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**Original Research Article**

# Derangements in thyroid hormone status in seriously ill patients: does it matter?

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## ABSTRACT

**Background:** Derangements in stress hormone levels i.e. steroids, thyroid hormones is routinely encountered in almost all the seriously ill patients, which have been found to be associated with morbidity and mortality. The present study was planned to assess the thyroid hormone derangements in seriously ill patients, with respect to mortality.
**Methods:** The present study was a retrospective, observational, record-based study done at Krishna Institute of Medical Sciences, Karad, Maharashtra, India.
**Results:** Out of total 170 patients, 108 were females (63.5%) and 62 (36.4%) were males. On age wise analysis, it was found that majority of the patients were in the age group >50 years comprising of 78 (45.8%) patients. Thyroid hormonal status was deranged in 94 patients (55%), out of which 53 (31%) died and 41 patients (24%) were alive. Most common derangement was seen in free T3 (triiodothyronine), with 60% of the patients showing lowered values, 35% showing raised values and 5% showing normal values. T4 (thyroxine) levels were normal in major bulk of the patients.
**Conclusions:** Serum T3 levels should be routinely done in critically ill patients, to detect any thyroid disorders, which might go undetected until it is too late.

**Keywords:** Hormone, T3, T4, Thyroid, Thyroxine, Triiodothyronine

## INTRODUCTION

Derangements in stress hormone levels i.e. steroids, thyroid hormones is routinely encountered in almost all the seriously ill patients.[1,2] These hormonal alterations have been found to be associated with morbidity and mortality outcomes in seriously ill patients.[3,4] Numerous studies have been done to assess the role of thyroid derangements in predicting outcomes in terms of morbidity and mortality in critically ill patients.[5]

These derangements in thyroid hormone levels during serious illness is termed as euthyroid sick syndrome (ESS) or non-thyroid illness syndrome (NTIS).[6,7] These derangements occur in the form of reduced serum levels of total as well as free T3 i.e. triiodothyronine, increased reverse T3 concentration, while TSH i.e. thyroid stimulating hormone and T4 i.e. thyroxine have mostly reduced or normal serum concentration values.[8] There are clinical types of ESS, which are encountered:

- ESS with reduced T3- seen in less severe illness
- ESS with reduced T4- seen in very severe illness
- ESS with reduced TSH[9]

Diminished serum levels of T3 is the most common finding cited in seriously ill patients in the thyroid hormone derangement category.[5] Physiologically, thyroid gland synthesize and secretes 1/5th amount of T4 secretion, as T3. Peripheral conversion of T4 to T3 by removal of 1 iodine atom is done by deiodinase enzyme, which contributes to major bulk of T3. The enzyme also clears off rT3.[10] It has been found in one study that activity of deiodinase is drastically reduced in patients with serious illness. This leads to reduced formation of T3 from T4, and accumulation of rT3.[11] Furthermore, there is accelerated clearance of T4 owing to stress induced metabolism, which increases the formation of rT3.[11,12]

Assessment of thyroid derangements, as prognostic indicator of morbidity and mortality indicator were done in the past. The results of these studies were inconsistent and highly variable, ranging from reduced free T3 in deceased patients in some study to normal levels in other study.[13,14]

Thyroid hormone status, as a prognosticator in seriously ill patients is not clear. To get more clarity on this issue, the present study was planned to assess the thyroid hormone derangements in seriously ill patients, with respect to mortality.

## METHODS

The present study was a retrospective, observational, record based study done at Krishna Institute of Medical Sciences, Karad, Maharashtra, India. Patient records were retrieved from Medical Records Department. Study period was of one year i.e. from January 2019 to January 2019. Patient selection criteria was as follows,

### *Inclusion criteria*

Records of all patients admitted to intensive care unit (ICU), irrespective of diagnosis were included in the study. Records of patients, whose age was more than 18 years were included, irrespective of sex. The records with complete investigation of T4, T3, fT3, fT4 and TSH were included.

### *Exclusion criteria*

Patients with previous history or positive family history of thyroid disorders, pregnancy, hormonal therapy in 6 months prior to admission were excluded from the study.

Demographic details like age, sex, co-morbidities, diagnosis, vital parameters, fT3, fT4, TSH levels were noted. All the data was entered into predesigned format in Microsoft Excel 2007. Numerical data was expressed as n (%), while categorical data was presented as mean±SD. Unpaired t test was applied for continuous variables and Fischer's test for categorical variables. Ethics committee approval was taken prior to the start of the study, from Institutional Ethics Committee.

Normal range for serum thyroid hormones was taken as:

- T3: 1.1-2.1 nmol/lit
- T4: 65-150 nmol/lit
- fT3: 3.5-6.5 µIU/lit
- fT4: 11-25 pmol/lit
- TSH: 0.3-4.7 µIU/lit

## RESULTS

Out of total 170 patients, 108 were females (63.5%) and 62 (36.4%) were males. On age wise analysis, it was found that majority of the patients were in the age group >50 years comprising of 78 (45.8%) patients, followed by 39 (22.9%) patients in 41 to 50 years group, 26 (15.2%) patients in 31 to 40 years age group and least in age group <20 years (Table 1).

**Table 1: Demographic details of the patients.**

| Item | Sub-category | n (%) |
|---|---|---|
| Age | <20 yrs | 8(4.7) |
| | 21 to 30 | 19(11.1) |
| | 31 to 40 | 26(15.2) |
| | 41 to 50 | 39(22.9) |
| | >50 | 78(45.8) |
| Sex | Male | 62(36.4) |
| | Female | 108(63.5) |

On analysing diagnosis of patients, it was found that majority of the patients had sepsis, comprising of 32% of the total patients, followed by renal failure in 18% of the cases, respiratory failure and diabetic ketoacidosis (DKA) in 15% of the patients, and myocardial infarction in 11% of the patients (Figure 1).

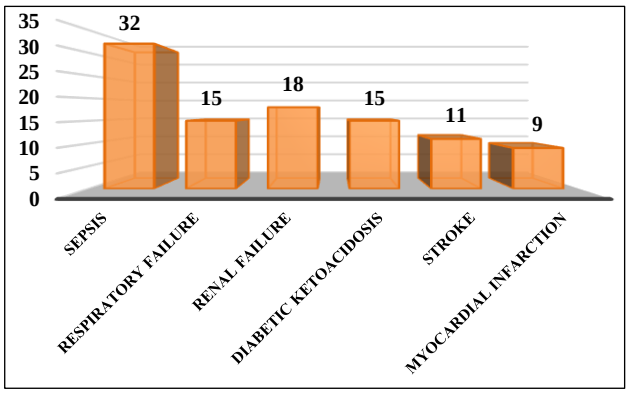


**Figure 1: Main diagnosis in the patients.**

Thyroid hormonal status was deranged in 94 patients (55%), out of which 53 (31%) died and 41 patients (24%) were alive. Normal thyroid hormonal status was seen in

76 patients (45%), out of which 54 were alive (32%), and 22 were deceased (13%) (Table 2).

**Table 2: Thyroid hormone status in patients.**

| Thyroid status | Live | Deceased | Total |
|---|---|---|---|
| Deranged | 41 (24.1) | 53 (31.1) | 94 (55%) |
| Normal | 54 (32) | 22 (13) | 76 (45%) |

Mean T3 was reduced to 0.9±0.21 in alive and 1.19±0.48 in deceased patients, and this was statistically significant. Rest all the parameters of thyroid functions were within normal range and there was no statistically significant difference between alive and deceased patient groups (Table 3).

**Table 3: Mean values of thyroid function test parameters in alive and deceased patients.**

| Mean | Alive | Deceased | P value |
|---|---|---|---|
| T3 | 0.9±0.21 | 1.19±0.48 | <0.001 |
| T4 | 78.2±30.1 | 79.4±36.5 | >0.05 |
| fT3 | 4.11±1.8 | 4.2±2.1 | >0.05 |
| fT4 | 17.6±2.1 | 18.1±2.8 | >0.05 |
| TSH | 2.91±4.1 | 3±3.9 | >0.05 |

Most common derangement was seen in fT3, with 60% of the patients showing lowered values, 35% showing raised values and 5% showing normal values. Majority had normal fT4 values, while TSH was high in 12% of the cases and low in 8% of the cases (Figure 2).

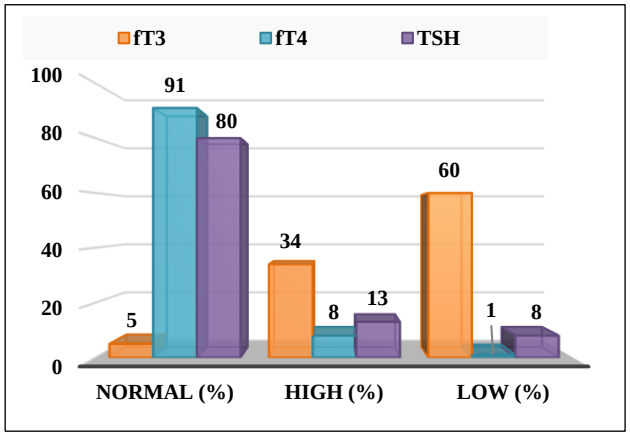


**Figure 2: Thyroid hormone status in patients.**

## DISCUSSION

Majority of the critically ill patients in the present study were females. Female to male ratio was 1.74:1. Similar sex preponderance was found in other study.[9] This sex predilection can be ascribed to high detection rate of thyroid disorder, owing to its high prevalence in females.[11] Apart from this, multiple factors are postulated to be responsible for such difference in prevalence between male and females. These include different levels of physical activities, body mass index, eating habits, etc.[15]

Most common comorbidity in the present study was sepsis. Similar trend was found in one such study.[16] Sepsis is characterized by profound release of pro-inflammatory cytokines likes interleukins, tumor necrosis factor. This cytokine is known to inhibit the thyroid hormone synthesis and functions at multiple steps.[17,18]

Abnormal thyroid hormonal status was found in 55% of the patients in the present study. This was more or less in corroboration with that of other such study.[9] Most common derangement was reduction in fT3, which was seen in 60% patients. This is incidence is low as compared to that of other study, which reported low fT3 in >80% of the critically ill patients.[16] These findings have added more evidence to the observations in earlier studies that ESS is more common in seriously ill patients admitted to intensive care units.

In the present study, majority of the mortality was associated with reduced fT3. Similarly, reduced fT3 as well as T3 was associated with increased mortality in other studies.[5,15,16] Moreover, various serious illness like renal failure, DKA, stroke is associated with lowered low T3 levels in different studies.[19,20] This low fT3 levels in seriously ill patients is attributed to lowered activity of deiodinase enzyme. In contrast, fT4 levels are altered only in extreme and prolonged illness.[15] Apart from thyroid disorders, thyroid hormone derangements are also seen in non-thyroid disorders and these are collectively known as non-thyroid illness syndrome. Typically, serum levels of T3 and rT3 are lowered, while T4 also decreases with increasing severity of this syndrome.[21] These derangements are corrected once patients are stabilized.[22]

Major aim of doing thyroid status evaluation in seriously ill patients should be to detect any new thyroid disorders, which will warrant immediate treatment. ESS should be suspected when there are clinical symptoms suggestive of hypothyroidism like bradycardia, reduced core temperature of body, acidosis, etc. coupled with evidence of central hypothyroidism.[21] When clinical symptoms and signs are suggestive of hyperthyroidism and TSH values are reduced then true hyperthyroidism are less likely in critically ill patients.[21]

## CONCLUSION

In the present study, we found statistically significant association between lowered fT3 and increased mortality. Based on these observations and findings of other studies, authors recommend evaluation of T3 levels in critically ill patients, to detect any thyroid disorders, which might

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