

## A Study on Thyroid Profile in Females with Depression in Rayalaseema Region

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**Abstract:** AIM: Aim of the study is to see for the thyroid function (T3, T4, TSH), Lipid patterns and glycemic control in females newly diagnosed with depression attending Psychiatry Department, (I.P&O.P) Sri Venkateswara Medical College, Tirupati and compare them to the levels in normal females without depression. OBJECTIVES: To estimate serum levels of TSH, T3, T4 (Thyroid profile) in females newly diagnosed with depression and to estimate serum levels of TSH, T3, T4 (Thyroid profile), in age matched females without depression. To Compare the serum levels of TSH, T3, T4 (Thyroid profile) in females newly diagnosed with depression to that of normal females. MATERIAL AND METHODS: study subjects were selected from Psychiatry department, SVRRGH and study were conducted in department of Biochemistry. Two groups of subjects 50 each as group 1(cases) and group 2 (controls) were selected based on inclusion and exclusion criteria. Results of cases are compared with that of controls and are tabulated. Conclusion: study may be useful in understanding the risk factors of depression and this forms an area for the research work which if detected early can be managed accordingly and may prevent the morbidity and mortality due mood disorders like depression.

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### I. Introduction

Depression is known to mankind since many years. The World Health Organization has ranked depression fourth in a list most urgent health issues worldwide<sup>1</sup>. It is projected that depression will be second largest killer disease after heart disease by 2020 and second major leading cause of Disability Adjusted Life Years(DALYS)(1).

Etiology of depression, among mood disorders is although most frequently studied, yet it is far away from ideally understood. Increased activity in the Hypothalamo-pituitary-Adrenal (HPA) axis leads to depression and it is viewed as the "most vulnerable finding in biological psychiatry". Major Depressive Disorder (MDD) has been associated with significant changes in the Hypothalamic-pituitary-Thyroid axis<sup>2</sup>. Research findings have extended the relationship between thyroid and mood disorders. It has long been recognized that hypothyroidism can cause depressive symptoms and almost always in severe cases<sup>3,4</sup>. Patients with subclinical hypothyroidism have been noted to have a higher than normal life time prevalence of depression<sup>5-7</sup>. Depression leads to state of constant stress and which usually leads to activation of HPA axis this in turn may lead to metabolic disturbances<sup>8</sup>. The correlation between the serum lipids and depression is debatable. Many attempts have been done to find out the correlation of hypercholesterolemia with depression. While some reports say that low serum cholesterol is associated with depression, other demonstrate higher depressive scores and TSH values in patients with high cholesterol levels<sup>9-11</sup>. The conventional wisdom is that hypothyroidism may be reversible cause of depression. Depression is much more common in females than males thus females are a focus of special care.

### II. Material And Methods

A cross sectional study done after approval from ethical and dissertation committee in Sri Venkateswara Medical College, Tirupati. Informed written consent is taken from all patients participating in the study.

Study duration: From the date of scientific committee and ethical committee approval study was conducted for one year. Source of data: Study subjects were selected from Psychiatry department, SVRRGH and

study were conducted in department of Biochemistry. Sample size: Two groups of subjects 50 each as group 1(cases) and group 2 (controls) were selected based on inclusion and exclusion criteria.

Inclusion Criteria were Newly diagnosed female subjects with depression in the age group between 18-50, satisfying ICD10 criteria who have given informed written consent and exclusion Criteria includes Known cases of Diabetes/Hypertension/Alcoholism/Epilepsy. Patients on medication which can affect the levels of thyroid hormones. (steroids and anti-epileptics) ; Pregnant and lactating women. Psychiatric illness that mimic depression). Blood samples (about 5ml) were collected under aseptic conditions and transferred to dry clean tubes and allowed to clot and then sample is centrifuged at 3000 rpm for five minutes and then serum is separated and following parameters were estimated. Care was taken to procure serum free of hemolysis.

Parameters estimated in the study was Thyroid profile. Sample collected in to plain tubes and serum stored in 4°C, and samples collected are analyzed on weekly basis. CLIA Analyzer (BECKMAN COULTER – ACCESS 2) used for thyroid hormones estimation.

Serum TSH estimation: Serum is the preferred specimen type (free of hemolysis). If testing is to be done within 48 hours, samples can be refrigerated at 2 to 8°C. Freeze at - 20°C or colder for longer storage. The requested sample volume for the assay is 1.0 mL, and the minimum sample volume is 0.3 ML.

Equipment Used: 1. Beckman Coulter Access II. 2. Centrifuge 3. Refrigerator

Other materials used: 1. Reaction Vessels 2. Sample Cups 3. Latex gloves 4. Pipettes and tips

C. Reagents used: R1: Access hypersensitive hTSH Reagent ; R1a: Paramagnetic particles coated with goat anti-mouse IgG: mouse monoclonal anti-hTSH complexes suspended in TRIS buffered saline, with surfactant, bovine serum albumin (BSA), 0.1% sodium azide, and 0.1% ProClin™ 300. R1b: TRIS buffered saline with surfactant, BSA, protein (murine, goat), <0.1% sodium azide, and 0.1% ProClin™ 300. R1c: Goat anti-hTSH-alkaline phosphatase (bovine) conjugate in TRIS buffered saline, with surfactant, BSA, protein (goat), < 0.1% sodium azide, and 0.1% ProClin™ 300. Serum results are expressed as mIU/mL and an active calibration curve is required for all tests. For the Access TSH assay, calibration is required every 28 days or whenever new lot numbers of reagents are placed into use. Reference ranges: Serum TSH: 0.34 – 5.60 mIU/ML.

**TOTAL T3 ESTIMATION:** Summary of test principle and clinical relevance: The Access Total T3 Assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of triiodothyronine levels in human serum and plasma using the Access Immunoassay Systems. The Total T3 Assay is a competitive binding immunoenzymatic assay. Sample is added to reaction vessels with a stripping agent to dissociate T3 from the binding proteins. T3 in the sample competes with the T3 analogue coupled to biotin for anti-T3 alkaline phosphatase conjugate. Of the resulting antigen: antibody complexes, the T3 analogue: antibody complexes are bound to the streptavidin coated solid phase. Separation in a magnetic field and washing removes the sample T3; antibody complexes and other materials not bound to the solid phase. A chemiluminescent substrate, Lumi-Phos 530, is added to the reaction vessel and light generated by the reaction is measured with a luminometer. The light production is proportional to the amount of enzyme conjugate bound to the solid support. Reference ranges: Serum: 80-120 µg /dl

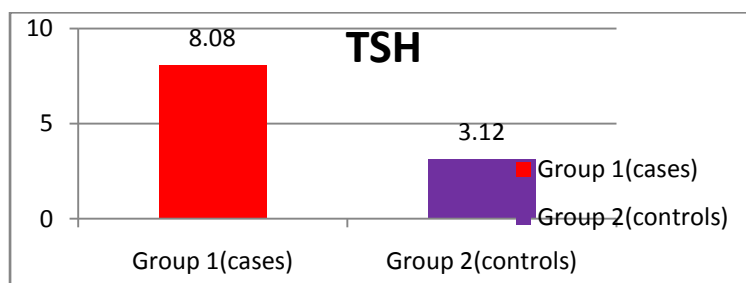
**TOTAL T4 ESTIMATION:** Test principle and clinical relevance: The Access Total T4 assay is a paramagnetic particle, chemiluminescent, competitive binding enzyme immunoassay (competitive binding immunoenzymatic assay) for the quantitative determination of total thyroxine (T4) in human serum, using the Access Immunoassay System. A sample is added to a reaction vessel with anti-thyroxine antibody, thyroxine-alkaline phosphatase conjugate, and paramagnetic particles coated with goat anti-mouse capture antibody and a stripping agent to dissociate all T4 from serum-binding proteins. Thyroxine in the sample competes with the thyroxine-alkaline phosphatase conjugate for binding sites on a limited amount of specific anti-thyroxine antibody. Resulting antigen: antibody complexes bind to the capture antibody on the solid phase. Separation in a magnetic field and washing removes materials not bound to the solid phase. A chemiluminescent substrate, Lumi-Phos 530, is added to the reaction vessel and light generated by the reaction is measured with a luminometer. The light production is inversely proportional to the concentration of T4 in the sample. Reference ranges (normal values): Serum: 6.09-12.23 µg/dL.

### **III. Results**

TSH (thyroid stimulating hormone): In the present study the mean value of serum TSH levels in group-1 is 8.1+/- 12.4 mIU/L and in group-2 the mean value is 3.1 +/- 4.0 mIU/L. P value is 0.0085 and there is significant difference between two groups. In group-1 the value is significantly increased compared to group-2.

**Table No.1:** Showing TSH VALUES IN TWO GROUPS

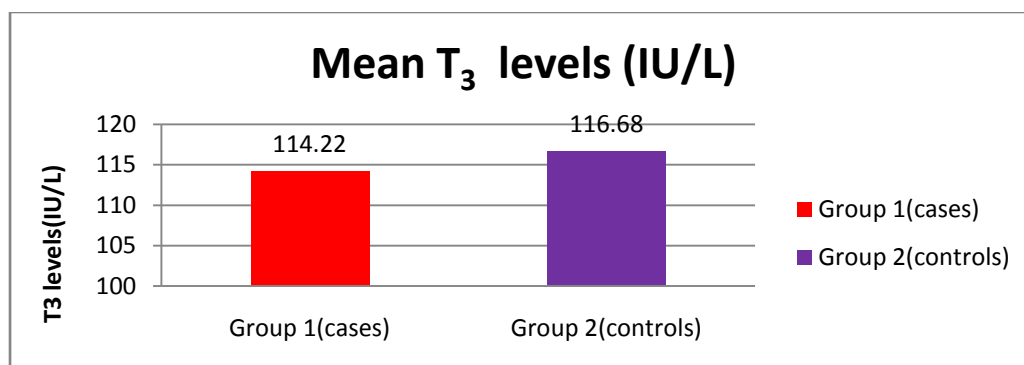
S.NO	Group	Mean+/-SD	P value
1	Group 1	8.1 +/- 12.4mIU/L	0.0085 (significant)
2	Group 2	3.1 +/- 4 mIU/L	



Serum T<sub>3</sub>: In the present study the mean value of serum T<sub>3</sub> level in group-1 is 114.2 +/- 39.9 IU/L and in group-2 the mean value is 116.7 +/- 46.1 IU/L. P value is 0.7761 which is statistically not significant. In group-1 the serum value of T<sub>3</sub> is not significantly increased compared to group-2.

**Table No.2:** Showing Serum T<sub>3</sub> VALUES - : Mean +/- SD T<sub>3</sub> levels (IU/L) in two groups

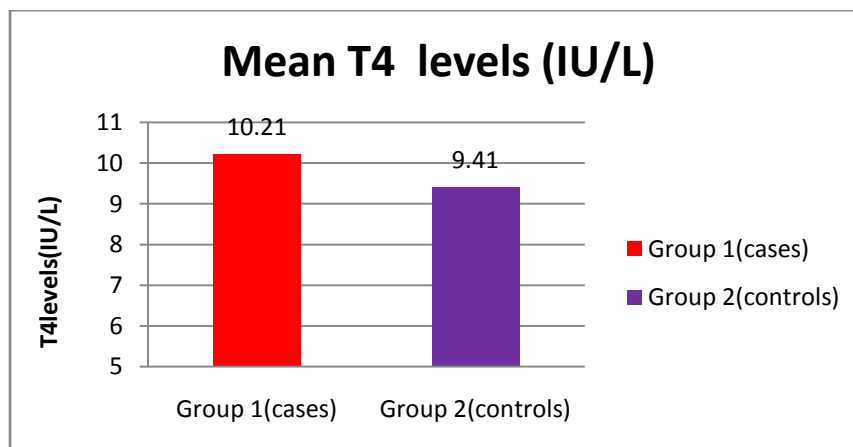
S.NO	Group	Mean+/-SD	P value
1	Group 1	114.2 +/- 39.9 IU/L	0.7761 (not significant)
2	Group 2	116.7 +/- 46.1 IU/L	



Serum T<sub>4</sub>: In the present study the mean value of serum T<sub>4</sub> level in group-1 is 10.2 +/- 3.3 IU/L and in group-2 the mean value is 9.4 +/- 3.3 IU/L. P value is 0.2242 which is statistically not significant. In group-1 the serum value of T<sub>4</sub> is not significantly lowered compared to group-2.

**Table No.3 :** Showing Mean +/- SD of T<sub>4</sub> levels (IU/L) in two groups.

S.NO	Group	Mean+/-SD	P value
1	Group 1	10.2 +/- 3.3 IU/L	0.2242 (not significant)
2	Group 2	9.4 +/- 3.3 IU/L	



#### IV. Discussion

Study was conducted by dividing the study subjects in to two groups group 1-includes women with depression fulfilling ICD 10 criteria and group 2- includes women without depression. The following investigations were done in both the cases and controls.

Depression is a important disorder of public health importance, related to its prevalence, the suffering, dysfunction, morbidity, and economic burden on the society. Depression in females is more common than males. The reports on overall burden of disease estimates the point prevalence of unipolar depressive episodes to be 1.9% for men and 3.2% for women, and the one-year prevalence has been estimated to be 5.8% for men and 9.5% for women. It is estimated that by the year 2020, the burden of depression will increase to 5.7% of the total burden of psychiatric disorders and it would be the second leading cause of disability-adjusted life years (DALYs)<sup>12</sup>.

Reddy and Chandrasekhar<sup>13</sup> carried out a metanalysis which shows that urban people are more prone to depression compared to rural people. Nandi *et.al*<sup>14</sup> studied psychiatric morbidity of the elderly population of a rural community in West Bengal and found that prevalence of depression was more common in old aged females especially widowed in the rural community. Psychiatric morbidity was more prevalent in those who were socially, economically, and educationally disadvantaged<sup>15</sup> symptomatology of depression were analyzed in order of frequency were sadness, depressed mood, somatic symptoms and signs, suicidal ideas, lack of energy, anxiety or tension, inability to fall asleep, early awakening, hopelessness, irritability and inability to enjoy<sup>94-15</sup>.

Diagnostic criteria for depression ICD-10 are used as an agreed list of ten depressive symptoms<sup>16</sup>

Key symptoms:

- Persistent sadness or low mood (and/or)
- Loss of interests or pleasure
- Fatigue or low energy

At least one of these, most days, most of the time for at least 2 weeks

If any of above present, ask about associated symptoms:

- Disturbed sleep
- Poor concentration or indecisiveness
- Low self-confidence
- Poor or increased appetite
- Suicidal thoughts or acts
- Agitation or slowing of movements
- Guilt or self-blame

The 10 symptoms mentioned above defines the degree of depression and management is based on that particular degree

- Not depressed (less than four symptoms)
- Mild depression (four symptoms)
- Moderate depression (five to six symptoms)
- Severe depression (seven or more symptoms, with or without psychotic symptoms)

Symptoms should be present for a month or more and every symptom should be present for most of every day.

Comparison of the parameters between two groups:

**Table No 4: Showing Thyroid profile between Cases & Controls**

Analyte	Cases	Controls	P-Value
TSH	8.1 +/- 12.4 mIU/L	3.1 +/- 4 mIU/L	0.0085
T <sub>3</sub>	114.2 +/- 39.9IU/L	116.7 +/- 40.1 IU/L	0.7761
T <sub>4</sub>	10.2+/-3.3 IU/L	9.4 +/- 3.3 IU/L	0.2242

Several thyroid abnormalities have been associated with mood disorders particularly depression. However, the vast majority of patients with depression do not have biochemical evidence of thyroid dysfunction<sup>17-18</sup>. When thyroid abnormalities exist, they consist mainly of elevated T4 levels, low T3, elevated rT3, blunted TSH response to TRH, positive antithyroid antibodies, and elevated cerebrospinal fluid (CSF) TRH concentrations.

T<sub>4</sub> : Studies examining total T4 levels in patients with depression have shown inconsistent results. Serum T4 levels in the upper range of normal or slightly higher have been reported in depressed patients as compared to healthy controls. Chopra et al. studies found that T4 levels found to regress after successful treatment of depression<sup>19</sup>. One mechanism explaining the increase in T4 seen in depression is the activation of hypothalamic TRH producing neurons and subsequent increase in thyroid function secondary to the rise in cortisol associated with depression<sup>20-22</sup>. In addition, it has been shown that elevated serum T4 levels fall after successful treatment of depression.

In the present study the mean value of serum T4 level in group-1 is 10.2+/- 3.3 IU/L and in group-2 the mean value is 9.4 +/-3.3 IU/L. P value is 0.2258 which is statistically not significant. In group-1 the serum value of T4 is not significantly raised compared to group-2. May be study may get significant p-value if the study was done on larger population sample

T<sub>3</sub>: Serum T3 levels are supposed to be lowered according to some studies as T3 is used along the antidepressants in treatment resistant depression. Previously T3 was used as mono therapy for depression but later on T3 was used for acceleration, augmentation and enhancement of depression drug therapies<sup>22-23</sup> indirectly prompting that depressive cases usually will be having decreased levels of T3. There is reduced deiodinization occur in peripheries of the body leading raised T4 and decreased levels of T3 and also increased levels of rT3<sup>23</sup>.

In the present study the mean value of serum T3 level in group-1 is 114.2+/- 39.9 IU/L and in group-2 the mean value is 116.7 +/-46.1 IU/L. P value is 0.7761 which is statistically not significant. In group-2 the serum value of T3 is not significantly increased compared to group-1.

TSH: Depression is associated to various endogenous circadian rhythms abnormalities such as diurnal mood variation, abnormalities in core body temperature, cortisol secretion, and sleep-wake cycle etc.<sup>24</sup> Depression is also linked to an abnormal diurnal TSH rhythm as well. An absent TSH nocturnal surge<sup>25</sup> has been noted in depression and a lower basal TSH has been reported in major depression as opposed to non major depression<sup>26</sup>. Blunted TSH response to TRH was reported in about 25–30% of depressed subjects compared to healthy subjects<sup>27-31</sup>.

The prolonged release of TRH in depression may be seen as a compensatory response to the decreased 5HT activity in an attempt to normalize 5HT function and maintain normal levels of thyroid hormones<sup>113</sup>. An alternative explanation is that the blunted TSH response may be induced by the hypercortisolism associated with depression or the elevated thyroid hormone levels mediated by adrenergic mechanisms<sup>33-34</sup>.

In addition, TRH has been postulated in early studies to have an antidepressant effect. Previously TRH was given as treatment with a dose of 500 µg parenterally to unipolar depressed women led to a significant improvement in depression ratings<sup>26,27</sup>.

In the present study the mean value of serum TSH levels in group-1 is 8.1 +/- 12.4 mIU/L and in group-2 the mean value is 3.1 +/- 4 mIU/L. P value is 0.0085 and there is significant difference between two groups. In group-1 the value is significantly increased compared to group-2. The present study is in tandem to the previously conducted studies.

## V. Summary And Conclusion

The present study includes totally 100 subjects divided in to 2 groups group-1 includes cases (Newly diagnosed women with depression) and group-2 includes cases (Age matched women without depression). By testing for all these parameters we found that HPA (Hypothalamo pituitary adrenal axis plays vital role in mood disorders. Excess of cortisol due to various reasons may be the root cause of mood disorders. Hence this study may be useful in understanding the risk factors of depression and this forms an area for the research work which

if detected early can be managed accordingly and may prevent the morbidity and mortality due mood disorders like depression.

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