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# 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 ($T_4$) was significantly higher in depressives. Total triiodothyronine ($T_3$) 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 $T_4$ and total $T_3$ 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 ($T_4$), total triiodothyronine ($T_3$), 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 ($T_4$) and free thyroxin ($FT_4$) 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; Rinieris 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 Sokolov et al. (1994) reported elevated $T_4$ (but not $FT_4$) in depressed adolescent patients as compared to controls. Similarly, conflicting findings have been reported about total triiodothyronine ($T_3$) during acute depressive illness (normal level of $T_3$ as reported by Kirkegaard et al.,1977; Rinieris et al.,1978; Kirkegaard and Faber,1981; Kjellman et al.,1983; Callaway+ et al.,1984; Roy-Byrne et al.,1984 and decreased $T_3$ 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 ($T_4$) or free thyroxin (F-$T_4$) "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 ($T_4$) and total triiodothyronine ($T_3$) in depressive patients and

higher levels in manics as compared to controls. Same authors, in another study (Boral et al.,1980) again found low levels of total thyroxin ($T_4$) and total triiodothyronine ($T_3$) 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 at 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 ($T_4$), total triiodothyronine ($T_3$) 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
COMPARISON OF SOCIO-DEMOGRAPHIC VARIABLES BETWEEN DEPRESSIVE AND CONTROL GROUPS

| Variable | Depressives (N=33) | Controls (N=31) | $X^2$/t | p |
|---|---|---|---|---|
| Age | Mean±SD 32.45±11.26 | Mean±SD 31.03±12.28 | 0.49 | NS |
| 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 | | |
| Housewife | 09 | 02 | 6.01 | NS |
| Student | 06 | 08 | | |
| Unemployed | 00 | 03 | | |
| Socio-economic status | | | | |
| Low | 28 | 28 | 0.44 | NS |
| Middle | 05 | 03 | | |

TABLE 2
COMPARISON OF TOTAL $T_3$, TOTAL $T_4$ AND TSH BETWEEN DEPRESSIVE AND THE CONTROL GROUPS

| Variable | Depressives (N=33) Mean±SD | Controls (N=31) Mean±SD | t | p |
|---|---|---|---|---|
| Total $T_4$ (µg/100 ml) | 8 3222±3 047 | 6 972±1.590 | 2.25 | <0.05 |
| Total $T_3$ (ng/ml) | 1 299±0 932 | 1 608±0.314 | 1.79 | NS |
| TSH (µIU/ml) | 2.380±2.308 | 2.280±1.263 | 0.21 | NS |
| $T_3/T_4$ | 0.156 | 0.231 | | |

TABLE 3
COMPARISON OF TOTAL $T_3$, TOTAL $T_4$ AND TSH IN THE DEPRESSIVE GROUP WITH RESPECT TO IMPORTANT CLINICAL VARIABLES

| Variable | Total $T_3$ (ng/ml) Mean±SD | t | Total $T_4$ (µg/100 ml) Mean±SD | t | TSH (µIU/ml) Mean±SD | t |
|---|---|---|---|---|---|---|
| Psychotic features | | | | | | |
| Present (N=9) | 1.172±0.419 | 0.473$^{NS}$ | 7.578±2.63 | 0.855$^{NS}$ | 3.867±3.200 | 2.436* |
| Absent (N=24) | 1.347±1.067 | | 8.601±3.193 | | 1.821±1.631 | |
| Somatic syndrome | | | | | | |
| Present (N=25) | 1.352±1.064 | 0.580$^{NS}$ | 8.744±3.323 | 1.430$^{NS}$ | 2.667±2.544 | 1.285$^{NS}$ |
| 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 | 0.804$^{NS}$ | 8.001±3.059 | 0.656$^{NS}$ | 2.164±1.627 | |
| Poor (N=15) | 1.55±0.477 | | 8.707±3.093 | | 2.637±2.972 | 0.580$^{NS}$ |

* $p < 0.05$

Table 2 shows the comparison of mean values of total thyroxin ($T_4$), total triiodothyronine ($T_3$) and thyroid stimulating hormone (TSH) between the depressive and the control groups. The mean value of total thyroxin ($T_4$) was significantly higher in the depressive group as compared to the control group ($p<0.05$). The mean value of total triiodothyronine ($T_3$) 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 ($T_3/T_4$) was higher in control group as compared to the depressive group.

Table 3 shows the mean values of total $T_4$, total $T_3$ 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 $T_3$ and total $T_4$. 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 $T_3$, total $T_4$ 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-naïve 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 ($T_4$) 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 ($T_4$) 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 ($T_4$) 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 ($T_4$) 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 ($T_3$) during acute depression is less consistent. Takahashi et al. (1974) found marginally elevated $T_3$ during acute depression whereas most of the other studies reported either normal or decreased total $T_3$ 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 ($T_4$) and decreased triiodothyronine ($T_3$) during acute depression and concluded that this finding may indicate that there is some defect in the conversion of thyroxin ($T_4$) to triiodothyronine ($T_3$). We found that the mean value of total triiodothyronine ($T_3$) 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, alongwith elevated levels of total thyroxin ($T_4$) and decreased triiodothyronine to thyroxin ratio ($T_3$/ $T_4$), the decreased triiodothyronine ($T_3$) in depressive patients indicate that the conversion of thyroxin ($T_4$) to triiodothyronine ($T_3$) 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 ($T_4$), total triiodothyronine ($T_3$) 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 ($T_3$) 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 ($T_4$) and total triiodothyronine ($T_3$). Even in the absence of low values of total thyroxin ($T_4$) and total triiodothyronine ($T_3$), 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-Cabal et al.,1986; Joffe et al.,1992). We found a total of a 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 aetiopathological significance of altered thyroid functioning in depressive illness.

## REFERENCES

**Bauer,M.S. & Whybrow,P.C. (1988)** Thyroid hormones and the central nervous

system in affective illness : interactions that may have clinical significance. *Integrated Psychiatry*, 6, 75-100.

**Baumgartner,A., Graf,K.J., Kurte,I. & Meinhold,H. (1988)** The hypothalamic pituitary-thyroid axis in psychiatric patients and healthy subjects : Parts 1-4. Part 2- Repeated measurements of thyroxin, free thyroxin, triiodothyronine, free triiodothyronine and reverse triiodothyronine in patients with major depressive disorders and schizophrenia and healthy subjects. *Psychiatry Research*, 24, 271-332.

**Boral,G.C., Ghosh,A.B., Pal,S.K., Ghosh, K.K. & Nandi,D.N. (1979)** Thyroid functions in manic depressive psychosis (circular). *Indian Journal of Psychiatry*, 21, 271-273.

**Boral,G.C., Ghosh,A.B., Pal,S.K., Ghosh,K.K. & Nandi,D.N. (1980)** Thyroid functions in depression. *Indian Journal of Psychiatry*, 22, 353-355.

**Callaway,S.P., Dolan,R., Fonagy,P., deSouze,U.F.A. & Waheling,A. (1984)** Endocrine changes and clinical profiles in depression. II-The thyrotropin releasing hormone test. *Psychological Medicine*, 14, 759.

**Diaz Cabal,R., Pearlman,C. & Kawecki, A. (1986)** Hyperthyroidism in a patient with agitated depression : resolution after convulsive therapy. *Journal of Clinical Psychiatry*, 47, 322-323.

**Gold,M.S., Pottash,A.L.C., Mueller,E.A. & Extein,I.R.L. (1981)** Grades of thyroid failure in 100 depressed and anergic psychiatric inpatients. *American Journal of Psychiatry*, 138, 253-255.

**Hamilton,M. (1967)** Development of a rating scale for primary depressive illness. *The British Journal of Social and Clinical Psychology*, 6, 278-296.

**Joffe,R.T. & Levitt,A.J. (1990)** Thyroid function in psychotic depression. *Psychiatry Research*, 33, 321-322.

**Joffe,R.T. (1990)** A perspective on the thyroid and depression. *Canadian Journal of Psychiatry*, 35, 754-758.

**Joffe,R.T., Bagby,R.M. & Levitt,A.J. (1992)** The thyroid and melancholia. *Psychiatry Research*, 42, 73-80.

**Joffe,R.T., Blank,D.W., Post,R.M. & Unde,T.W. (1985)** Decreased triiodothyronine in depression : A preliminary report. *Biological Psychiatry*, 20, 922-925.

**Joffe,R.T., Roy-Byrne,P.P., Unde,T.W. & Post,R.M. (1984)** Thyroid function and affective illness : A reappraisal. *Biological Psychiatry*, 19, 1658.

**Kirkegaard,C. & Faber,J. (1981)** Altered serum levels of thyroxin, triiodothyronine and diiodothyronine in endogenous depression. *Acta Endocrinology*, 96, 199.

**Kirkegaard,C., Bjorum,N., Cohn,D., Faber,J., Lauridsen,U.B. & Nerup,J. (1977)** Studies on the influence of biogenic amines and psychoactive drugs on the prognostic value of the TRH stimulation test in endogenous depression. *Psychoneuroendocrinology*, 2, 131.

**Kirkegaard,C., Eskildsen,P.C. & Bjorum,N. (1981)** Parallel changes of the response to thyrotropin, growth hormone and prolactin to thyrotropin releasing hormone in endogenous depression. *Psychoneuroendocrinology*, 6, 253.

**Kjellman,B.F., Ljunggren,J.G., BeckFriis, J. & Wetterberg,L. (1983)** Reverse $T_3$ levels in affective disorders. *Psychiatry Research*, 10, 1.

**Linnoila,M., Lamberg,B.A., Potter,W.Z., Gold,P.W. & Goodwin,F.K. (1982)** High reverse $T_3$ levels in manic and unipolar depressed women. *Psychiatry Research*, 6, 271.

**Linnoila,M., Lamberg,B.A., Rosberg, G., Katonen,S.L. & Welin,M.G. (1979)** Thyroid hormones and TSH, prolactin and LH response to repeated TRH and LRH injections in depressed patients. *Acta Psychiatric Scandinavica*, 59, 536.

**Loosen,P.T. & Prange,A.J. Jr. (1982)** Serum thyrotropin response to thyrotropin releasing hormone in psychiatric patients : A review. *American Journal of Psychiatry*, 139, 405-416.

**Muller,B. & Boning,J. (1988)** Changes in the pituitary-thyroid-axis accompanying major affective disorder. *Acta Psychiatrica Scandinavica*, 77, 143-150.

**Orsulak,P.J., Crewley,G., Schlesser, M.A., Giles,D., Fairchild,C. & Rush,J.A. (1985)** Free triiodothyronine ($T_3$) and thyroxin ($T_4$) in a group of unipolar depressed patients and normal subjects. *Biological Psychiatry*, 20, 1047.

**Rinieris,P., Christodoulou,G.N., Souvalzoglou,A., Koutras,D.A. & Stefanis,C. (1978)** Free thyroxin index in psychotic and neurotic depression. *Acta Psychiatrica Scandinavica*, 58, 56.

**Roy-Byrne,P.P., Joffe,R.T., Unde,T.W. & Post,R.M. (1984)** Carbamazepine and thyroid function in affectively ill patients : Clinical and theoretical implications. *Archives of General Psychiatry*, 41, 1150-1153.

**Sokolov,S.T.H., Kutcher,S.P. & Joffe, R.T. (1994)** Basal thyroid indices in adolescent depression and bipolar disorder (1994) *Journal of American Academy of Child and Adolescent Psychiatry*, 33, 469-475.

**Sternback,H.A., Gwirtsman,H.E. & Gerner,R.H. (1985)** The TRH stimulation test and reverse $T_3$ in depression. *Journal of Affective Disorder*, 8, 267-270.

**Takahashi,S., Kondo,H. & Yoshimura, M. (1973)** Antidepressant effect of TRH and the plasma thyrotropin levels in depression. *Folia Neurologica Japanica*, 27, 305-314.

**Takahashi,S., Kondo,H., Joshimura,M. & Ochi,Y. (1974)** Thyrotropin response and TRH in depressive illness : Relation to clinical subtypes and duration of depressive episode. *Folia Psychiatrica Neurologica Japanica*, 28, 355-365.

**Whybrow,P.C. & Prange,A.J. Jr. (1981)** A hypothesis of thyroid catecholamine receptor intraction : Its relevance to affective illness. *Archives of General Psychiatry*, 38, 106-113.

**Whybrow,P.C., Coppen,A., Prange,A.J. Jr., Noguera,R. & Bailey,J.E. (1972)** Thyroid function and the response to liothyronine in depression. *Archives of General Psychiatry*, 26, 242-245.

**World Health Organization (1992)** International Classification of Disease (ICD-10) Geneva : World Health Organization.

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