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# Thyroid and Cortisol Changes in Critical Illness

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## *Abstract*

*It is known that metabolic and hormonal reactions that are responses to acute critical illnesses affect every organ and tissue in the body, however, only little is understood about the underlying mechanisms. Correction of these hormone levels as early as possible can lead to reduced stay in hospital and better prognosis. The present study aims to determine the thyroid and cortisol changes in acute severely ill patients and to assess their relationship with the severity of illness. The present prospective observational study was conducted in sixty critically ill patients grouped according to APACHE II score. The baseline characters that were used to calculate the APACHE II score were 1. Temperature, 2, heart rate, 3 hematocrit, 4 sodium levels, 5 potassium levels, 6 WBC count 7, pH, 8 pO2 10 respiratory rates 11 GCS. Blood samples were collected from patients at 1 and 8 days of admission by aseptic venipuncture. The samples were processed and levels of FT3, FT4, TSH and cortisol levels were assessed using standard protocol. The obtained data were recorded and subjected to statistical analysis. Groups were compared using one-way ANOVA with post hoc Tukey HSD. Comparison among groups was done student t-Test method. Pearson chi-square test or Fisher exact test (2-tailed) was used to compare proportions. The p-value less than 0.05 was considered significant. The results showed the normal values of various parameters in the 3 groups and will serve as a reference for the Indian population.*

***Keywords:*** *Critical Illness, Cortisol, Mortality Prediction, Normal Values, Thyroid.*

## Introduction

Critical illness is a condition in which the patient requires intensive medical support for survival of vital organs. The causes of critical illness vary from surgery to severe disease conditions [1, 2, 3]. Hence during critical illness, the body elicits responses that affect every organ in the body and the underlying mechanism is still unknown. These changes include stress, hyperglycemia, muscle wasting and changes in hormonal levels. Among these, the endocrine response to critical illness is very complex and dynamic, particularly with the adrenal and thyroid systems. Changes in levels of thyroid hormone are seen in critically ill patients who never reported a previous history of thyroid dysfunction.

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It is a well-known fact that the thyroid gland plays an important role in regulating metabolism, growth, and development by secretion of hormones such as thyroxine (T4) and triiodothyronine (T3). In critical illness, changes occur in the hypothalamic-pituitary-thyroid (HPT) axis which leads to euthyroid sick syndrome or non-thyroidal illness syndrome (NTIS). This condition is characterized by decreased T3 levels, normal to low levels of T4, and normal to decreased thyroid-stimulating hormone (TSH) levels despite the absence of intrinsic thyroid disease in patients. The pathophysiology of NTIS involves alterations in thyroid hormone production, peripheral conversion of T4 to T3, and increased degradation of thyroid hormones. During critical illness, cytokines and inflammatory mediators such as tumour necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) play a significant role in these hormonal changes. Reduced activity of deiodinases, enzymes responsible for the conversion of T4 to T3, further contributes to decreased T3 levels [4]. NTIS is a result of immediate response to critical illness and macronutrient restriction in the acute phase. However, the pathogenesis in chronic critical illness is more complex and associated with the suppression of hypothalamic thyrotropin-releasing hormone, thereby decreasing thyroid-stimulating hormone despite low plasma thyroid hormone. In some patients distinguishing between NTIS and severe hypothyroidism, is a challenge and infusion of hypothalamic-releasing factors may improve the thyroid axis in patients with NTIS.

Changes in thyroid function parameters are rarely isolated and frequently associated with changes in other endocrine axes such as cortisol levels [5, 6]. Cortisol, a glucocorticoid produced by the adrenal cortex, is essential for the body's response to stress. It modulates various physiological processes, including metabolism, immune response, and cardiovascular function. In critically ill patients, the hypothalamic-pituitary-adrenal (HPA) axis is often activated, resulting in elevated cortisol levels. This response is part of the body's adaptive mechanism to cope with severe stress. However, dysregulation of the HPA axis can occur, leading to either insufficient or excessive cortisol production. Adrenal insufficiency in critically ill patients, characterized by inadequate cortisol response, is associated with increased mortality and morbidity. Conversely, hypercortisolism can contribute to complications such as hyperglycemia, immunosuppression, and muscle wasting. The interaction between thyroid hormones and cortisol is complex and multifaceted. Cortisol can influence thyroid hormone metabolism and action at various levels, including the regulation of deiodinase activity and thyroid hormone receptor expression. Additionally, the stress-induced activation of the HPA axis and the subsequent increase in cortisol levels can modulate the HPT axis, leading to alterations in thyroid function.

Critical illness is associated with increased systemic cortisol availability, a vital part of the stress response. Stress can cause a life-threatening adrenal crisis when a disease of the hypothalamic-pituitary-adrenal (HPA) axis is present and not adequately treated with stress doses of hydrocortisone. Hence understanding these changes is vital to improve prognosis in patients under intensive care. For instance, in the absence of adrenal insufficiency, stress doses of hydrocortisone can be used to reduce the high vasopressor need in patients suffering from septic shock [7]. In this direction, administration of corticosteroids may have long-term side effects. In a study, it was reported that 5-year mortality was more in ICU survivors who had a longer ICU stay. Therefore, the use of glucocorticoids during critical illness has been identified as an independent ICU risk factor [8]. Further, patients who had suffered from respiratory muscle weakness during their stay in the ICU

had worse physical function 5 years after discharge [9].

Thus, understanding the endocrine changes and correction of these hormone levels as early as possible may reduce the hospitalization duration, thereby improving the prognosis of the patients. However, there is a lacuna in the literature regarding the level of these hormones at various timelines in critically ill patients classified according to the APACHE II classification in India. With the available data, we aimed to determine the thyroid and cortisol changes in acute severely ill patients and to assess their relationship with the severity of illness.

## Materials and Methods

### Study Design, Sample Size and Study Duration

The present prospective observational study was conducted on sixty critically ill patients admitted to the Intensive Care Unit of Sri Ramachandra University for 1 year and 10 months.

### Participant Selection

The purpose of the study was explained to the guardians of critically ill patients and guardians who signed the informed consent alone were recruited in the study based on the inclusion and exclusion criteria.

### The Inclusion Criteria

Patients with Acute Physiology and Chronic health evaluation APACHE II score >10 and without pre-existing endocrinopathies, intra cranial diseases, poisoning, and patients under medications that affect the endocrine axis were included in the study [10].

### Exclusion Criteria

Patients with preexisting endocrinopathies, intra-cranial diseases, poisoning, and patients under medications that affect the endocrine axis were excluded from the study.

### Data Collection

Demographic details of the patients and baseline parameters were recorded by a trained examiner. Based on the details recorded APACHE II score was calculated and the samples were divided into three groups as described below.

### APACHE II Score

### Acute Physiology Score

To calculate APACHE II scored the twelve physiological variables such as (temperature, mean arterial pressure, heart rate, respiratory rate, A-a $PO_2$ ($Fio_2$ > 50%) or $PaO_2$ ($Fio_2$ <50%), arterial PH or $HCO_3$, serum sodium, potassium and creatinine, hematocrit, white blood cell count and GCS) were also recorded. The sum of the 12 individual variable points was done to obtain the Acute physiology score.

### Score for the Age of the Participants

Based on the age of the patient a score was given as follows < 44 years 0 points; 45–54 years were scored as 2; 55–64 years was scored as 3; 65–74 years were scored as 5; and ≥ 75 years were scored as 6.

### The score for Chronic Health Status

For elective postoperative patients with immunocompromise or a history of severe organ insufficiency were scored a 2; Non-operative patients or postoperative patients under emergency with immunocompromise or severe organ insufficiency were scored 5.

### Calculation of APACHE II Score

The sum of age, chronic health status score and acute physiology score were calculated as APACHE score and the values ranged between 0 and 71[10].

### Study Groups

The patients were divided into three groups based on the APACHE Score as

1. Group A: mild (24), score 10 to 16.

2. Group B: moderate (22) score 16 to 20.
3. Group C: severe (14) score >20.

### Sample Collection

Blood samples were collected from patients at 8:00 am within 72 hours of admission and after 7 days of admission by aseptic venipuncture. Briefly, the site was cleaned with an antiseptic and the placement of an elastic band was done around the upper arm for the application of pressure. A sterile needle was inserted into the vein after palpation and 5 ml of blood was drawn under an aseptic condition. The elastic band was removed, hemostasis was achieved by the application of pressure and a bandage was placed.

### Sample Processing

The obtained blood sample was collected and placed in a rack for half to an hour to allow the coagulation process at room temperature. Centrifugation was done at 3,000 revolutions per sixty-second for 5 minutes. The serum was separated and stored at -20 degrees Celsius until use. The samples were labelled properly to ensure accuracy.

### FT3, FT4, TSH and Cortisol Analysis

The samples were processed and levels of FT3, FT4, TSH and cortisol levels were assessed using standard protocol. Briefly, the obtained serum separated from whole blood was analyzed for TSH, free T3, and free T4 on Abbott ARCHITECT i2000SR (Abbott, Chicago, USA) using the chemiluminescent microparticle immunoassay (CMIA) technology. Determination of cortisol in serum samples was done with an Abbott ARCHITECT i1000SR (Abbott, Chicago, USA) using the CMIA technology. Strict adherence to the manufacturer's protocol was done.

## Statistical Analysis

The obtained data were recorded and subjected to statistical analysis using SPSS software version 21. The continuous variable was expressed as Mean ± SD. Discrete variables were expressed as numbers (%) in each study group as well as total cases. Groups were compared using one-way ANOVA with post hoc Tukey HSD. Comparison among groups was done student t-Test method. The Pearson chi-square test or Fisher's exact test (2-tailed) was used to compare proportions. The p-value was less than 0.05 and was considered significant.

## Results

### Demographic Data

In the present study group, the mean age in Group A was 47.56, B was 48.73 and C was 46.21. Considering gender distribution Group A had 96% (23/24) males and 4 % (1/24) females, group 2 had 68.2% (15/22) males and 31.8% (7/22) females whereas Group C had 64.3% (9/14) males and 35.7% (5/14) females. Thus, the findings demonstrate that critical illness is more common in male members. The results are depicted in Table 1.

**Table 1.** Demographic Details of the Study Population

| | | A | B | C | P Value |
|---|---|---|---|---|---|
| **Age** | **Mean** | 47.56 | 48.73 | 4621 | 0.902 |
| | **SD** | 16.5 | 12.61 | 20.34 | |
| **Sex** | **Male** | 24 | 15 | 9 | 0.022* |
| | **Female** | 1 | 7 | 5 | |

**Survival Rate**

Considering the outcome or survival rate all patients were alive in Group A (100%) whereas six patients out of twenty-two in Group B expired, giving a survival rate of 72.7%. The survival rate was lowest in Group C (35.75%), 9 out of 14 expired. The results are depicted in Table 2 and Graph 1.

**Table 2.** Outcome Analysis of Study Participants

| Outcome Analysis | Group A | Group B | Group C | Statistical Significance |
|---|---|---|---|---|
| **Survived** | 25 | 16 | 5 | 0* |
| **Expired** | 0 | 6 | 9 | |

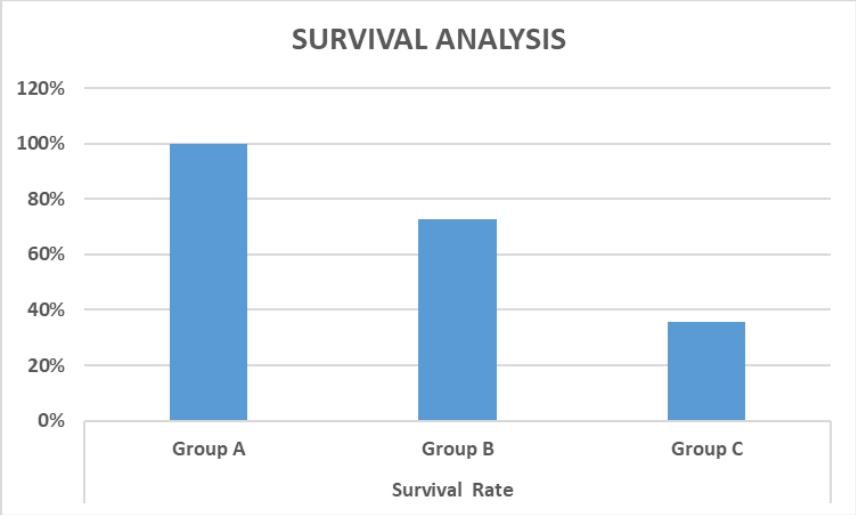


**Figure 1:** Survival Rate of Study Participants

**Physiologic Parameters**

Temperature was significantly different among the groups with the source of variation being the B vs C group(P=0.003). Heart rate was similar in all groups (P>0.05). Haematocrit (PCV) was different among the groups where B and C were similar, and A was different. Sodium values showed the difference between A-C(P=0.00) and B - C (P=0.002). Potassium differed among A–C (p=0.00) and B –C (P=0.006). There was no statistical difference in the WBC count. Creatinine values differed among A-B and A-C. pH value differed from A-C and B-C. pO2 did not vary significantly. Respiratory rate differed among A-C (P=0.004) and B-C (p=0.005). GCS varied significantly among all the groups. Initial MWCNTs are treated with ammonium hydroxide and hydrogen peroxide for oxidization of MWCNTs and again carboxylated by treatment with hydrochloric acid. HCL was used to produce covalently functionalized MWCNTs after successfully functionalized characterization analytically. The results are depicted in table 3.

**Table 3**. Comparison of Mean Physiologic Parameters between the Study Groups

| Parameters | Groups | | | P Value | Turkeys HSD p Value | | |
|---|---|---|---|---|---|---|---|
| | A | B | C | | A vs B | Avs C | B vs C |
| **Temperature (°F)** | 100.29±2.079 | 99.13±1.751 | 101.3±1.6541 | 0.0004* | 0.094 | 0.239 | 0.003* |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Heart Rate (Beats/min)** | 101.48±16.696 | 94.45±17.204 | 105.21±25.204 | 0.23 | 0.427 | 0.83 | 0.237 |
| **Haematocrit (PCV)** | 35.19±8.611 | 27.45±8.105 | 22.86±6.521 | 0.000* | 0.005* | 0.000* | 0.221 |
| **Sodium (mMol/L)** | 132.92±6.144 | 130.68±9.732 | 120.862.071 | 0.000* | 0.595 | 0.000* | 0.002 |
| **Potassium (mMol/L)** | 4.04±0.548 | 3.85±0.817 | 3.09±-.692 | 0.000* | 0.639 | 0.000* | 0.006 |
| **WBC (x10$^3$ cu mm)** | 11.94±11.430 | 9.183±6.298 | 12.545±9.865 | 0.496 | 0.583 | 0.981 | 0.558 |
| **Creatinine (mg/dl)** | 0.952±0.2347 | 1.482±0.7500 | 1.643±0.8045 | 0.002* | 0.012* | 0.004* | 0.721 |
| **pH** | 7.3608±0.0655 | 7.3564±0.07537 | 7.4264±0.01038 | 0.024* | 0.98 | 0.041* | 0.032* |
| **$pO_2$ (mmHg)** | 95.96±15.282 | 95.32±17.937 | 88.86±14.701 | 0.388 | 0.99 | 0.392 | 0.477 |
| **Respiratory Rate (min$^{-1}$)** | 26.88±7.780 | 26.95±6.321 | 35.57±9.280 | 0.002* | 0.999 | 0.004* | 0.005* |
| **GCS** | 14.6±0.645 | 12.55±2.874 | 6.93±1,685 | 0.000* | 0.002 | 0.000* | 0.000* |

## Thyroid and Cortisol Profile

### FT3

FT3 was significantly different among the three groups, with Group A having the highest value, followed by Group B and C. About the 8th day value, they were statistically similar(p=0.2). Only in group B, there was a significant difference between day 1 and 8. Incidence of decrease in FT3 (Day 1) levels was observed in group C and FT3(Day 8) levels showed significant decrease in both group B and C, which signifies increase in severity with a decrease in FT3 levels. The results are depicted in table 4.

**Table 4**. Comparison of Mean FT 3 Values on Days 1 and 8 in the Study Groups

| **Parameter** | A | B | C | P value intergroup | Post hoc A vs B | Post Hoc A vs C | Post Hoc B vs C |
|---|---|---|---|---|---|---|---|
| **FT3 (Day1) (µg/dl)** | 2.475 | 2.1157 | 1.2167 | 0.000* | 0.386 | 0.000* | 0.002* |
| **FT3 (Day8) (µg/dl)** | 4.8754 | 1.7405 | 1.0775 | 0.289 | 0.393 | 0.376 | 0.971 |
| P value intra-group | **0.346** | 0.000* | **0.175** | -- | | | |

### FT4

There was no significant difference between FT4 from day 1 and day 8. However, on day 8 there was a significant difference between the groups. The result is depicted in table 5.

**Table 5**. Comparison of Mean FT 4 Values on day 1 and 8 in the Study Groups

| **Parameter** | A | B | C | P value intergroup | Post hoc A vs B | Post Hoc A vs C | Post Hoc B vs C |
|---|---|---|---|---|---|---|---|
| **FT4 (Day1) (µg/dl)** | 1.3458 | 1.0829 | 1.33 | 0.113 | 0.172 | 0.964 | 0.176 |
| **FT4 (Day8) (µg/dl)** | 1.7046 | 1.0467 | 1.0025 | 0.007* | 0.015* | 0.031* | 0.986 |

| | | | | |
|---|---|---|---|---|
| P value intra-group | **0.116** | **0.546** | **0.085** | |

**TSH**

An increase in TSH level was noted in group C in the day 1 sample following which there was a decrease in TSH levels on day 8. However, TSH in both A and B groups stayed within the normal range. The results are depicted in table 6.

**Table 6.** Comparison of mean TSH Values on days 1 and 8 in the Study Groups

| **Parameter** | A | B | C | P value intergroup | Post hoc A vs B | Post Hoc A vs C | Post Hoc B vs C |
|---|---|---|---|---|---|---|---|
| **TSH (Day1) (µg/dl)** | 3.1464 | 4.3633 | 6.0958 | 0.034* | 0.739 | 0.028* | 0.134 |
| **TSH (Day8) (µg/dl)** | 3.1 | 3.3971 | 4.04 | 0.384 | 0.86 | 0.35 | 0.626 |
| P value intra-group | **0.713** | **0.156** | 0.048* | -- | | | |

**Cortisol**

The cortisol level increased with the severity of the illness as in groups B and C with a significant decrease in their levels after one week but elevated above normal levels. Group A did not show any rise in cortisol levels from baseline. The results are depicted in table 7.

**Table 7.** Comparison of Mean TSH Values on day 1 and 8 in the Study Groups

| **Parameter** | A | B | C | P value intergroup | Post hoc A vs B | Post Hoc A vs C | Post Hoc B vs C |
|---|---|---|---|---|---|---|---|
| **Cortisol (Day1) (µg/dl)** | 18.1556 | 23.5705 | 26.8167 | 0.031* | 0.219 | 0.028* | 0.498 |
| **Cortisol (Day8) (µg/dl)** | 15.3026 | 20.5224 | 22.7308 | 0.005* | 0.037 | 0.010* | 0.656 |
| P value intra-group | 0.000* | 0.001* | 0.003* | -- | | | |

**Overall Comparison**

Group C had decreased levels of T3 and FT4 compared to groups A and B and increased cortisol levels from baseline compared to other groups representing the severity of the illness. TSH level also increased in group C compared to groups A and B.

Group C had decreased levels of FT3 (Day 8), and FT4 (Day 8) compared to groups A and B and an increase in cortisol levels from baseline compared to other groups representing the severity of illness. TSH (Day 8) levels did not show much difference among groups. The results are depicted in Figure 1.

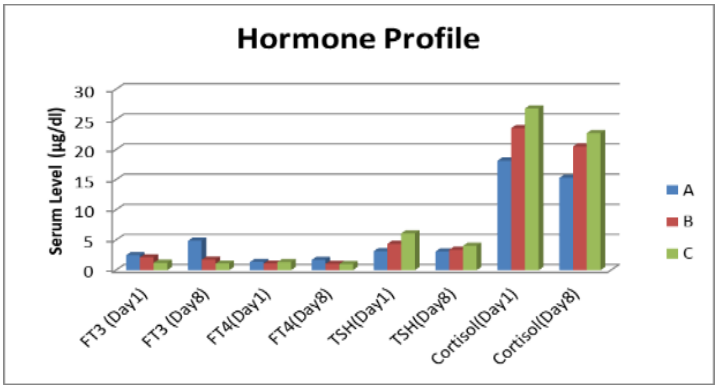


**Figure 2:** Comparison of Hormone profile of Patients in the Study Groups

## Discussion

As we all know, thyroid hormone which is a collection of T3 and T4 is vital for the body's normal metabolism and secretion of the same is stimulated by the Thyroid stimulating hormone or the TSH. Cortisol is yet another important hormone associated with stress. Previous studies have reported that race and ethnicity are associated with differences in hormone levels. [11]. Normal serum TSH levels are tightly regulated within an individual, suggesting a genetic 'set point' for individual thyroid hormone levels [12]. Previous studies have demonstrated variation in TSH levels between non-Hispanic whites and Mexican Americans or non-Hispanic blacks [13]. Similar differences are seen in cortisol and its diurnal variation [14]. Therefore, it is essential to estimate the levels of these hormones according to the population.

Hormone levels not only vary with race and ethnicity but also vary in health and disease. Critical illness is one such condition that is associated with variations in hormonal levels due to severe disease or surgery wherein the patient requires intensive care to survive. [15]. These changes are known to be associated with disease severity and survival [16,17]. Since thyroid hormones play a vital role in growth modulation, metabolism and immunity, several research has reported that thyroid dysfunction is directly related to the survival rate of individuals requiring intensive care [18, 19, 20].

Considering the above factors with hormone changes concerning critical illness and ethnicity we aimed to determine the thyroid and cortisol changes in the critically ill patients belonging to the population in the capital city of Tamil Nadu State of South India. This is a prospective observational study that was done in 61 critically ill patients grouped based on APACHE II score. In addition, we also analyzed the viral physiological parameters.

It has been seen that age and sex did not contribute to the severity of illness. However, the result on age cannot be over-generalized as the range of age was narrow in this study. Further, the sex ratio could not be equalized due to constraints in collecting a sufficient number of patients. Empirically, these values did not change with age and sex within this study. Hypotension is one of the cornerstones in critical illness which requires ionotropic support which in turn will affect the neuro-endocrine axis [21]. Hypotension, commonly seen in critically ill patients, significantly impacts the neuroendocrine axis, particularly the hypothalamic-pituitary-adrenal axis and the sympathetic-adrenal-medullary system. Hypotension activates the HPA axis, initiating the release of corticotropin-releasing hormone (CRH) from the hypothalamus. CRH prompts the anterior pituitary to secrete adrenocorticotropic hormone (ACTH), which then stimulates cortisol production from the adrenal cortex. Cortisol helps maintain blood pressure by enhancing vascular sensitivity to catecholamines and promoting

gluconeogenesis. In critically ill patients, cortisol levels often rise to counteract hypotension. Chronic hypotension can impair the HPA axis' feedback mechanism, potentially leading to adrenal insufficiency over time. The SAM system, involving the release of catecholamines from the adrenal medulla, is also activated by hypotension. Increased catecholamine release boosts heart rate, myocardial contractility, and vascular resistance to restore blood pressure. Prolonged catecholamine exposure, however, can strain the cardiovascular system and damage organs. Understanding these interactions is crucial for optimizing treatment strategies and improving patient outcomes. Thus, hypotension was reported to be more severely ill patients when compared to others. However, in the current study, no such difference was noted among the groups which could be attributed to meticulous monitoring and immediate management.

We also analysed the hematocrit value. Hematocrit (Hct) value, the proportion of blood volume occupied by red blood cells, is a critical parameter in managing critically ill patients. It provides essential insights into a patient's oxygen-carrying capacity and overall hemodynamic status. Low hematocrit levels, often indicative of anaemia, can significantly impair oxygen delivery to tissues, exacerbating hypoxia and potentially leading to organ dysfunction. This is particularly concerning in critically ill patients, where oxygen demand is increased due to stress and illness. Monitoring HCT helps clinicians determine the need for interventions like blood transfusions, which can improve oxygenation and tissue perfusion. Conversely, high hematocrit levels can indicate polycythemia, which increases blood viscosity, raising the risk of thrombosis and impairing microcirculation. In critical care, maintaining optimal hematocrit levels is crucial for balancing adequate oxygen transport and minimizing vascular complications. Furthermore, hematocrit levels can reflect fluid balance in patients. For instance, low Hct might suggest hemodilution due to fluid overload, while high Hct could indicate hemoconcentration from dehydration. Thus, Hct values guide fluid management strategies, ensuring effective hydration without overloading the cardiovascular system. Haematocrit value gives clues regarding the haemodynamic stability of the patient which is essential for survival and to improve the clinical outcome [22]. In the current study, there was a decrease in hematocrit with an increase in severity.

The other important parameter is the sodium levels. Hyponatremia, a low sodium concentration in the blood, is common in critically ill patients and can complicate their management. It often results from factors such as fluid overload, medications, and underlying diseases like heart failure or liver cirrhosis. Hyponatremia can lead to symptoms ranging from mild confusion to severe neurological deficits like seizures and coma, particularly when sodium levels drop rapidly. Accurate diagnosis and management are crucial, involving careful monitoring and correction of sodium levels to avoid rapid shifts that could cause cerebral oedema. Thus, understanding and addressing hyponatremia is vital for improving outcomes in critically ill patients. Hyponatremia is one of the risk factors that support the severity of illness [23]. In this study, hyponatremia was found in all groups, most of them in the C group. Similarly, Hypokalemia was found in all three groups and values were statistically different. It is related directly to the severity of the disease [24].

White blood cell (WBC) count is a critical marker in assessing the immune response and detecting infections in critically ill patients. Elevated WBC counts, or leukocytosis, often indicate infection, inflammation, or stress, prompting further investigation and targeted treatment. Conversely, low WBC counts, or leukopenia, may suggest bone marrow suppression, severe infection, or immunosuppression, necessitating immediate

medical attention to prevent complications. Regular monitoring of WBC counts helps clinicians diagnose underlying conditions, gauge the severity of illness, and tailor appropriate therapeutic interventions, ensuring better patient outcomes in critical care settings. WBC count is important while evaluating sepsis and other inflammatory conditions which is also a contributing factor for the severity of illness [25]. In the current study, there was no significant difference between the groups.

Creatinine levels in critically ill patients are a crucial indicator of renal function and overall metabolic health. Elevated creatinine levels often signify acute kidney injury (AKI), which is common in critically ill patients due to factors like sepsis, dehydration, and the use of nephrotoxic drugs. Monitoring creatinine helps assess the severity of kidney impairment and guides therapeutic decisions. Persistent high creatinine levels can necessitate interventions like dialysis. Thus, regular monitoring of creatinine is essential for managing the renal health of critically ill patients and for predicting their prognosis. Creatinine shows organ insufficiency or failure which will play a major role in increasing the severity of illness [26]. In the current study also there is an increase in creatinine levels with an increase in severity.

PH levels in critically ill patients are a crucial indicator of acid-base balance and overall metabolic status. Normal blood pH ranges from 7.35 to 7.45. Deviations from this range, either acidosis (pH < 7.35) or alkalosis (pH > 7.45), can significantly impact cellular function and organ systems. Acidosis can result from conditions like sepsis, renal failure, or respiratory dysfunction, leading to decreased cardiac output and altered enzyme function. Alkalosis may arise from excessive vomiting, diuretic use, or hyperventilation, causing muscle weakness and arrhythmias. Monitoring and correcting pH imbalances are vital for stabilizing critically ill patients and optimizing their outcomes. Critically ill patients have alkalosis [27]. According to the current study, the C group had the most normal pH.

pO2, or partial pressure of oxygen, is a critical parameter in assessing the respiratory function of critically ill patients. Normal pO2 levels range from 75 to 100 mmHg. Deviations from this range indicate hypoxemia or hyperoxemia, both of which can have severe consequences. Hypoxemia (pO2 < 75 mmHg) suggests inadequate oxygenation, which may result from conditions such as ARDS, pneumonia, or sepsis, leading to tissue hypoxia and organ dysfunction. Hyperoxemia (pO2 > 100 mmHg) can occur with excessive supplemental oxygen and may cause oxidative stress and lung injury. Accurate monitoring and management of pO2 are essential for optimizing patient outcomes in critical care settings. There is no defined pO2 target for critically ill patients, irrespective of underlying aetiology. Therefore, deviation on both sides needs to be avoided [28]. In this study, pO2 did not differ among the groups. Respiratory rate is an important tool for predicting recovery or prolonged illness in critically ill patients [29]. In this study, the increase in respiratory rate was observed with an increase in severity. A decrease in the Glasgow Coma Scale increases the risk of outcome and severity of illness [30]. In the current study, it increased with severity.

According to previous reports, FT3 was the best predictor of ICU mortality [31]. In critical illness, there may be a decrease of FT3 within a few hours of onset of acute illness. Samples collected on day 1 showed a decrease in group C, but in other groups, it was within the normal range. About Day 8's value, it was normal in all groups, showing persistent non-thyroidal illness. Similarly, FT4 may be decreased in critical illness, however, in the current study it was within normal limits in all groups. About the 8$^{th}$ day value, all groups remained within normal limits. Decreasing FT4 levels show ongoing prolonged illness with increased severity and an increase signifies recovery [31].

TSH may be elevated at the onset of critical illness due to alteration of the hypothalamic-pituitary-thyroidal axis [32]. In the current study, elevated TSH was seen on the first day. The 8th-day TSH value was within the normal range for all groups. Levels were found in direct relation to the severity of illness. An increase in cortisol is directly related to severity [33]. A decrease in cortisol on day 8 shows recovery. Group A showed recovery, but B and C showed prolonged illness.

The effect of diseases, severe trauma, infection and surgery may result in severe stress and the outcome depends upon the neuroendocrine system. Thus, prolonged illness with low FT3, normal FT4 and normal TSH levels is known as low T3 syndrome or sick euthyroid syndrome (SES), since there is no preexisting thyroid disease. Diagnosis of sick euthyroid syndrome is difficult to assess in a sick patient.

Treatment of SES with thyroid hormone is controversial since prognosis and mortality do not depend upon the return of serum levels to normal range. The use of hormonal peptides may be beneficial but not much is reported about it. In chronic illnesses, cortisol loses diurnal variation of rhythm. Further, a negative feedback mechanism is lost due to the altered hypothalamic-pituitary-adrenal axis. In this study, 2 patients reported with adrenal insufficiency and mortality was seen before the $8^{th}$ day sample. Adrenal insufficiency must be diagnosed as early as possible. Therapy with hydrocortisone may improve the outcome.

The study has limitations such as low sample size, and unequal gender distribution. Also, the correlation of each parameter with survival could not be done owing to the low sample size. Further studies with larger sample sizes and samples representative of a particular study population are warranted to emphasize the importance of addressing endocrine changes in critically ill patients to improve the overall survival rate.

## Conclusion

This study has thrown valuable light on TSH, FT3, FT4 and Cortisol values in critically ill patients. It has also provided normal values (Those in group A) which can act as targets for patients in groups B and C. This stands as a rough guideline for clinicians in the Indian scenario. In the future, more such studies must be performed in a multicentric way to obtain more accurate and ethnicity-centred values for proper treatment in the ICU. This would not only reduce mortality but also reduce long-term morbidity.

## Conflict of Interest

The authors declare no conflict of interest.


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