

## Original Research Article

# Study of thyroid function in patients admitted in intensive care unit in a tertiary care centre

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## ABSTRACT

**Background:** Thyroid hormones play a key role in the maintenance of body growth by modulating metabolism and the immune system. These alterations in thyroid hormone levels are referred to as “euthyroid sick syndrome” or “non thyroidal illness syndrome” (NTIS), which is characterized by low serum levels of free and total triiodothyronine (T3) and high levels of reverse T3 (rT3) accompanied by normal or low levels of thyroxine (T4) and thyroid-stimulating hormone (TSH). During critical illness, changes in circulating hormone levels are a common phenomenon. These alterations are correlated with the severity of morbidity and the outcomes of patients in ICU.

**Methods:** This study was carried out at a tertiary care hospital. 100 patients of age above 18yrs, both sexes, admitted to intensive care units with following diseases Septicemia, ARF, Respiratory failure, CCF, DKA, Stroke were taken into the cross-sectional study. Relevant hematological and radiological examination are done. Fasting venous blood samples were collected immediately on admission to ICU from all patients and were subjected for hormone analyses. Samples were tested for total T3, total T4, and TSH. The hormone estimation was done by chemiluminescence assay.

**Results:** Patients (59%) had low T3 level, 41(41%) patients had normal T3, 31 patients (31%) had low T4, 69 patients (69%) had normal T4 level and TSH was low in 11 patients (11%), 76 patients (76%) had normal TSH and 14 patients (14%) slightly high. Our study showed low T3 (59%) is the commonest abnormality in ICU admitted patients. There is a significant relation present between T3 and mortality (p value-0.0001) and need for ventilation (p value 0.004).

**Conclusions:** Our study suggests that low T3 is an important marker of mortality in ICU admitted patients. We suggest that in ICU patients T3 levels should be done and used as a prognostic marker for mortality and need for ventilation.

**Keywords:** ICU, TSH, T3, T4

## INTRODUCTION

Thyroid hormones play a key role in the maintenance of body growth by modulating metabolism and the immune system. In the 20<sup>th</sup> century, researchers found that thyroid dysfunction is associated with the mortality of patients

admitted to the ICU.<sup>1</sup> These alterations in thyroid hormone levels are referred to as euthyroid sick syndrome.<sup>2</sup> It is also referred to as non-thyroidal illness syndrome (NTIS).<sup>3</sup> It is characterized by low serum levels of free and total triiodothyronine (T3) and high levels of reverse T3 (rT3) accompanied by normal or low

levels of thyroxine (T4) and thyroid-stimulating hormone (TSH).

Researchers in some studies demonstrated that triiodothyronine (T3) levels in nonsurvivors were significantly lower than those in survivors.<sup>4</sup> Low T3 is an important marker of mortality in critically ill patients. T4 and TSH did not vary between survivors and nonsurvivors.<sup>5</sup> Whereas other researchers showed that there was no association.<sup>6</sup>

Therefore, undertook study of medical ICU patients to detect the independent predictors of ICU mortality on the basis of thyroid hormone levels (TT3, TT4, TSH,) and to evaluate the ability of thyroid hormone level to predict ICU mortality.

Research objective was to study the thyroid dysfunction in critically ill patients admitted in intensive care units and its relation to the mortality and severity of disease.

## METHODS

### Sample size

This study was carried out in a tertiary care, teaching hospital in south India. 100 patients admitted and treated as in-patients in the intensive care unit (ICU) are taken for this cross sectional study.

### Inclusion criteria

Patients of age above 18yrs, both sexes, admitted to intensive care units with following diseases were included septicemia, Acute renal failure, respiratory failure, congestive cardiac failure, diabetic ketoacidosis, stroke.

### Exclusion criteria

- History of any thyroid diseases, such as hyperthyroidism, hypothyroidism and thyroid tumors
- Thyroid nodule found by physical examination when admitted to the ICU
- Pregnancy
- Within the previous 6 months undergoing any hormonal therapy
- Patients receiving massive blood transfusion or having steroid or dopamine therapy and drugs known to interfere with thyroid hormone metabolism e.g. rifampicin, ketoconazole, antiepileptics.

### Procedure

Patients fulfilling inclusion and exclusion criteria are taken into study.

All the patients had a detailed clinical examination and were managed appropriate to their primary condition.

Relevant hematological and radiological examination are done. Fasting venous blood samples were collected immediately on admission to ICU from all patients and were subjected for hormone analyses. Samples were tested for total T3, total T4, and TSH. The hormone estimation was done by chemiluminescence assay. The normal reference range for thyroid hormones in our laboratory are TSH (0.3-6.02 $\mu$ U/ml), T3 (0.5-2ng/mL), T4 (4.4-12 $\mu$ g/dL). Any deviation of the hormone results from the normal ranges is considered to be abnormal (low or elevated).

### Statistical analysis

Summary data were entered in MS-Excel and analyzed in SPSS V22 software. Descriptive statistics, mann-whitney u test, logistic regression, ROC curves were applied. P values were reported for all statistical tests and a value of <0.05 was considered to be significant.

## RESULTS

Out of 100 critically ill patients out of which 17 patients had Sepsis, 18 had acute renal failure, 19 patients had acute respiratory failure, 19 patients had Diabetic ketoacidosis, 16 patients had congestive Cardiac failure, and 11 patients had stroke.

T3, T4 and TSH analysis were done, 59 Patients (59%) had low T3 level, 41(41%) patients had normal T3, 31 patients (31%) had low T4, 69 patients (69%) had normal T4 level and TSH was low in 11 patients (11%), 76 patients (76%) had normal TSH and 14 patients (14%) slightly high.

Out of 100 critically ill patients, 28 patients (28%) had died, 8 patients with sepsis, 4 patients with acute renal failure, 6 patients with acute respiratory failure, 2 patients with DKA, 5 patients with CCF with and 3 patients with stroke had died in our study.

In this study, of 17 patients of sepsis, 14 patients (82.35%) had low serum T3 level, 11(64%) patients had low T4 level and TSH is low in 7(41%) patients. Compared to the other critically ill patients, sepsis patients have more decrease in TSH and T4.

Out of 100 critically ill patients, 18 patients had acute renal failure out of which 7 had low serum T3 level, 5 Patients low serum T4 level and 18 had near normal range serum TSH.

In this study, 19 patients of acute respiratory failure, 11 patients (57.8%) had low serum T3 level, 6 (31.5%) patients had low T4 level and TSH is low in (5%) patients.

In this study, of 19 patients of diabetic ketoacidosis, 8 patients (42.1%) had low serum T3 level, 4 (21%) patients had low T4 level and TSH is low in (10%) patients which shows most of them had low T3 levels.

In this study, of 16 patients of congestive cardiac failure 8 patients (50%) had low serum T3 level, 2 (12.5%) patients had low T4 level and TSH is normal in all patients which shows most of them had low T3 levels.

In this study, of 11 patients of stroke 10 patients (90%) had low serum T3 level, 1 (0.9%) patients had low T4 level and all patients had TSH normal which shows most of them had low T3 levels. low T3 levels might represent an integrative measure of multiple harmful pathological processes occurring simultaneously in patients with critical illness, such as inflammation status and cardiac dysfunction, which are associated with adverse outcomes. There, was a significant relation between T3 and mortality with p value 0.0001 (Table 1).

**Table 1: Relationship between T3 and mortality.**

Variable	Mortality	N	Minimum	Maximum	Mean	SD	P-value
T3	No	72	0.10	1.75	0.63	0.45	0.0001
	Yes	28	0.10	1.70	0.40	0.46	
	Total	100	0.10	1.75	0.56	0.46	

**Table 2: Relationship between T4 and mortality.**

Variable	Mortality	N	Minimum	Maximum	Mean	SD	P-value
T4	No	72	1.41	11.99	5.72	2.15	0.65
	Yes	28	1.41	11.74	5.58	2.89	
	Total	100	1.41	11.99	5.68	2.36	

**Table 3: Relationship between TSH and mortality.**

Variable	Mortality	N	Minimum	Maximum	Mean	SD	P-value
TSH	No	72	0.10	8.90	2.91	2.18	0.16
	Yes	28	0.10	8.30	3.75	2.44	
	Total	100	0.10	8.90	3.14	2.28	

**Table 4: Relation between T3 and need for ventilation.**

Need	T3						P-Value
	N	Minimum	Maximum	Mean	SD		
No	41	0.16	1.75	0.67	0.43	0.004	
Yes	59	0.10	1.75	0.49	0.47		
Total	100	0.10	1.75	0.56	0.46		

In the acute phase of critical illness, the alterations in thyroid hormones present as decreased T3 and increased T4 and rT3, as well as normal TSH. There is no significant relation between T4 and mortality with p value 0.65 (Table 2). TSH level are commonly within the normal range and only in prolonged illness may be low. There is no significant relation between TSH and mortality with p value 0.16 (Table 3). There is significant relation between T3 and need for ventilation with p value 0.004 (Table 4).

**DISCUSSION**

Critical illness is often associated with alterations in thyroid hormone concentrations in patients with no previous intrinsic thyroid disease. The non-thyroidal illness syndrome, also known as the low T3 syndrome or

euthyroid sick syndrome, describes a condition characterized by abnormal thyroid function tests encountered in patients with acute or chronic systemic illnesses. This syndrome includes low serum levels of triiodothyronine (T3) and high levels of reverse T3, with normal or low levels of thyroxine (T4) and normal or low levels of thyroid-stimulating hormone (TSH). Out of 100 critically ill patients out of which 17 patients had Sepsis, 18 had acute renal failure, 19 patients had acute respiratory failure, 19 patients had diabetic ketoacidosis, 16 patients had congestive cardiac failure, and 11 patients had stroke. T3, T4 and TSH analysis were done, 59 Patients (59%) had low T3 level, 41 (41%) patients had normal T3, 31 patients (31%) had low T4, 69 patients (69%) had normal T4 level and TSH was low in 11 patients (11%), 76 patients (76%) had normal TSH and 14 patients (14%) slightly high. Out of 100 critically ill

patients, 28 Patients(28%) had died, 8 patients with sepsis, 4 patients with acute renal failure, 6 patients with acute respiratory failure, 2 patients with DKA, 5 patients with CCF with and 3 patients with stroke had died in our study. Anna G, Karageorgopoulos ADE et al, decreased thyroid function at baseline might be associated with a worse outcome of patients with sepsis or septic shock.<sup>7</sup> Several inflammatory cytokines, such as IL1b, IL6, and TNF-a, can suppress, via direct or indirect pathways, the thyroid function at different levels.<sup>8,9</sup> In sepsis, the increase in the production of pro-inflammatory cytokines is more pronounced than that in other types of critical illness.<sup>10,11</sup> A relationship between serum triiodothyronine (T3) and several markers of inflammation, nutrition and endothelial activation in patients with chronic renal failure (CRF) has been documented.<sup>12,13</sup> Hu, Yan-Yan et al, showed euthyroid sick syndrome are associated with the severity of DKA.<sup>14</sup> Serum TT3 and TT3/TT4 ratio were lower in severe COPD compared to moderate COPD.<sup>15</sup> Shafran DM, Debra L. Isaac: the rate of HF decompensation is significantly lower in patients with normal TFTs than in those with unmeasured or abnormal TFTs.<sup>16</sup> Clinical studies have also found that low T3 syndromes have a negative prognostic effect in patients with heart failure.<sup>17</sup> Pande A et al, conducted a study on patients of acute hemorrhagic stroke, high mortality rates were observed in patients with a low T3 and T4. Consequently, low T3 and low T4 predict a poor outcome in patients of hemorrhagic stroke.<sup>18</sup>

## CONCLUSION

Our study showed low T3 (59%) is the commonest abnormality in ICU admitted patients. There is a significant relation present between T3 and mortality (p value 0.0001) and need for ventilation (p value 0.004). Our study didn't show any significant relation between T4, TSH and mortality. We suggest that in ICU patients T3 levels should be done and used as a prognostic marker for mortality and need for ventilation. The evaluation of altered thyroid function parameters in systemic illness and stress remains a complex issue and presents many diagnostic problems because changes occur at all levels of the hypothalamic-pituitary-thyroid axis.

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