration in TSH level depicts the biochemical status of hypothalamus. The most interesting finding of this study was decreased levels of T4 in the diseased cases as compared to control. It could therefore be hypothesized that unlike other organs which require T_3, the brain obtains T4 from a saturable carrier, transthyretin(TTR), which carries T4 across the blood brain barrier. Once T4 is converted to T3 in the brain, through the action of 5'deiodinase type II, the increase level of T3 (active) and T4 negatively feedback the secretion of TSH.

In the present study a total of six depressive patients were found to have thyroid abnormalities: Overt hypothyroidism (n=3), sub-clinical hypothyroidism (n=2) and hyperthyroidism (n=1). A number of previous studies suggested that the thyroid function

of depressed patient to be within the normal range while overt thyroid dysfunction being extremely uncommon[11,12,13]. It is reported that most patients with depression may have alteration in their thyroid function including slight elevation of serum T4 level, blunted TSH response to TRH stimulation and loss of the nocturnal TSH rise and this may reflect brain hypothyroidism in the context of systemic euthyroidism[14].

In conclusion this study therefore points towards presence of thyroid dysfunction among the depressives which most often characterized as a "Lower Thyroid Syndrome". Thus inclusion of thyroid screening test among depressive patients may be helpful in proper management of cases. However, there is a need to continue the research effort in this field to further clarify the aetiopathological significance of altered thyroid function in depressive illness in a larger population.

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