

Thyroid Dysfunction in Critically ill Surgical Patients in a Tertiary Care Hospital in Mysore, India

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Abstract

Background: During critical illness, patients with no history of thyroid disorders may experience multiple changes in their thyroid hormone levels as a part of neuroendocrine stress response. Such changes are termed as euthyroid sick syndrome. The extent of change correlates with the severity of the illness and its outcomes in critically ill patients.

Objectives: The aim of this study was to identify critically ill surgical patients and grade them clinically according to the Acute Physiology and Chronic Health Evaluation II (APACHE II) severity scale and evaluate the thyroid function tests (TFTs) and to document the outcome and relate the APACHE II severity scale with TFTs.

Methods: A descriptive, observational hospital-based study was conducted on critically ill patients admitted to the Surgical Intensive Care Unit who fulfilled the inclusion criteria. All data were entered into Microsoft Excel sheet and were analyzed using GraphPad InStat software.

Results: The majority of the patients belonged to geriatric age group (49%) and were male (58%). Cardiovascular diseases (45%) constituted the major morbidity. The majority had APACHE II score ≥ 20 (71%) and succumbed (48%) to their illness within 10 days. The majority of them had a low total triiodothyronine (T3) (57%), and there was a significant inverse correlation ($P = 0.0132$) between severity of illness and low serum total T3 levels whereas there was no relationship between total thyroxine or thyroid-stimulating hormone levels and severity of illness.

Conclusions: Serum T3 has a significant inverse relationship to the severity of critically ill patients.

Keywords: Acute Physiology and Chronic Health Evaluation II, critically ill, thyroid dysfunction

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I. Introduction

- The endocrine response to critical illness is complex. The physiological rationale behind these changes is to help body maintain homeostasis and is associated with the morbidity and mortality of patients.^[1]
- This is even more important in surgical patients who have increased metabolic demands due to post surgery status, sepsis and as a part of healing process.^[2]
- Changes in the levels of thyroid hormones, sex hormones, and corticosteroids are the predominant changes in critical illness as a part of neuroendocrine stress response.^[2]
- In the 20th century, studies found that thyroid dysfunction is associated with the increased morbidity and mortality of patients admitted to Intensive Care Unit (ICU).^[3]
- These alterations in thyroid hormone levels are referred by various terms such as euthyroid sick syndrome, sick euthyroid syndrome, nonthyroidal illness syndrome, and low triiodothyronine (T3) low thyroxine (T4) syndrome. It is characterized by low serum levels of free and total T3 and high levels of reverse T3 (rT3) accompanied by normal or low levels of T4 and thyroid-stimulating hormone (TSH).^[4,5]
- A few studies have reported that alterations in thyroid hormone levels during nonthyroidal illness syndrome can act as independent predictors of mortality and morbidity in critically ill patients, thus proposing the inclusion of thyroid profile in these scoring systems of critically ill patients.^[3,6]
- Surgical conditions such as hollow viscus perforation, acute pancreatitis, infectious conditions (necrotizing

fasciitis, diabetic foot) and patients who have undergone major surgery have increased metabolic demands thus leading to catabolism.

- In this study, we tried to find out the relationship between critical illness (based on the Acute Physiology and Chronic Health Evaluation II [APACHE II] score) and thyroid dysfunction and outcome.

II. Methods

After obtaining approval from the Institution Ethics Committee, 100 consecutive consenting patients admitted to the Surgical ICU with critical illness were included in this hospital-based descriptive study. Admission to ICU was based on the clinical condition of the patient, unrelated to the objective of the study.

Inclusion criteria

- Patients >18 years of age admitted to the Surgical ICU with critical illness.

Exclusion criteria

- Patient with known history of thyroid disorders
- Patient with intake of drugs altering thyroid hormone levels
- Pregnant patients

After obtaining written informed consent from patients or their legal guardian, who fulfilled the inclusion criteria, details of the patients were recorded on a pretested structured pro forma which included the demographic details, detailed case history, and APACHE II score. A thorough physical examination was done and relevant investigations were performed.

All collected data were entered into Microsoft Excel sheet and analyzed with the help of GraphPad InStat version 3.1 for and percentage and Chi-square data were calculated.

Chi-square test was performed for quality variable, and $P < 0.05$ was considered statistically significant.

Thyroid hormones were assessed using chemiluminescence immunoassay.

The normal reference range for thyroid function tests (TFT) in our laboratory is as follows:

TSH: 0.39-4.94 mIU/L,

Total T3: 58-185 ng/dL,

Total T4: 4.4-11.6 µg/dL.

III. Results

The majority (49%) of study population belonged to the geriatric age group with a mean age of 59 years. The majority (58%) of the study population were males. The most common cases were Hollow viscus perforation (30%) followed by wound sepsis (26%), moderate and severe acute pancreatitis (23%) and others(21%) [intestinal obstruction, patients who have undergone major surgery].

Most common co-morbidities were LRTI (30%) followed by diabetes mellitus (23%).

Most of the study participants (39%) had APACHE II score of 20–24 across all participants, and both sexes and least participants (4%) had APACHE II score of above 34 [Figure 1].

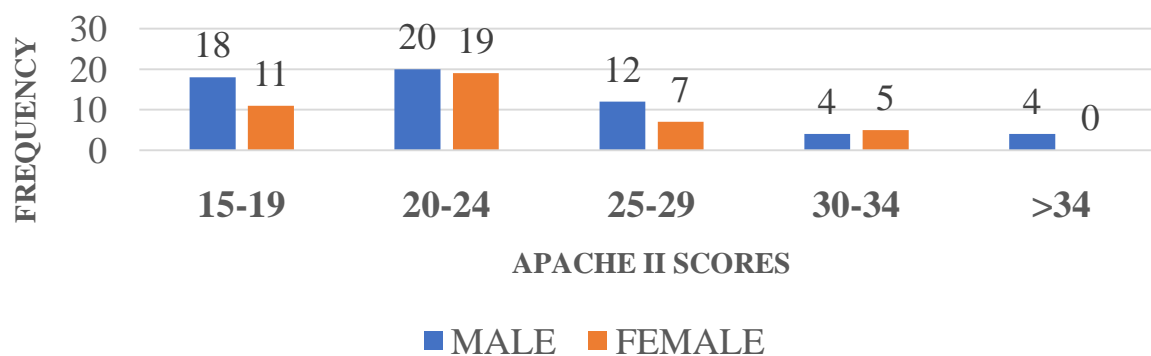


Figure 1: Distribution of patients according to Acute Physiology and Chronic Health Evaluation II score

Forty-three percent of the patients had normal total T3 levels followed by reduced total T3 levels in 58% [Figure 2].

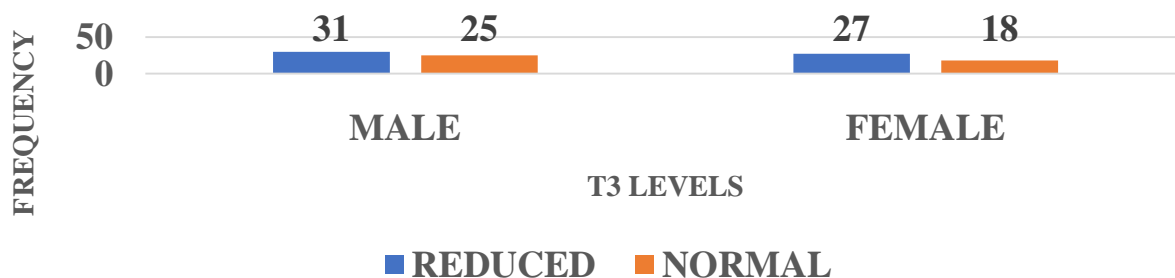


Figure 2: Distribution of patients according to total triiodothyronine levels

Eighty-one percent of the patients had normal total T4 levels followed by reduced total T4 levels in 19% [Figure 3].

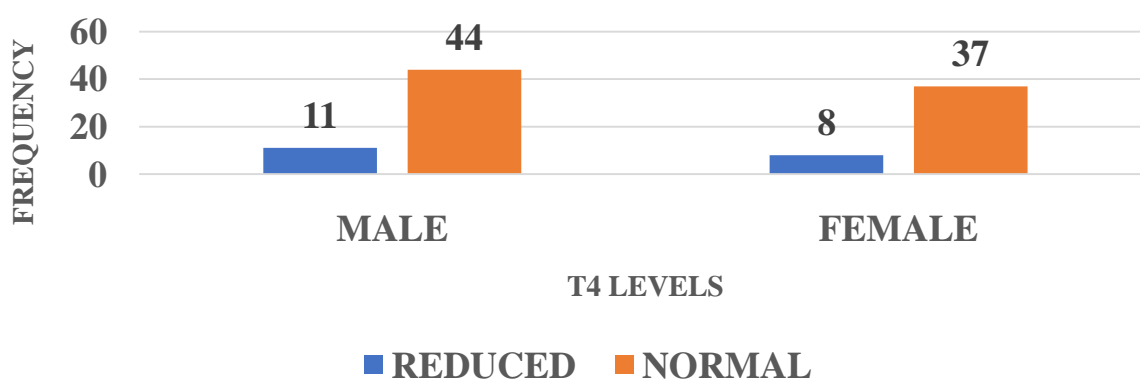


Figure 3: Distribution of patients according to total T4 levels

Eighty percent of the patients had normal TSH levels, followed by increased TSH levels in 14% and reduced TSH levels in 6% [Figure 4].

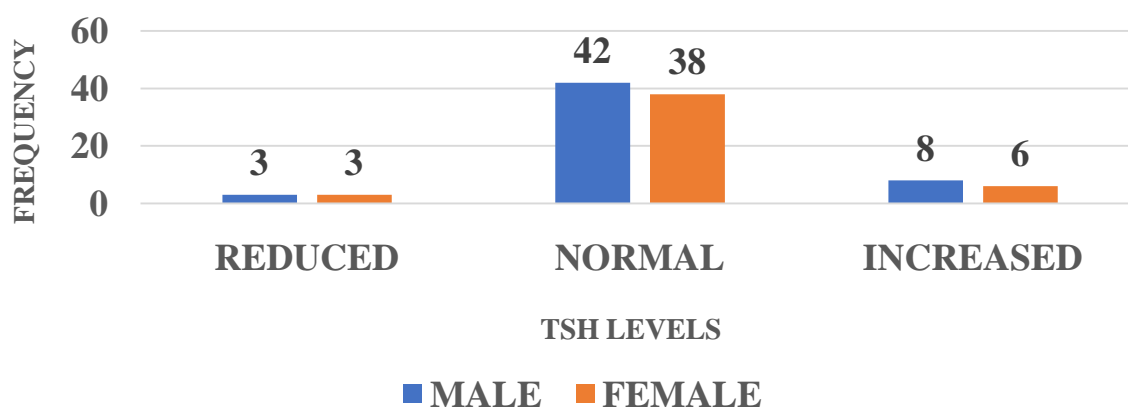


Figure 4: Distribution of patients according to thyroid-stimulating hormone levels

There was no significant difference in the distribution of total T3, total T4, and TSH levels between males and females.

With increasing APACHE II score, there was an increase in percentage of patients with decreased total T3 levels compared to normal total T3 levels at similar APACHE II score and the above distribution was found to be statistically significant (Chi-square for trend with 1 degree of freedom; P = 0.0233), and patients with normal total T3 levels had increased survival compared to patients with decreased total T3 levels which was

also statistically significant (two-sided $P < 0.0001$, Fisher's exact test with Yates correction) [Table 1].

Table 1: Distribution of total triiodothyronine with respect to Acute Physiology and Chronic Health Evaluation II score and outcome

APACHE II Score	T3 decreased (n)	T3 normal (n)
15-19	16	13
20-24	13	21
25-29	13	6
30-34	12	2
>34	3	1
Total	57(17 Survived and 40 expired)	43(33 survived and 10 expired)

The distribution of patients with normal and decreased total T4 levels was similar in trend with increasing APACHE II score (Chi-square for trend with 1 degree of freedom; $P = 0.6406$), with no significant difference in total T4 levels between patients of survived and nonsurvived group ($P = 0.8088$, Fisher's exact test with Yates correction) [Table 2].

Table 2: Distribution of total thyroxine with respect to Acute Physiology and Chronic Health Evaluation II score and outcome

APACHE II Score	T4 decreased (n)	T4 normal (n)
15-19	4	24
20-24	7	31
25-29	4	14
30-34	2	10
>34	2	2
Total	19 (10 Survived and 9 expired)	81 (42 Survived and 39 expired)

The distribution of patients with increased, normal, and decreased TSH levels was similar in trend with increasing APACHE II score (for decreased TSH: Chi-square for trend with 1 degree of freedom; $P = 0.8758$ and for increased TSH: Chi-square for trend with 1 degree of freedom; $P = 0.4548$), with no significant difference in TSH levels between patients of survived and nonsurvived group (for decreased TSH: $P = 0.1056$, Fisher's exact test with Yates correction and for increased TSH: $P = 0.1408$, Fisher's exact test with Yates correction) [Table 3].

Table 3: Distribution of thyroid-stimulating hormone with respect to Acute Physiology and Chronic Health Evaluation II score and outcome

APACHE II Score	TSH decreased (n)	TSH normal (n)	TSH increased (n)
15-19	1	21	5
20-24	3	31	4
25-29	2	16	3
30-34	0	8	2
>34	0	4	0
Total	6 (1 Survived and 5 expired)	80 (41 Survived and 39 expired)	14 (10 Survived and 4 expired)

IV. Discussion

Nonthyroidal illness syndrome is characterized by the changes in thyroid hormonal levels in acute and chronic illness due to nonthyroidal illness thought to be caused by the inhibition of enzyme 5-deiodinase by various mechanisms which catalyze T4 to T3 conversion as a part of neuroendocrine stress response^[5,6]. In acute illness, changes usually seen are low T3 with increased T4 and rT3. Whereas in chronic phase of illness, low levels of T3, T4, and TSH are seen^[7,8]. To date, it is not clear whether these changes are normal adaptive response to stress or pathological requiring treatment.

In our study with 100 patients, mean age was 59 years. Forty-nine belonged to geriatric age group followed by 37 in middle age. Fifty-eight were male. There was no significant difference in the thyroid profile across different age groups and between the genders.

The most common cases were Hollow viscus perforation (30%) followed by wound sepsis (26%), severe acute pancreatitis (23%) and others (21%) [intestinal obstruction, patients who have undergone major surgery]. Most common co-morbidities were LRTI (30%) followed by diabetes mellitus (23%) with no significant difference in the thyroid profile among different diseases. Mean APACHE II score was 22.74; about two-third of the study population belonged to APACHE II score of more than 20 with no significant difference in the gender across the APACHE II groups.

The patients were followed up to 25 days from the day of admission. Of 100 patients admitted, 45 patients succumbed to their illnesses. The mortality was more when compared to other studies^[5,9,10]. It may be possible as this is the only referral hospital in Mysore district and very critically ill patients were referred from other nearby districts of the state, in the final stages of their illnesses (mean APACHE II score was more than the other studies). There was no significant difference in mortality between the two genders.

Fifty-seven patients had low total T3 in which 16 of them also had low total T4 and 8 of them had low TSH. Thus, isolated decreased total T3 was found in 33 patients. Nineteen patients had low total T4 in which 16 of them also had low total T3 and 3 of them had low TSH, 4 of them had increased TSH and 9 had normal TSH. Thus, isolated decreased total T4 was found in 3 patients only.

TSH levels of the patients showed mixed pattern; 80 had normal TSH, 14 had increased TSH, and 6 had low TSH levels.

The comparison of thyroid hormone levels of our study with other studies [5,9,10] showed similar distribution pattern except that for TSH which was increased when compared to other studies as depicted in other studies [Table 4].

Table 4: Comparison of T.F.T among different studies and present study

STUDIES	Zargar AH <i>et al.</i>	K.V.S. Hari Kumar <i>et al.</i> (%)	Wang <i>et al.</i> (%)	Present study (%)
Percent of low T3	45	61	4.79	57
Percent of low T4	16.7	16	11.4	19
Percent of TSH dysfunction	13.4	7	3.54	20

Of the 48 patients who expired, 37 of them had low total T3 levels whereas 11 of them had normal total T3. Whereas in the survival group, 17 had low total T3 levels and 33 had normal total T3 levels. Thus, low total T3 is a very strong predictor of outcome in critically ill patients with $P = 0.0001$.

In the study, we categorized patients into five classes based on the APACHE II scores. As the APACHE II score increased, the percentage of the people with low total T3 also increased at par with the same APACHE II score group. Total T3 is decreased in 44.8% of the patients who were in the 15–19 APACHE II score range whereas it decreased in more than 75% of the patients whose APACHE II scores are more than 30, which is statistically significant with $P = 0.0235$ with Chi-square for trend with 1 degree of freedom.

Total T4 was decreased in 19 patients but the percentage of people with decreased total T4 levels was nearly 20% across all APACHE II score groups. However, 50% patients had decreased total T4 with APACHE II score more than 34. Thus, low total T4 levels had no significance with severity of illness. Of 19 patients with low total T4, 9 expired and 10 survived. Among the normal total T4 group, 42 survived and 39 expired. Thus, decreased total T4 levels have no significance in predicting the outcome of patients who are critically ill.

Eighty patients had normal TSH levels; 14 had increased levels, rest 6 had decreased levels. Thus, TSH levels showed mixed pattern with no significant relation with the APACHE II scores, i.e., severity of illness. Of 48 patients expired, 39 had normal TSH, 4 had increased TSH, and 5 had decreased TSH levels. Whereas in the survival group, 41 patients had normal TSH, 10 had increased TSH, and 1 had decreased TSH levels. Thus, TSH levels had no significance in predicting the outcome in critically ill patients.

The limitations of this study are that it is a single-center study with a small sample size with patients also coming from hilly areas. Thus, availability of control group (baseline TFT) would have increased the validity of the results.

Few more limitations or drawbacks of this study were non-measurement of free T3, free T4, rT3, serial hormone levels, and recording of the time of onset of the critical illness (thyroid dysfunction in critically ill based on the time from the onset of critical illness could have been further assessed) and nonavailability of data on use of medications such as heparin, dopamine, glucocorticoids, and amiodarone that could have potentially interfered with the TFT.

V. Conclusion

Low T3 is an important prognostic indicator in critically ill patients and can be combined with APACHE II score to predict the severity of illness and outcome in critically ill patients and thus early intervention.

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