BASAL THYROID FUNCTIONS IN FIRST EPISODE DEPRESSIVE ILLNESS: A CONTROLLED STUDY

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ABSTRACT

Significant but subtle abnormalities in the thyroid functions in depressive patients, have been reported. Basal thyroid functions of 33 drug naive depressive patients having first episode of illness were compared with 31 healthy matched controls. The mean value of total thyroxin (T4) was significantly higher in depressives. Total triiodothyronine (T3) was lower in depressive patients but the difference was not significant. The mean value of thyroid stimulating hormone (TSH) was comparable in the two groups. No significant difference was found with respect to total T4 and total T3 when depressive patients with various subtypes of depression were compared. But depressive patients with psychotic features had significantly higher mean value of TSH as compared to those without them. The findings are discussed in relation to the available literature.

Key words: First-episode, depressive illness, total thyroxine (T4), total triiodothyronine (T3), thyroid stimulating hormone (TSH)

The possibility of a relationship between thyroid gland, brain and behaviour has captured the attention of clinicians and researchers for more than two centuries (Whybrow and Prange, 1981). Although, a relationship between clinical disorders of the thyroid gland and psychiatric morbidity has been well established, the significance of the association between thyroid functioning and primary psychiatric disorders is much less clear.

Many studies in seventies and eighties reported elevated total thyroxin (T4) and free thyroxin (FT4) levels in acute depressive illness which normalized after recovery (Whybrow et al., 1972; Takahashi et al., 1974; Kirkegaard et al., 1981; Linnoila et al., 1982). However, others found either no difference or decreased level of thyroxin during acute phase of depression. (Kirkegaard et al., 1977; Rinieri et al., 1978; Linnoila et al., 1979, Kjellman et al., 1983; Callaway et al., 1984; Joffe et al., 1985; Sternback et al., 1985; Baumgartner et al., 1988). A study by Sokclov et al. (1994) reported elevated T4 (but not FT4) in depressed adolescent patients as compared to controls. Similarly, conflicting findings have been reported about total triiodothyronine (T3) during acute depressive illness (normal level of T3 as reported by Kirkegaard et al., 1977; Rinieri et al., 1978; Kirkegaard and Faber, 1981; Kjellman et al., 1983; Callaway et al., 1984; Roy-Byrne et al., 1984 and decreased T3 level as reported by Linnoila et al., 1979, Joffe et al., 1985, Orsulak et al., 1985). Thus various studies have yielded a conflicting data about changes in thyroid functioning during acute depression. However, the most consistent findings have been elevated total Thyroxin (T4) or free thyroxin (F-T4) "within the euthyroid range" that decrease with treatment (Joffe, 1990).

In India, very little work has been done in this field. Boral et al. (1979) studied 12 patients of manic depressive psychosis and found lower levels of total thyroxin (T4) and total triiodothyronine (T3) in depressive patients and
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higher levels in manics as compared to controls. Same authors, in another study (Boral et al., 1980) again found low levels of total thyroxin (T₄) and total triiodothyronine (T₃) and elevated thyrotropin (TSH) in depressed patients.

The present study was planned to study the basal thyroid functions in drug naive patients with first episode of depression and to compare the findings with normal controls.

**MATERIAL AND METHOD**

Between Jan. and Dec. 1997, 33 drug naive depressive patients in the age range of 18-60 years, having first episode of illness reporting at OPD of our institute and diagnosed as per DCR (Diagnostic Criteria for Research) of ICD-10 (WHO, 1992) were selected. 31 healthy controls were taken from dermatological clinic. A careful history, thorough physical examination and relevant laboratory investigations were performed to rule out any evidence of endocrinological, hepatic, renal, cardiac or other chronic systemic illness, significant alcoholism or other substance abuse and pregnancy or oral contraceptive use (in case of female subjects). The depressive patients were rated on Hamilton’s depressive rating scale (Hamilton, 1967) to assess the severity of depression. The controls were matched with the depressive patients with respect to age, sex and socio economic status.

The blood sample was drawn in the fasting state between 8 am to 9 am and total thyroxin (T₄), total triiodothyronine (T₃) and thyroid stimulating hormone (TSH) were estimated using enzyme-immuno assay. The results obtained were analysed using statistical package of social sciences, version - 7.0 (SPSS-7.0).

**RESULTS**

Table 1 shows the comparison of socio-demographic variables between the depressive and the control groups. There was no significant difference between the two groups with respect to age, sex, marital status, socio-economic status, domicile, education and occupation. In the control group, more Muslims were represented than the depressive group, probably because the controls represented the local population attending the skin clinic as compared to the depressive group which came from a vast catchment area.

### Table 1

| Variable               | Depressives (N=33) | Controls (N=31) | X²/t | p    |
|------------------------|--------------------|-----------------|------|------|
| Age                    | Mean±SD            | Mean±SD         | 0.49 | NS   |
|                        | 32.45±11.26        | 31.03±12.28     |      |      |
| Sex                    | Male               | 20              | 17   | 0.25 | NS   |
|                        | Female             | 13              | 14   |      |      |
| Marital status         | Married            | 27              | 23   | 0.54 | NS   |
|                        | Unmarried          | 06              | 08   |      |      |
| Domicile               | Rural              | 23              | 24   | 0.5  | NS   |
|                        | Urban              | 10              | 07   |      |      |
| Religion               | Hindu              | 25              | 17   | 3.4  | <0.05|
|                        | Non-Hindu          | 08              | 14   |      |      |
| Education              | Upto class 5th     | 11              | 15   |      |      |
|                        | 6th to XII         | 16              | 12   | 1.52 | NS   |
|                        | Above Intermediate | 06              | 04   |      |      |
| Occupation             | Employed           | 18              | 18   | 6.01 | NS   |
|                        | Housewife          | 09              | 02   |      |      |
|                        | Student            | 06              | 08   |      |      |
|                        | Unemployed         | 00              | 03   |      |      |
| Socio-economic status  | Low                | 28              | 28   | 0.44 | NS   |
|                        | Middle             | 05              | 03   |      |      |

### Table 2

| Variable | Depressives (N=33) | Controls (N=31) | t    | p    |
|----------|--------------------|-----------------|------|------|
| Total T₄ (µg/100 ml) | 8.322±3.047       | 6.972±1.590     | 2.25 | <0.05|
| Total T₃ (ng/ml)      | 1298±309.332      | 1608±31.234     | 1.79 | NS   |
| TSH (µU/ml)           | 2280±12.263       | 2280±12.263     | 0.21 | NS   |
| T₄/T₃                | 0.156             | 0.231           |      |      |
TABLE 3

COMPARISON OF TOTAL T₃, TOTAL T₄ AND TSH IN THE DEPRESSIVE GROUP WITH RESPECT TO IMPORTANT CLINICAL VARIABLES

| Variable               | Total T₃ (ng/ml) Mean±SD | Total T₄ (μg/100 ml) Mean±SD | TSH (μIU/ml) Mean±SD |
|------------------------|--------------------------|-----------------------------|---------------------|
| **Psychotic features** |                          |                             |                     |
| Present (N=9)          | 1.172±0.419              | 7.578±2.63                  | 3.867±3.200         |
| Absent (N=24)          | 1.347±1.087              | 8.601±3.193                 | 1.821±1.631         |
| **Somatic syndrome**   |                          |                             |                     |
| Present (N=25)         | 1.352±1.064              | 8.744±3.323                 | 2.867±2.544         |
|Absent (N=8)            | 1.134±0.226              | 7.003±1.393                 | 1.475±0.968         |
| **Premorbid global functioning** |          |                             |                     |
| Good (N=18)            | 1.419±1.189              | 8.001±3.069                 | 2.164±1.627         |
| Poor (N=15)            | 1.55±0.477               | 8.707±3.083                 | 2.637±2.972         |

*p < 0.05

Table 2 shows the comparison of mean values of total thyroxin (T₄), total triiodothyronine (T₃) and thyroid stimulating hormone (TSH) between the depressive and the control groups. The mean value of total thyroxin (T₄) was significantly higher in the depressive group as compared to the control group (p<0.05). The mean value of total triiodothyronine (T₃) was lower in case of depressives as compared to controls, although the difference just escaped the statistical significance. There was no difference between the mean value of thyroid stimulating hormone (TSH) between the two groups. The ratio of total triiodothyronine to total thyroxin (T₃/T₄) was higher in control group as compared to the depressive group.

Table 3 shows the mean values of total T₃, total T₄, and TSH in depressive patients with respect to important clinical variables. There was no significant difference between depressive patients with and without the presence of psychotic features and with and without the presence of somatic syndrome with respect to total T₃ and total T₄. However, depressive patients with psychotic features had significantly higher mean values of thyroid stimulating hormone (TSH) as compared to those without psychotic features (p<0.05). The depressive patients with good as well as poor premorbid global functioning had comparable values of total T₃, total T₄ and TSH.

The data was further analyzed to find out the frank as well as subclinical (Gold et al., 1981) thyroid abnormalities in the two groups. A total of 3 depressive patients (9%) had grade II hypothyroidism and one (3%) had grade I hypothyroidism. One (3%) depressive patient had frank hyperthyroidism. None of the controls had either hypo or hyperthyroidism.

DISCUSSION

Many of the previous studies done in this field had various methodological flaws in the sample selection e.g. including the patients having chronic resistant illness or being on psychotropic medication. The present study included only drug-naive patients having first episode of depressive illness. This way, the non-specific effects of chronicity of illness and pharmacological agents on thyroid functions were taken care of.

The most significant finding of the study was elevated levels of total thyroxin (T₄) in the depressive patients in the acute phase of illness as compared to healthy controls. This is in agreement with most of the earlier studies (Whybrow et al., 1972; Takahashi et al., 1974; Kirkegaard and Faber, 1981; Muller and Boning, 1988).

Bauer and Whybrow (1988) proposed that elevated total thyroxin (T₄) during acute
depression is a compensatory phenomenon so as to help in increasing the catecholamine neurotransmission for the alleviation of depressive affect. On the other hand, Joffe et al. (1984) and Joffe and Levitt (1990) proposed that relative increase in total thyroxin (T₄) during acute depression is not compensatory, but is pathological indicating a relative state of hyperthyroidism and a substantial decrease in thyroxin level is required for recovery. In this study, the levels of thyroxin (T₄) were not preformed after the recovery and this remains one of its limitations.

We did not find any difference with respect to thyroid stimulating hormone (TSH) levels between the depressive and the control groups. This finding is similar to most of the previous studies (Takahashi et al., 1973; Linnoila et al., 1979; Gold et al., 1981; Loosen and Prange, 1982).

The literature regarding total triiodothyronine (T₃) during acute depression is less consistent. Takahashi et al. (1974) found marginally elevated T₃ during acute depression whereas most of the other studies reported either normal or decreased total T₃ during acute depression (Kirkegaard and Faber, 1981; Kjellman et al., 1983; Sternback et al., 1985; Joffe et al., 1985; Orsulak et al., 1985; Baumgartner et al., 1988). Muller and Boning (1988) found elevated thyroxin (T₄) and decreased triiodothyronine (T₃) during acute depression and concluded that this finding may indicate that there is some defect in the conversion of thyroxin (T₄) to triiodothyronine (T₃). We found that the mean value of total triiodothyronine (T₃) was lower in depressive patients as compared to controls, though the difference just escaped statistical significance. The exact significance of this findings is not clear. However, along with elevated levels of total thyroxin (T₄) and decreased triiodothyronine to thyroxin ratio (T₃/T₄), the decreased triiodothyronine (T₃) in depressive patients indicate that the conversion of thyroxin (T₄) to triiodothyronine (T₃) may be defective in the depressive illness.

Joffe et al. (1992) did not find any difference between patients with melancholic and non-melancholic depression with respect to total thyroxin (T₄), total triiodothyronine (T₃) and thyroid stimulating hormone (TSH). In this study, we did not find any difference with respect to any of the thyroid parameters between the depressive patients with and without the presence of somatic syndrome. Joffe and Levitt (1990) found significantly lower total triiodothyronine (T₃) and significantly higher thyroid stimulating hormone (TSH) in patients with psychotic depression as compared to non-psychotic depression. Our study found that depressive patients with psychotic features had significantly higher (p<0.05) value of thyroid stimulating hormone (TSH) as compared to those without psychotic features, though there was no significant difference between the two with respect to total thyroxin (T₄) and total triiodothyronine (T₃). Even in the absence of low values of total thyroxin (T₄) and total triiodothyronine (T₃), elevated levels of thyroid stimulating hormone (TSH) indicate the presence of subclinical hypothyroidism in depressive patients with the presence of psychotic features as suggested by Joffe and Levitt (1990).

Apart from subtle changes in the thyroid functions, many studies have found overt thyroid abnormalities in a minority of depressive patients (Gold et al., 1981; Diaz-Caballero et al., 1986; Joffe et al., 1992). We found a total of 4 (12%) patients having grade I and grade II (Gold et al., 1981) hypothyroidism and 1 patient (3%) having frank hyperthyroidism.

In the conclusion, we would like to emphasize that this study supports the view that there are subtle but significant abnormalities in the basal level of thyroid hormones in acute depressive illness. There is a need to continue the research efforts in this field to further clarify the aetio-pathological significance of altered thyroid functioning in depressive illness.

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