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Original Research

Evaluation of thyroid hormone levels in critically ill patients

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Abstract

Aim: To analyse thyroid hormone levels in critically ill patients.

Material and Methods: This prospective hospital based study was carried out at Department of InternalMedicine over a period of twelve months, after the approval of the ethical committee. This study was carried out including 100 cases of critically ill patients admitted and treated in the intensive care unit (ICU), after considering the inclusion and exclusion criteria.

Results: Out of 100 patients included in study, 42 (42%) patients required Ventilator assistance, whereas 58 (58%) patients didn't required Ventilator. A total of 22 patients (22%) succumbed to their illness during ICU admission. 78 patients were survivors. The mean APACHE-II score was significantly higher among non-survivorscompared with survivors (25.52 ± 6.84 vs. 14.06 ± 5.71, $P < 0.01$). In our study, APACHE II score which is calculated within 24 hoursof ICU admission is compared with thyroid function tests which is taken on day1. The results obtained with this comparison is that on day 1 levels of FT3 and FT4 weresignificantly correlated with APACHE II scores whereas TSH levelwas not statistically significant.

Conclusion:We observed that FT3 and FT4 were the strongest predictor of ICU mortality compared to all other parameters included in our study. Further, the combination of FT3, FT4 levels and APACHE-II scores provided for a higher probability for predicting mortality in ICU patients.

Keywords: Critically Ill, FT3, TSH, FT4

Introduction: Critically ill patients in the intensive care unit (ICU) exhibit profound inflammation, overwhelming fluid overload with renal failure and ultimately, significant malnutrition with sarcopenia. Despite substantial improvements in the care of critically ill patients over the past decades, optimal management of endocrinologic problems in the ICU continues to vex clinicians.[1,2] Whether it is the use of glucocorticoids, maintaining ideal blood glucose level or accurately distinguishing between subclinical preexistent thyroid dysfunction or acute illness-induced dysfunction, much debate remains regarding how to properly address these topics in the ICU. Wedo, however, know that certain conditions such as sepsis, starvation, bone marrow transplantation, and myocardial infarction affect thyroid function and the degree of thyroid dysfunction seems to correlate with disease severity in critically ill patients[3,4].

Critical illness is often associated with alterations in thyroid hormone concentrations in patients with no previous intrinsic thyroid disease. Euthyroid Sick Syndrome (ESS) is the commonest endocrine change seen in critically illpatients[1]. It is characterized by low levels of free and total triiodothyronine (T3) and high levels of reverse T3 (rT3) with variable values of thyroxine (T4) and thyroid-stimulating hormone (TSH) in the low to normal range[5,6].

The most common thyroid hormonal change reported in critically ill patients is reduced serum T3 level. Under normal circumstances 100% of T4 and 10-20% of T3 are directly secreted by the thyroid gland. 5`deiodinase causes peripheral monodeiodination of T4 contributing to 80-90% of T3 and also increases the clearance of the inactive isomer reverse T3 (rT3) (which is derived by the action of 5` deiodinase on T4)[7].

Researchers in some studies demonstrated that triiodothyronine (T3) levels in non-survivors were significantly lower than those in survivors. Low T3 is an important marker of mortality in critically ill patients. T4and TSH did not vary between survivors and non-survivors, whereas other researchers showed that there was no association[8].

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The acute physiology and chronic health evaluation II (APACHE II) scoring system has been a widely accepted method to determine the outcomes in ICU patient with an accuracy level of 77%. It is a point score system based on the initial values of 12 routine physiologic measurements, age, and previous health status, which provide a measure of severity of the disease.

Due to variation in studies and availability of scanty data in this part of our country and also demographic profile of patients too is different in patients of this region, this hospital based observational study was being conducted to evaluate the thyroid hormone levels in critically ill patients admitted to ICU. Through this study we tried to find abnormalities in thyroid hormone levels in this set of patients. APACHE II score was used to assess the severity of illness of these patients and prognosticate the outcome.

Material and Methods: This study was carried out among critically ill patients admitted and treated in the intensive care unit (ICU) were taken for this prospective hospital based study during the defined study period.

Inclusion criteria: All adult patients of both sexes admitted to medical Intensive Care Unit(MICU).

Exclusion criteria:

1. Known case of thyroid diseases such as hyperthyroidism, hypothyroidism and thyroid tumors.
2. Thyroid swelling found by physical examination when admitted to the ICU.
3. Pregnancy.
4. Patients receiving massive blood transfusion or on drugs known to interfere with thyroid hormone metabolism.

Sample Size: 100

Methodology:

1. Patients fulfilling inclusion and exclusion criteria were taken into study.
2. Detailed clinical examination was carried out.
3. Baseline demographic and clinical characteristics of the eligible patients were recorded.
4. Fasting venous blood samples were collected on admission to ICU from all critically ill patients and were subjected for thyroid hormone analysis by VIDAS-ELISA.
5. They were also be evaluated for body temperature, blood pressure, pulse rate, respiratory rate, and impairment of consciousness on the Glasgow coma scale.
6. Arterial blood gas analysis, complete blood count, liver function test, renal function test were interpreted and the APACHE II score will be calculated.
7. Course and the outcome of these patients were followed in the hospital.
   Data was collected and subjected to statistical analysis.

Statistical analysis: Data so collected was tabulated in an excelsheet, under the guidance of statistician.The means and standard deviations of the measurementsper group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc. Chicago, USA). Difference between two groups was determined using student t-test as well as chi square test and the levelof significance was set at $p < 0.05$.

Results: This study was carried out including 100 cases of critically ill patients admitted and treated in the intensive care unit (ICU), after considering the inclusion and exclusion criteria. The written informed consent for clinical examination & lab investigations was obtained either from patient or attendant. In the present trial maximum patient belong to 41-50 years age group (n=34, 34%), followed by 31-40 years age group (n=28, 28%), <30 years age group (n=23,23%) and least no. of patients were in >50 years age group (n=15, 15%). Maximum patients were male (n=69, 69%) and rest were females (n=31, 31%). (Table 1)

Table 1: Age and gender distribution among the study subjects

Age Group (in years)	**N**	**%**
<30	23	23
31-40	28	28
41-50	34	34
>50	15	15
Gender	**N**	**%**
Male	69	69

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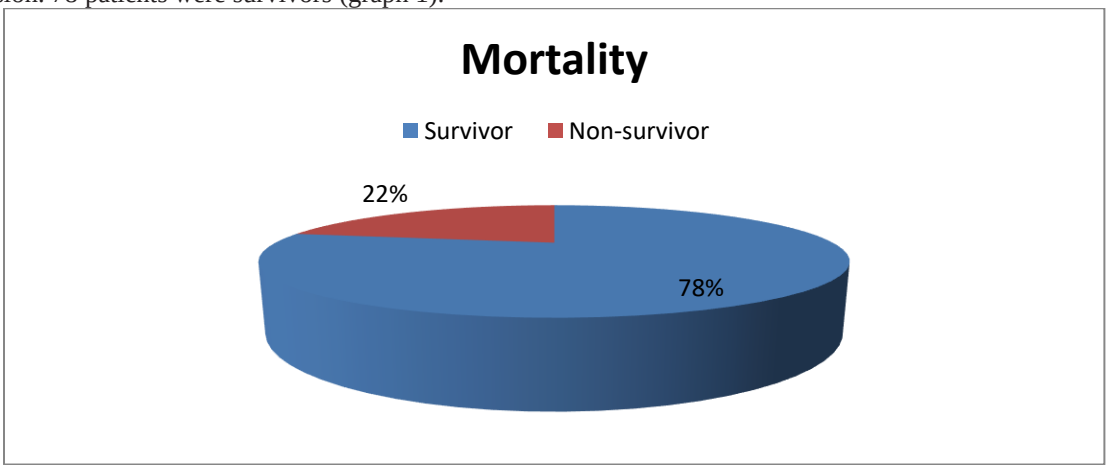
Female	31	31
Total	100	100

Of the total 100 patients involved in study, a total of 22 patients (22%) succumbed to their illness during ICU admission. 78 patients were survivors (graph 1).



Graph 1: Outcome among the study subjects

In present study, of the total 78 survivors, 25 patients (32.05%) required Ventilator assistance and 53 patients (67.95%) didn't require Ventilator and among the non survivors, 17 (77.27%) required ventilator assistance and 5 patients (22.73%) didn't require Ventilator. The p value was statistically significant. (Table 2)

Table 2: Outcome among the study subjects according to Ventilator requirement

Ventilator Requirement	Survivor		Non-survivor		p value
	N=78	%	N=22	%	
Yes	25	32.05	17	77.27	0.007*
No	53	67.95	5	22.73	

*: statistically significant

The mean APACHE-II score was significantly higher among non-survivorscompared with survivors (25.52 ± 6.84 vs. 14.06 ± 5.71, $P < 0.01$). (Table 3)

Table 3: Outcome among the study subjects according to APACHE-II score

Outcome	APACHE-II score		p value
	Mean	SD	
Survivor	14.06	5.71	<0.01*
Non-Survivor	25.52	6.84	

*: statistically significant

The mean level of both FT3 and FT4 were lower in non-survivors (2.98, 13.39) as compared to survivors (3.82,15.71), the p value was statistically significant ($P < 0.01$). The mean level of TSH was lower in non-survivors (2.63) as compared to survivors (4.07), but p value was not statistically significant. (Table 4)

Table 4: Outcome among the study subjects according to thyroid profile

Thyroid Profile	Survivor		Non-survivor		p value
	Mean	SD	Mean	SD	
TSH	4.07	8.31	2.63	3.02	0.11
FT3	3.82	0.47	2.98	0.33	<0.01*
FT4	15.71	1.28	13.39	1.06	<0.01*

*: statistically significant

In our study, APACHE II score which is calculated within 24 hoursof ICU admission is compared with thyroid function tests which is taken onday1. The results obtained with this comparison is that on day 1 levels of FT3 and

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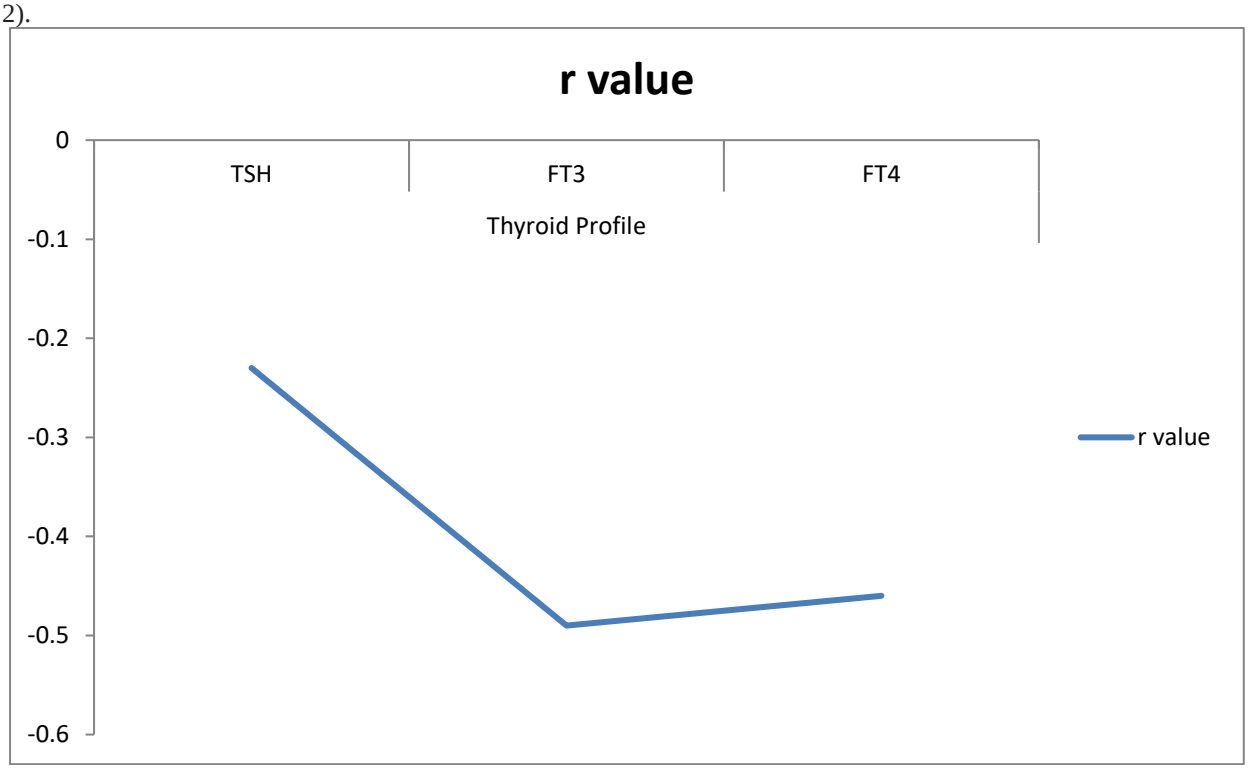
FT4 weresignificantly correlated with APACHE II scores whereas TSH levelwas not statistically significant (graph 2).



Graph 2: Correlation between thyroid profile and APACHE-II score

Discussion: In the present trial maximum patients belong to 41-50 years age group (34%) and least no. of patients were in >50 years age group (15%). Of the total 100 patients included in study, maximum patients were male (n=69, 69%) and rest were females. According to findings of Suresh *et al*[9], majority (49%) of study population belonged to the geriatric age group with a mean age of 59 years. The majority (55%) of the study population was males. The result was not in accordance to findings of Gutch *et al*[10], who found that there was a minor difference between the no. of male and female patients, and also that mean age of the study population was 38.99±18.32 years.

Out of 100 patients included in study, 42% patients required Ventilator assistance, whereas 58% patients didn't required Ventilator. Of the total 78 survivors, 32.05% patients required Ventilator assistance and 67.95% patients didn't required Ventilator. And among the non survivors, 77.27% required Ventilator assistance and only 22.73% patients didn't required Ventilator. The p value was statistically significant. So it can be said that, majority of survivors did not require ventilator assistance but maximum non survivors required Ventilator support.

APACHE II scores were calculated for all the 100 patients to assess whether thyroid function tests could independently predict the outcome of the patients. The mean APACHE-II score was 18.37±9.04. It was significantly higher among non-survivors compared with survivors (25.52±6.84 vs. 14.06±5.7, $P < 0.01$). So, it can be said APACHE II score affects the outcome of the patients. Results were in accordance with findings of Gutch *et al*[10], according to which mean APACHE II scores was significantly higher among non-survivors compared with survivors (25.00 ± 9.75 vs. 14.83 ± 5.95, $P < 0.001$). According to findings of Suresh *et al*[9], *the m*ean APACHE II score was 22.72; about two-third of the study population belonged to APACHE II score of more than 20.

The mean value of TSH was 3.27±6.91, FT3 was 3.42±0.36 and FT4 was 14.79±1.17. The mean level of both FT3 and FT4 were lower in non-survivors (2.98, 13.39) as compared to survivors (3.82,15.71), the p value was statistically significant ($P < 0.01$). The mean level of TSH was lower in non-survivors (2.63) as compared to survivors (4.07), but p value was not statistically significant. Results were in accordance with findings of Gutch *et al*[10], according to which the levels of both fT3 and fT4 were lower in non-survivors as compared to survivors ($P < 0.001$). Again the thyroid profile was compared with APACHE II scores in predicting the outcome. The levels of FT3 and FT4 were significantly correlated with APACHE II scores whereas TSH level was not statistically significant. Wang et al in 2012 did a study on relation between thyroid function and ICU mortality also showed that low T3 can predict the mortality of the patients.

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Previous studies conducted to demonstrate any association between thyroid hormone levels and prognosis in critically ill patients yielded inconsistent results. Either they could not establish an association between fT3 and adverse outcomes or they found association between T4, T3, TSH and FT4. Such results may be ascribed to small sample sizes and different population included in the different studies.[11-13] However, a large-scale study[14] involving 480 adult patients admitted to the ICU demonstrated that fT3 was the most powerful predictor of ICU mortality among other indicators and that addition of fT3 to APACHE-II score improved the ability to predict mortality.

In the Indian scenario, very few studies have been performed to determine any relationship between thyroid hormone levels and prognosis of ICU-admitted patients. A study of 100 ICU-admitted patients showed that low T3 was an important marker of prognosis in critically ill patients compared to HbA1C, prolactin, T4, and TSH levels.[13] Yet, another study of 100 ICU-admitted patients showed a similar relationship between low T3 levels and severity of critically ill patients.[14]

There are few limitations of the following study. Firstly, the single-center study with small sample size, so the findings of the present study could not be generalized. Secondly, the inclusion of some patients with undetected thyroid disease before ICU admission may not be ruled out in the present study, even though we tested patients by palpation of the thyroid carefully when they were admitted to the ICU to exclude those with thyroid nodules.

Conclusion: It was observed that FT3 and FT4 were the strongest predictor of ICU mortality compared to all other parameters included in our study. Further, the combination of FT3, FT4 levels along with APACHE-II scores can be used as a predictor of poor prognosis in ICU patients. Early recognition and appropriate treatment of abnormal thyroid functions may assist in recovery of critically ill patients admitted in ICU. The concept of relative thyroid insufficiency in the ICU warrants further research to better characterize patients that may benefit from this therapy.

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