

## THYROID FUNCTION ABNORMALITIES IN PATIENTS ADMITTED IN MEDICAL INTENSIVE CARE UNIT

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### ABSTRACT

**Objectives:** The aim of the study was to assess the thyroid hormone levels in patients admitted in intensive care unit (ICU) for various critical medical conditions.

**Methods:** This was a prospective and observational study conducted in the department of medicine of a tertiary care medical college. One hundred and twenty patients admitted in medical ICU for various medical conditions were included in this study on the basis of a predefined inclusion and exclusion criteria. A detailed history with respect to demographic details such as age, gender, and body mass index was noted. APACHE II score of the patients were noted with an objective to assess the severity of the illness. The incidence of thyroid function abnormalities as well as the analysis of patients' outcome in terms of thyroid function abnormalities was determined.  $p < 0.05$  was taken as statistically significant.

**Results:** Out of these 120 patients, there were 78 (65%) were males and 42 (35%) were females with a M: F ratio of 1:1.0.53. The mean age of patients was found to be  $44.52 \pm 11.27$  years. The most common indication for admission was diabetic ketoacidosis (23.33%) followed by stroke (15.00%) and renal failure (11.67%). Thyroid function abnormalities were seen in 26 (21.67%) patients. These abnormalities were seen in patients with diabetic ketoacidosis (4.17%), congestive cardiac failure (4.17%), stroke (3.33%), renal failure (2.50%), hypertensive crisis, and multiorgan dysfunction (2.50%). Mortality was found to be significantly high in patients having thyroid function abnormalities as compared to those who had normal thyroid function.

**Conclusion:** Thyroid function abnormalities are common in patients admitted in ICU and are associated with adverse outcome.

**Keywords:** Intensive care unit, APACHE II, Thyroid function test, Mortality.

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### INTRODUCTION

Critical illness often results in changes in circulating hormone levels. These changes correlate with morbidity as well as outcome in intensive care units (ICU). A wide range of endocrinological abnormalities is encountered in patients admitted in medical ICUs (MICU) for various life-threatening conditions and the challenge before the treating physician is to know whether these endocrinological abnormalities are cause or result of medical conditions for which the patient is admitted in ICU [1]. Moreover, it is also crucial to understand the difference between a pre-existing endocrinological abnormality and one that is recent and is associated with the conditions such as sepsis, immunosuppression, autoimmune disorder, or drug induced because the management will differ depending on the etiology of such as endocrinological abnormality [2].

Irrespective of the etiology any significant medical illness requiring admission in ICU for considerable time period is likely to be associated with alteration of various hormonal levels [3]. The etiology of such a hormonal imbalance may be diverse and a specific etiological diagnosis is necessary for appropriate management. Common hormonal abnormalities seen in patients admitted in ICUs include abnormalities of glucose metabolism (hyperglycemia and hypoglycemia), changes in insulin secretion, and sensitivity. Stress and sepsis associated with ICU admission and therapeutic interventions can also lead to changes in the hypothalamic-pituitary-adrenal axis, resulting in abnormalities of cortisol production and increased levels of inflammatory mediators [4]. In addition, patients in the ICU are at increased risk for developing "critical illness-related corticosteroid insufficiency," which is characterized by inability of the adrenal glands to produce sufficient cortisol in response to stress [5].

Thyroid function abnormalities such as hypothyroidism and hyperthyroidism are also commonly seen in patients admitted in ICU. These thyroid function abnormalities in many instances are first diagnosed during ICU stay with no previous history of thyroid dysfunction [6]. The abnormalities of thyroid function in these patients may consist of abnormalities of production, binding of thyroid hormone to binding protein, and peripheral metabolism as well as altered regulation of thyroid hormone by thyroid stimulating hormone (TSH) [7]. Various studies have reported reduced T3 levels to be the most common thyroid function abnormality in patients admitted in ICU. The common cause of this abnormality appears to be changes in the peripheral metabolism of the thyroid hormones as well as release of acute phase reactants such as interleukin 6 [8]. In critically ill but conscious patients' hypothyroidism may present clinically as fatigue, weakness, cold intolerance, and constipation. Moreover, hemodynamic instability such as bradycardia or hypotension can also be seen in these patients. A high index of suspicion is required on the part of treating physician for diagnosis of various hormonal abnormalities in these patients [3].

Assessing and treating these endocrinological abnormalities including thyroid function abnormalities as well as hemodynamic instability associated with thyroid dysfunction is one of the essential components of management of these patients and can have a significant impact on a patient's recovery and overall health outcomes [9]. We undertook this observational study to assess the thyroid hormone levels in patients admitted in ICU for various critical medical conditions.

### Aims and objectives

The aim of the study was to assess the thyroid hormone levels in patients admitted in ICU for various critical medical conditions.

**METHODS**

This was a prospective and observational study conducted in the department of medicine of a tertiary care medical college. The institutional ethical committee approved the study. One hundred and twenty patients admitted in MICU for various medical conditions were included in this study on the basis of a predefined inclusion and exclusion criteria. The primary outcome of the study was to evaluate thyroid function abnormalities in studied cases. A detailed history with respect to demographic details such as age, gender, and body mass index was noted. A detailed history was taken and through clinical examination was done with respect to primary condition for which patients were admitted in medical ICU. All hematological investigations were reviewed. If any imaging investigations such as X-ray, ultrasound, or computed tomography were done then its findings were also reviewed. Any significant past or family history with respect to thyroid function abnormalities was also enquired and noted. Any drug history with respect to intake of drugs likely to be interfering with thyroid functions such as amiodarone, lithium, tricyclic antidepressants, metformin, rifampicin, and lithium was also noted. History of comorbid systemic illnesses such as diabetes mellitus, hypertension, coronary artery disease, and bronchial asthma was also noted. APACHE II score of the patients was noted with an objective to assess the severity of the illness [10].

The blood samples for thyroid function tests were collected in the morning hours. The hormone estimation was done by Electrochemiluminescence immunoassay method. The normal reference values for T3, T4, and TSH were taken to be 0.5–2 ng/mL, 4.5–13.2 µg/dL, and 0.39–4.6 mIU/l. Depending on the results of T3, T4, and TSH reports, patients were diagnosed to be having hypothyroidism or hyperthyroidism. The incidence of thyroid function abnormalities as well as the analysis of patients' outcome in terms of thyroid function abnormalities was determined.

Sample size was calculated according to the previous reference studies, when thyroid function abnormalities were studied in patients admitted in in-patient department. The minimum sample size of least 80 patients was calculated by Open Epi-Version 3 online software, a 10% difference could be determined between the group at 80% power and 5% significance ( $\alpha=0.05, \beta=0.80$ ). On the basis of minimum sample size calculation done by Epi-Version 3, we have included 120 patients in our study.

SPSS 21.0 software was used for statistical analysis and  $p<0.05$  was taken as statistically significant.

**Inclusion criteria**

The following criteria were included in the study:

1. Patients admitted in ICU for various medical conditions.
2. Patients of both genders.
3. Age between 18 and 60 years.
4. Those gave informed consent to be part of the study.

**Exclusion criteria**

The following criteria were excluded from the study:

1. Those Who refused consent.
2. Patients having history of thyroid function abnormalities before admission in ICU.
3. Patients on drugs likely to affect thyroid functions.
4. Pregnant patients.
5. Any history of benign or malignant thyroid conditions in past.

**RESULTS**

Our study consisted of total 120 patients. Out of these 120 patients, there were 78 (65%) were males and 42 (35%) were females with a M: F ratio of 1:1.053 (Fig. 1).

The most common affected age group was found to be between 51 and 60 years (46.67%) followed by 41–50 years (27.50%) and 31–40 years

(15.83%). Only 12 (10%) patients were found to be below the age of 30 years. The mean age of patients was found to be  $44.52 \pm 11.27$  years (Table 1).

The analysis of patients on the basis of primary pathology for which they were admitted in the ICU showed that out of 120 patients, the most common indication for admission was diabetic ketoacidosis (23.33%) followed by stroke (15.00%) and renal failure (11.67%). The other indications for which patients were admitted included

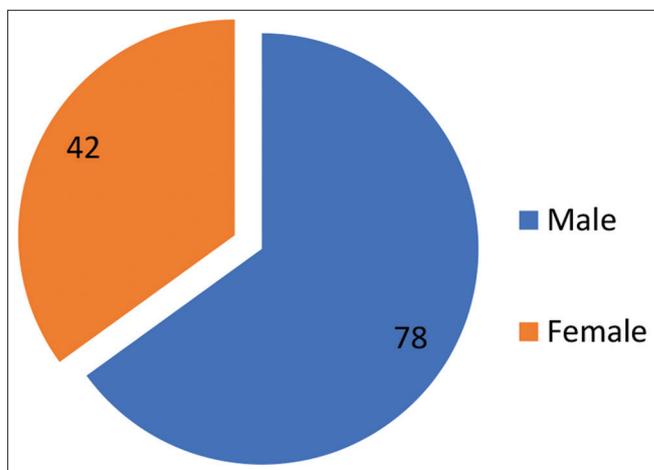


Fig. 1: Gender distribution of the studied cases

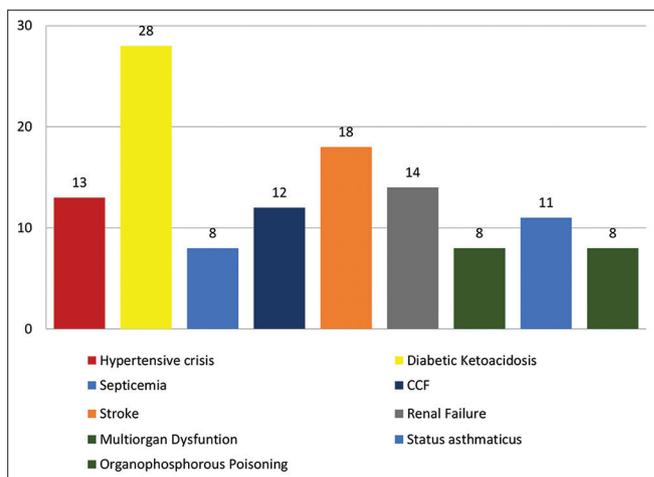


Fig. 2: Indications for admission in Medical Intensive care unit

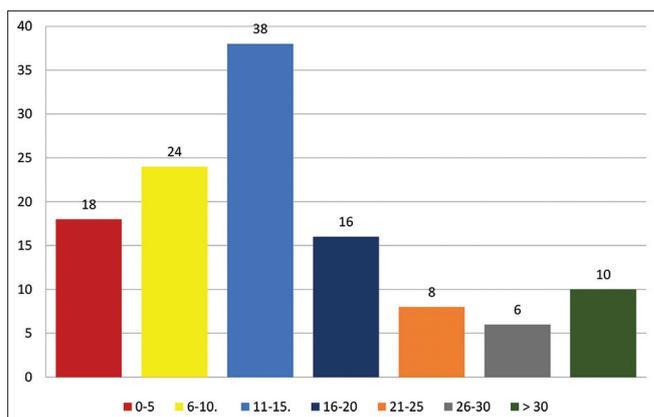


Fig. 3: APACHE II Score for determination of severity of illness

congestive cardiac failure (10.83%), hypertensive crisis (10%), and status asthmaticus (9.17%) (Fig. 2).

The severity of illness of the patients admitted in ICU was assessed using APACHE-II Score. Out of the studied cases, 38 (31.67%) patients had APACHE II score between 11 and 15 whereas 24 (20.00%) patients had APACHE II score between 6 and 10. Eighteen (15.00%) patients had APACHE II Score below 5 whereas 10 (8.33%) patients had APACHE II score above 30. The mean APACHE II score in studied cases was found to be 20.40±9.12 (Fig. 3).

The analysis of thyroid function tests in studied cases showed that thyroid function abnormalities were seen in 26 (21.67%) patients. These abnormalities were seen in patients with diabetic ketoacidosis (4.17%), congestive cardiac failure (4.17%), stroke (3.33%), renal failure (2.50%), hypertensive crisis, and multiorgan dysfunction (2.50%). Thyroid function abnormalities were less common in patients with status asthmaticus (0.83%). Thyroid function was normal in all patients with organophosphorus poisoning (Table 2).

The most common thyroid function abnormality seen in patient was isolated reduced T3 levels which were seen in 14 (11.67%) patients followed by isolated reduced T4 levels which were seen in 6 (5%) patients. Low TSH and low TSH and Low T4 was seen in 3 (2.50%) patients each (Table 3).

**Table 1: Age distribution of the studied cases**

Age group (years)	Number of cases (%)
18–30	12 (10.00)
31–40	38 (15.83)
41–50	42 (27.50)
51–60	64 (46.67)
Total	120 (100.00)
Mean age (years)	44.52±11.27

**Table 2: Thyroid function test in patients with various pathologies**

Etiology of ICU admission	Normal, number of cases (%)	Abnormal, number of cases (%)
Hypertensive crisis	10 (8.33)	3 (2.50)
Diabetic ketoacidosis	23 (19.17)	5 (4.17)
Septicemia	3 (2.50)	5 (4.17)
CCF	10 (8.33)	2 (1.67)
Stroke	14 (11.67)	4 (3.33)
Renal failure	11 (9.17)	3 (2.50)
Multiorgan dysfunction	5 (4.17)	3 (2.50)
Status asthmaticus	10 (8.33)	1 (0.83)
Organophosphorus poisoning	8 (6.67)	0
Total	94 (78.33)	26 (21.67)

ICU: Intensive care unit, CCF: Congestive Cardiac Failure

The analysis of mortality among the studied cases showed that 94 (78.33%) patients recovered and 26 (21.67%) patients died. The analysis of the cases who succumbed with respect to APACHE II score and thyroid function status showed that out of 26 patients who expired, 22 patients had APACHE Score more than 20. The mean APACHE score in patients who survived and who expired was found to be 12.57±8.13 and 48.73±20.19 respectively. The APACHE II score was high in patient who expired as compared to those who survived and the difference was found to be statistically highly significant ( $p < 0.0001$ ) (Table 4).

Similarly, out of 26 patients who expired 19 patients were found to have abnormal thyroid function test whereas out of 94 patients who recovered only 7 (5.83%) patients had abnormal thyroid function test. Thyroid function abnormalities were common in patients who expired as compared to those who recovered and the difference was found to be statistically highly significant ( $p < 0.0001$ ) (Table 5).

## DISCUSSION

The study comprised of 120 patients admitted in MICU for various life-threatening medical conditions. The analysis of cases on the basis of gender and age distribution showed that there were 78 (65%) males and 42 (35%) females with a M: F ratio of 1:1.0.53. The mean age of the studied cases was found to be 44.52±11.27 years.

The analysis of thyroid function tests in studied cases showed that thyroid function abnormalities were seen in 26 (21.67%) patients. Most common abnormality in our study was found to be isolated decrease in T3 levels. A similar study was conducted by Sekhar *et al.* In this study, 100 patients of age above 18 years and admitted to ICU for various serious medical conditions were included in the study [11]. 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. The study found that 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. On the basis of these findings, the authors concluded that low T3 is an important marker of mortality in ICU admitted patients. Similar low T3 levels in patients admitted in ICU were also reported by the authors such as Suresh *et al.* [12] and Kumar *et al.* [13].

In our study septicemia, diabetic ketoacidosis, multiorgan dysfunction, stroke, and renal failure were commonly associated with thyroid function abnormalities whereas in all patients admitted with organophosphorus poisoning thyroid function were found to be normal. In a similar study, Kumar *et al.* reported patients with sepsis, acute renal failure, acute respiratory failure, diabetic ketoacidosis, and congestive cardiac failure to be commonly associated with thyroid function abnormalities [14]. Similar patient profile was also reported by the authors such as Bhavana *et al.* [15] and Chethan *et al.* [16].

**Table 3: Various thyroid function abnormalities in studied cases**

Etiology of ICU admission	Abnormal TFT	Low T3	Low T4	Low TSH	Combination of low TSH and low T4
Hypertensive crisis	3	2	1	0	0
Diabetic ketoacidosis	5	3	1	1	0
Septicemia	5	3	1	0	1
CCF	2	1	1	0	0
Stroke	4	2	1	1	0
Renal failure	3	2	1	0	0
Multiorgan dysfunction	3	0	0	1	2
Status asthmaticus	1	1	0	0	0
organophosphorus poisoning	0	0	0	0	0
Total	26	14	6	3	3

TFT: Thyroid function test, TSH: Thyroid stimulating hormone, ICU: Intensive care unit, CCF: Congestive Cardiac Failure

**Table 4: APACHE II score and mortality in studied cases**

APACHE II score	Mean±SD score	p-value
Recovered	12.57±8.13	<0.0001 (HS)
Expired	48.73±20.19	

HS: Highly significant, SD: Standard deviation, APACHE: Acute Physiology And Chronic Health Evaluation

**Table 5: Thyroid function abnormalities and mortality in studied cases**

Outcome	Normal	Abnormal	p-value
Recovered	87	7	<0.0001 (HS)
Expired	7	19	
Total	94	26	

HS: Highly significant

In our study, out of 26 patients who expired 19 patients were found to have abnormal thyroid function test whereas out of 94 patients who recovered only seven patients had abnormal thyroid function test. Thyroid function abnormalities were common in patients who expired as compared to those who recovered and the difference was found to be statistically significant. In a similar study of 100 critically ill patients conducted by Kajal *et al.* found that the mean value of TSH was 3.27±6.91 [17]. The mean value of FT3 was 3.42±0.36. The mean value of FT4 was 14.79±1.17. A total of 22 patients (22%) succumbed to their illness during ICU admission. The mean level of both FT3 and FT4 was lower in non-survivors (2.98, 13.39) as compared to survivors (3.82, 15.71). The mean level of TSH was lower in non-survivors (2.63) as compared to survivors (4.07). The study concluded that FT3 and FT4 were lesser in non-survivors as compared to survivors with significant difference and FT3 and FT4 were best independent predictors of ICU mortality. Similar relationship between thyroid function abnormalities and mortality was also reported by the authors such as Wang *et al.* [18] and Bose *et al.* [19].

## CONCLUSION

Thyroid function abnormalities are common in patients admitted in ICUs. Prompt diagnosis and appropriate management of these thyroid function abnormalities is essential for optimal care of patients. Uncorrected thyroid function is found to be associated with adverse outcome such as increased mortality rate.

## AUTHOR CONTRIBUTION

AK- Concept and design of the study, interpreted the results, prepared first draft of manuscript and critical revision of the manuscript, statistically analyzed and interpreted, reviewed the literature, and manuscript preparation; SK- statistically analyzed and interpreted data, preparation of manuscript, and revision of the manuscript. NJ-Concept and coordination of the overall study.

## CONFLICTS OF INTEREST

None.

## SOURCE OF FUNDING

None.

## REFERENCES

- Bajwa SJ, Jindal R. Endocrine emergencies in critically ill patients: Challenges in diagnosis and management. *Indian J Endocrinol Metab* 2012;16:722-7. doi: 10.4103/2230-8210.100661, PMID 23087855, PMID PMC3475895
- Hassan-Smith Z, Cooper MS. Overview of the endocrine response to critical illness: How to measure it and when to treat. *Best Pract Res Clin Endocrinol Metab* 2011;25:705-17. doi: 10.1016/j.beem.2011.04.002, PMID 21925072
- Martinez FJ, Lash RW. Endocrinologic and metabolic complications in the intensive care unit. *Clin Chest Med* 1999;20:401-21, ix. doi: 10.1016/s0272-5231(05)70149-0, PMID 10386264
- Alarif AA, van den Berghe GH, Snider RH, Becker KL, Mueller B, Nylen ES. *Endocrine Markers and Mediators in Critical Illness*. 3<sup>rd</sup> ed. Philadelphia, PA: J B Lippincott Publishers Co.; 2001.
- Annane D, Pastores SM, Arlt W, Balk RA, Beishuizen A, Briegel J, *et al.* Critical illness-related corticosteroid insufficiency (CIRCI): A narrative review from a multispecialty task force of the society of critical care medicine (SCCM) and the European society of intensive care medicine (ESICM). *Intensive Care Med* 2017;43:1781-92. doi: 10.1007/s00134-017-4914-x. PMID 28940017
- Pimentel L, Hansen KN. Thyroid disease in the emergency department: A clinical and laboratory review. *J Emerg Med* 2005;28:201-9. doi: 10.1016/j.jemermed.2004.08.020, PMID 15707817
- Fliers E, Bianco AC, Langouche L, Boelen A. Thyroid function in critically ill patients. *Lancet Diabetes Endocrinol* 2015;3:816-25. doi: 10.1016/S2213-8587(15)00225-9. PMID 26071885, PMID PMC4979220
- Yamazaki K, Yamada E, Kanaji Y, Shizume K, Wang DS, Maruo N, *et al.* Interleukin-6 (IL-6) inhibits thyroid function in the presence of soluble IL-6 receptor in cultured human thyroid follicles. *Endocrinology* 1996;137:4857-63. doi: 10.1210/endo.137.11.8895357, PMID 8895357
- Qari FA. Thyroid function status and its impact on clinical outcome in patients admitted to critical care. *Pak J Med Sci* 2015;31:915-9. doi: 10.12669/pjms.314.7497, PMID 26430429, PMID PMC4590373
- Knaus WA, Draper EA, Wagner DP, Zimmerman JE. Apache II: A severity of disease classification system. *Crit Care Med* 1985;13:818-29. doi: 10.1097/00003246-198510000-00009, PMID 3928249
- Sekhar TV, Appalaneni R, Jada A, Pinnamaneni S. Study of thyroid function in patients admitted in intensive care unit in a tertiary care centre. *Int J Res Med Sci* 2018;6:2717-21. doi: 10.18203/2320-6012.ijrms20183257
- Suresh M, Srivastava NK, Jain AK, Nandy P. Thyroid dysfunction in critically ill patients in a tertiary care hospital in Sikkim, India. *Thyroid Res Pract* 2017;14:58-62. doi: 10.4103/trp.trp\_16\_16
- Kumar KV, Kapoor U, Kalia R, Chandra NS, Singh P, Nangia R. Low triiodothyronine predicts mortality in critically ill patients. *Indian J Endocrinol Metab* 2013;17:285-8. doi: 10.4103/2230-8210.109715, PMID 23776904
- Kumar CA, Arepalli SK, Chintalapudi V, Suresh B. Study of thyroid function in patients admitted in intensive care unit. *Int J Res Med Sci* 2022;11:54-61. doi: 10.18203/2320-6012.ijrms20223258
- Bhavana I, Kommineni R, Kusuma G. Study on assessment of thyroid status among critically ill patients admitted in a tertiary care hospital. *J Assoc Physicians India* 2019;67:46-8.
- Chethan KL, Shiva K. Thyroid status among critically ill patients admitted in the intensive care unit of the government tertiary care hospital in Mandya: A retrospective study. *Int J Adv Med* 2020;7:401-3.
- Kajal M, Vishvanayak TS, Singh VK, Krishna H, Lalit A, Leekha S. Thyroid function abnormalities in critically ill patients. *Acad J Med* 2021;4:67-72.
- Wang F, Pan W, Wang H, Wang S, Pan S, Ge J. Relationship between thyroid function and ICU mortality: A prospective observation study. *Crit Care* 2012;16:R11. doi: 10.1186/cc11151, PMID 22257427
- Bose P, Dasarathan R, Murugesan AS, Chenthil KS. Relationship between thyroid function and ICU mortality (sick euthyroid syndrome). *Int J Adv Med* 2017;4:1266-70. doi: 10.18203/2349-3933.ijam20173662