Original Research Article

Assessment of thyroid profile in critically ill patients by using SOFA score in a tertiary care hospital

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A B S T R A C T

Background: It has been noted in many studies that there are hormonal imbalances in critically ill patients. We have undertaken this study to clarify whether thyroid profile can independently predict mortality & disease severity in ICU patients and whether there is any correlation between the thyroid profile & SOFAS scores.

Materials and Methods: Current study was cross sectional in nature conducted on 152 critically ill sepsis patients. All patients fulfilling eligibility criteria of our study were included.

Results: There were 85 (55.92%) survivors & 67 (44.08%) non-survivors in the study. Mean age of the survivors was 58.33 + 12.56 years vs. 62.46 + 14.22 years among non-survivors. Mean FT3 level was significantly more reduced among non-survivors (1.5 ± 0.77 pmol/l) than the survivors (2.02 ± 0.66 pmol/l). Mean FT4 level though decreased, it did not differ between the two groups. While mean TSH level was significantly raised among non-survivors (5.23 ± 0.96 μIU/l) than the survivors (4.92 ± 0.96 μIU/l). Serum FT3 levels in both the groups were negatively correlated with disease severity i.e. duration of mechanical ventilation, duration of ICU stay & with SOFA scores.

Conclusion: FT3 can be used as a proxy indicator of SOFA scores for assessing disease severity & predicting prognosis of critically ill patients in ICU.

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1. Introduction

Sequential organ failure assessment (SOFA) score, was used to assess extent of organ failure among patients in ICU. Earlier acute physiology and chronic health evaluation II (APACHE II) score and sepsis related organ failure assessment (SOFAS) score have been used to predict hospital associated mortality in these patients.

It has been noted in many studies that there are hormonal imbalances in critically ill patients. Peculiar changes have been observed in thyroid hormones that have been called non-thyroidal illness syndrome (NTIS). [1,2] Commonly reported changes were low levels of total triiodothyronine and low free triodothyronine with changes in levels of thyroxine and free thyroxine in prolonged critical illnesses. [3] These changes attributed to decreased peripheral deiodination of thyroid hormones along with altered binding to thyroid hormone binding proteins. These changes in thyroid profile could be associated with increased mortality & disease severity. [4,5] But according to some studies there was no such association exist. [6,7]

Hence to evaluate such conflicting evidence, we have undertaken this study to clarify whether thyroid profile can independently predict mortality & disease severity in patients of ICU and whether there is any correlation between the thyroid profile & SOFAS score among patients critically ill.

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2. Objectives

1. To evaluate the SOFA scores of critically ill patients admitted in ICU.
2. To evaluate thyroid stimulating hormone (TSH), free triiodothyronine (fT3), and free thyroxine (fT4) parameters of patients admitted in ICU with critically illness.
3. To determine the correlation of thyroid profile of these patients with disease severity and SOFA scores.

3. Materials and Methods

A cross sectional study conducted over a period of two moths from February 2022 to March 2022. The Institutional Ethical committee approval for the start of study has been taken. Informed consent was also taken from cases. All cases who have fulfilled our inclusion and exclusion criteria admitted in ICU of our tertiary care institute were taken up for the study until fulfilling the required sample size.

A total of 152 critically ill subjects with sepsis were recruited in the study according to eligibility criteria. Criteria for severe sepsis used in our study was those given by American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM).[8] Sepsis was defined by the presence of any two of the following conditions amongst cases 1) Temperature >38ºC or 2) pulse >90 beats/min, 3) White blood cell count > 12,000 or < 4,000 cells/mm2 and 4) Respiratory rate > 20 breaths/min or PaCO2 < 32 mmHg. Patients stayed < 24 hours in the ICU and patients with abnormalities of thyroid gland, thyroid gland enlargement was excluded. Patients transferred from another ICU were also excluded from the study.

Sample size was calculated with n = [DEFF*Np(1-p)]/ [(d^2/Z$^2_{1-\alpha\ /2}$*(N-1)+p*(1-p)] using OPENEPI software version 3. Kaukonen K et al[9] in their study, found proportion of sepsis admission among ICU was 11.1%. Considering this, at 95% confidence interval and absolute precision of 5%, sample size came out to be 152.

3.1. Method of assessment

Questionnaire of semi structured questions was used as data collection tool. Thorough clinical evaluation was done. SOFA scores based on six variables i.e. respiratory, hepatic, cardiovascular, coagulation, renal, and neurological were calculated within the first 24 hours of admission to determine the initial severity of illness & predict the association with the thyroid profile. Degree of dysfunction in these systems graded from 0-4, so SOFA score ranges from 0-24. Organ failure was defined as a SOFA score of 3 or greater.[10] fT3, fT4, and TSH concentrations were measured within the first 24 hours, Blood samples were obtained only in the morning at 8:00AM on the day following ICU admission. The normal values for TSH, FT3 and FT4 were 0.3-4.5 μIU/l, 3.5-6.5pmol/l, and 11.5-23

pmol/l respectively. Data was analyzed using IBM SPSS version 20. Means were compared by using student t test while qualitative variables compared by using Chi square & Fischer exact test of significance.

4. Results

In the present cross sectional study there were 85 (55.92%) survivors & 67 (44.08%) non-survivors in 152 critically ill patients admitted in ICU. Mean age of the survivors was 58.33 + 12.56 years vs 62.46 + 14.22 years among non-survivors. Majority of the patients were males among both the groups. Common comorbidities were CHD, diabetes, hypertension & COPD. These two groups did not differ significantly according to age, gender & comorbidities (p>0.05). (Table 1)

Mean duration of mechanical ventilation among non-survivors was 14.8 + 13.4 days & it was significantly more than the survivors (7.1 + 5.7 days) (p<0.001). Mean duration of ICU stay among non-survivors (21.6 + 18.3 days) also significantly more than the survivors (9.6 + 4.4 days) (p<0.001). (Table 1) Mean SOFA score among non-survivors (15.5 + 3.7) was significantly more than the survivors (5.8 + 1.9) (p<0.001). (Table 2)

Most common source of infection among survivors was chest infections (25.88%), followed by abdomen (22.35%), blood (17.65%), urine (14.12%), skin (10.59%) & others (9.41%) while among non-survivors it was blood infections (31.34%) followed by chest (25.37%), skin (14.93%), urine (13.43%), abdomen (10.45%) & others (4.48%). Two groups did not differ significantly according to source of infection except for blood which was significantly more important source of infection among non-survivors (p=0.04). Most common causative organism among survivors was E. coli (25.88%), followed by klebsiella (22.35%), streptococci (15.29%), pseudomonas (8.24%), MRSA (4.71%) & others (23.52%) while among non-survivors it was MRSA (25.37%) followed by klebsiella (20.90%), pseudomonas (17.91%), E. coli (14.93%), streptococci (10.45%) & others (10.45%). Two groups did not differ according to causative organisms except for MRSA which was significantly more important causative organism in non-survivors (p=0.0001). (Table 2)

On laboratory evaluation we found that mean hemoglobin among non-survivors (10.3 + 2.5 gm/dl) did not differ significantly from survivors (10.6 + 1.2 gm/dl). Mean total leucocyte count among non-survivors (21.5 + 5.8x10^3 cells/mm^3) was significantly raised than the survivors (14.1 + 2.1x10^3 cells/mm^3). Mean serum albumin level was significantly more in survivors (2.8 + 0.7 gm/dl) than the non-survivors (1.5 + 0.4 gm/dl).

Mean FT3 level was significantly more reduced among non-survivors (1.5 ± 0.77 pmol/l) than the survivors (2.02 ± 0.66 pmol/l). Mean FT4 level though decreased, it did not differ between the two groups. While mean TSH level

Table 1: Baseline characteristics of study subjects.

S.No.	Baseline characteristic		Survivors (n=85)	Non-survivors (n=67)	P
1	Frequency	No. (%)	85 (55.92)	67 (44.08)	–
2	Age (years)	Mean + SD	58.33 + 12.56	62.46 + 14.22	0.06
4	Gender	Male	49 (57.65)	36 (53.73)	0.62
		Female	36 (42.35)	31 (46.27)	
		CHD	4 (4.71)	3 (4.48)	0.69
5	Comorbidities	DM	12 (14.12)	10 (14.93)	0.88
		HTN	17 (20)	15 (22.39)	0.71
		COPD	02 (2.35)	03 (4.48)	0.51
6	Duration of mechanical ventilation (days)	Mean + SD	7.1 + 5.7	14.8 + 13.4	**<0.001**
7	Duration of ICU stay (days)	Mean + SD	9.6 + 4.4	21.6 + 18.3	**<0.001**

Table 2: Source of infection, causative organism and SOFA scores among study subjects.

S.No.	Baseline characteristic		Survivors (n=85)	Non-survivors (n=67)	P
1	SOFA score	Mean + SD	5.8 + 1.9	15.5 + 3.7	**<0.001**
2	Source of infection	Chest	22 (25.88)	17 (25.37)	0.09
		Skin	09 (10.59)	10 (14.93)	0.42
		Blood	15 (17.65)	21 (31.34)	**0.04**
		Urine	12 (14.12)	09 (13.43)	0.9
		Abdomen	19 (22.35)	07 (10.45)	0.052
		Others	08 (9.41)	03 (4.48)	0.28
4	Causative organism	E. coli	22 (25.88)	10 (14.93)	0.09
		Klebsiella	19 (22.35)	14 (20.90)	0.82
		MRSA	04 (4.71)	17 (25.37)	**0.0001**
		Pseodomonas	07 (8.24)	12 (17.91)	0.07
		Streptococci	13 (15.29)	07 (10.45)	0.38
		Others	20 (23.52)	07 (10.45)	**0.03**

Table 3: Laboratory profile of survivors & non-survivors.

Lab. Parameter	Survivors (n=85) Value (Mean + SD)	Non-survivors (n=67) Value (Mean + SD)	P
Hb (gm/dl)	10.6 + 1.2	10.3 + 2.5	3.38
TLC ($\times 10^3$ cells/cmm)	14.1 + 2.1	21.5 + 5.8	**<0.001**
Serum albumin (mg/dl)	2.8 + 0.7	1.5 + 0.4	**<0.001**
FT3 (pmol/l)	2.02 ± 0.66	1.5 ± 0.77	**<0.001**
FT4 (pmol/l)	1.15 ± 0.39	1.08 ± 0.42	0.29
TSH (μIU/l)	4.92 ± 0.96	5.23 ± 0.96	**0.04**

Table 4: Correlation of FT3 with disease severity and SOFA scores among survivors.

Parameters	FT3	
	R	P
Duration of mechanical ventilation	-0.355	0.04
Duration of ICU stay	-0.487	**0.03**
SOFA score	-0.534	0.04

Table 5: Correlation of FT3 with disease severity and SOFA scores among non-survivors.

Parameters	FT3	
	R	P
Duration of mechanical ventilation	-0.433	0.006
Duration of ICU stay	-0.587	0.03
SOFA score	-0.612	0.002

was significantly raised among non-survivors (5.23 ± 0.96 μIU/l) than the survivors (4.92 ± 0.96 μIU/l). (Table 3)

In this study, serum FT3 levels among survivors were negatively correlated with duration of mechanical ventilation (-0.355), duration of ICU stay (-0.487) & SOFA scores (-0.534) & the correlation was found to be significant (p<0.05). Also among survivors serum FT3 levels were negatively correlated with duration of mechanical ventilation (-0.355), duration of ICU stay (-0.487) & SOFA scores (-0.534) & the correlation was found to be significant (p<0.05). (Tables 4 and 5)

5. Discussion

In the current study, of the 152 critically ill septic patients admitted in ICU, 85 (55.92%) were survivors & 67 (44.08%) were non-survivors with majority of them were males in both the groups. In the study by Mohamed Hosny et al[11] there were 51.2% survivors & 48.8% non-survivors. Consistently Richa Giri et al[12] found 44.0% mortality with mean age of non-survivors was 57±11.96 years. Indicators of disease severity i.e. mean duration of mechanical ventilation & mean duration of ICU stay was significantly more among non-survivors than the survivors (p<0.001). Gutch M et al[13] in their study reported quite higher proportion of survivors (70%). Another study by Feilong Wang et al[14] reported 80.33% survivors out of 480 patients. Indicator for organ failure i.e. mean SOFA score was also significantly more among non-survivors than the survivors (p<0.001). Similarly, Mohamed Hosny et al[11] observed prolonged duration of mechanical ventilation, duration of ICU stay & increased SOFA scores among non-survivors ICU patients.

Sources of infections among our septic patients were chest, blood, urine, skin, abdomen etc. but two groups did not differ significantly according to sources of infection except for blood which was significantly more important source of infection among non-survivors (p=0.04). This finding is consistent with Mohamed Hosny et al[11] but in their study abdominal infections were the significant source of infection among non-survivors. Causative organisms were E.coli, klebsiella, pseudomonas, streptococci, MRSA but the two groups did not differ according to causative organisms except for MRSA which was significantly more important causative organism in non-survivors (p=0.0001). This is in line with Mohamed Hosny et al.[11]

In our study, there was significant leukocytosis & hypoalbunemia among non-survivors than survivors (p<0.0001). Mean FT3 & FT4 level severely reduced in our patients while TSH levels are increased. Mean FT3 was significantly reduced among non-survivors (p<0.001). This is consistent with Mevlüt Türe et al,[15] Richa Giri et al.[12] We also found that serum FT3 levels in both the groups were negatively correlated with disease severity i.e. duration of mechanical ventilation, duration of ICU

stay & with SOFA scores. Similar findings are reported by Mohamed Hosny et al,[11] Arvind Mishra et al[16] who reported that lower values of serum fT3 and T3 levels were clinically significantly associated with mortality, Mayer et. al.[17] found lowest FT3 levels among patients with severe sepsis (0.8 nmol/l) and septic shock (0.8 nmol/l), Mevlüt Türe et al[15] according to whom serum fT3 levels have additional value apart from SOFA and APACHE II scores in predicting short-term mortality in patients of ICU, Richa Giri et al[12] noted FT3 as the strong predictor of ICU mortality.

6. Conclusion

From the findings of this study we can conclude that thyroid function test, particularly free tri-idiothyronine (FT3) can be used as a proxy indicator of SOFA scores for assessing disease severity & predicting prognosis of critically ill patients in ICU.

7. Conflict of Interest

None.

8. Conflict of Interest

None.

References

1. Berghe GVD. Endocrine evaluation of patients with critical illness. *Endocrinol Metab Clin North Am*. 2003;32(2):385–410.
2. Peeters RP, Wouters PJ, Kaptein E, Van Toor H, Visser TJ. Van den Berghe G. Reduced activation and increased inactivation of thyroid hormone in tissues of critically ill patients. *J Clin Endocrinol Metab*. 2003;88(7):3202–11.
3. Mciver B, Gorman CA. Euthyroid sick syndrome: an overview. *Thyroid*. 1997;7(1):125–32.
4. Docter R, Krenning EP, De Jong M, Hennemann G. The sick euthyroid syndrome: Changes in thyroid hormone serum parameters and hormone metabolism. *Clin Endocrinol (Oxf)*. 1993;39(5):499–518.
5. Stouthard JM, Van Der Poll T, Endert E, Bakker PJ, Veenhof CH, Sauerwein HP, et al. Effects of acute and chronic interleukin‐6 administration on thyroid hormone metabolism in humans. *J Clin Endocrinol Metab*. 1994;79(5):1342–6.
6. Chinga‐Alayo E, Villena J, Evans AT, Zimic M. Thyroid hormone levels improve the prediction of mortality among patients admitted to the intensive care unit. *Intensive Care Med*. 2005;31(10):1356–61.
7. Peeters RP, Debaveye Y, Fliers E, Visser TJ. Changes within the thyroid axis during critical illness. *Crit Care Clin*. 2006;22(1):41–55.
8. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Crit Care Med*. 1992;20(6):864–74.
9. Kaukonen K, Bailey M, Suzuki S, Pilcher D, Bellomo R. Mortality Related to Severe Sepsis and Septic Shock Among Critically Ill Patients in Australia and New Zealand. *JAMA*. 2000;311(13):1308–16.
10. Vincent JL, Moreno R, Takala J. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure: on behalf of the Working Group on Sepsis-Related Problems of the

European Society of Intensive Care Medicine. *Intensive Care Me.* 1996;22(7):707–10.

11. Hosny M, Atef RR, Abed D, N. Predictive value of thyroid hormone assessment in septic patients in comparison with C-reactive protein. *Egypt J Crit Care Med [Internet]*. 2015;3(2-3):55–61.

12. Giri R, Yadav PK, Agarwal S, Kumar L. Assessment of prognostic value of FT3, FT4 and TSH among critically ill patients. *Int J Adv Med*. 2021;8(6):775–80.

13. Van BG. Endocrine evaluation of patients with critical illness. *Endocrinol Metab Clin North Am*. 2003;32(2):385–410.

14. Wang F, Pan W, Wang H, Wang S, Pan S, Ge J, et al. Relationship between thyroid function and ICU mortality: a prospective observation study. *Crit Care*. 2012;16(1):11. doi:10.1186/cc11151.

15. Türe M, Memiş D, Kurt I, Pamukçu†Z. Predictive value of thyroid hormones on the first day in adult respiratory distress syndrome patients admitted to ICU: comparison with SOFA and APACHE II scores. *Ann Saudi Med*. 2005;25(6):466–72.

16. Mishra A, Saini R, Mittal M, Himanshu D, Gupta KK, Mahdi AA, et al. Prognostic efficacy of thyroid profile with sequential organ failure assessment score in predicting mortality in intensive care unit patients. *Thyroid Res Pract*. 2019;16(3):113–20.

17. Meyer S, Schuetz P, Wieland M, Nusbaumer C, Mueller B, Christ-Crain M, et al. Low triiodothyronine syndrome: a prognostic marker for outcome in sepsis. *Endocrine*. 2011;39(2):167–74.

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