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Original article

Non-Thyroidal Illness Syndrome as a Predictor for Mortality in ICU Patients

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Abstract:

Background: Thyroid hormones (TH) are essential for cellular growth, differentiation, and energetic regulation. Critical illness is frequently associated with alterations in TH metabolism not caused by abnormalities of the hypothalamic-pituitary-thyroid function. These changes, collectively known as non-thyroidal illness syndrome (NTIS). This study aimed to investigate the role of NTIS in prediction of mortality in ICU Patients. **Methods:** This prospective cohort study was carried out on 50 ICU patients in the Department of Intensive Care Unit in Benha University Hospitals. After diagnosis of NTIS patients were categorized into two groups: Non-NTIS group and NTIS group. **Results:** Multivariate regression analysis identified ALT, SAPS III, APACHE II, sepsis, ARDS, mechanical ventilation, liver cell failure, and ICU length of stay as significant independent predictors of NTIS. For in-hospital mortality, WBC count, albumin, ALT, NTIS, APACHE II score, ARDS, need for mechanical ventilation, liver cell failure, and ICU length of stay were identified as significant predictors. Our ROC curve analysis demonstrated that both fT3 and fT4 levels have good diagnostic performance in predicting in-hospital mortality. A cut-off value of fT3 < 2 pmol/L showed 90.8% sensitivity and 81.3% specificity, while fT4 < 10 pmol/L demonstrated 90.9% sensitivity and 85.2% specificity. **Conclusions:** our study demonstrates that NTIS is common among ICU patients and is associated with increased disease severity, higher complication rates, and increased mortality. The strong predictive value of fT3 and fT4 levels for in-hospital mortality suggests that thyroid function tests could be valuable additions to prognostic models in the ICU setting.

Keywords: Non-Thyroidal Illness Syndrome; NTIS; Mortality; ICU

Abbreviations:
TH: Thyroid hormones.
NTIS: non-thyroidal illness syndrome.
TSH: thyroid stimulating hormone.

Introduction

Non-thyroidal Illness Syndrome (NTIS) or Low T3-(/T4-) Syndrome describes a decrease in free serum thyroid hormones without a corresponding increase in thyroid stimulating hormone (TSH) in the absence of manifest thyroidal illness. It is a phenomenon frequently seen in critically ill patients and is associated with several severe complications such as sepsis, multiple organ failure, prolonged mechanical ventilation, extended stay on intensive care unit (ICU), and increased mortality [(1)]**.** The entire pathogenesis of NTIS is not yet completely understood, but it seems to be induced by pro-inflammatory cytokines, increased levels of endogenous or exogenous corticosteroids and certain drugs [(2)]**.** Subsequently, the conversion of thyroxine (T4) to triiodothyronine (T3) in the tissue is inhibited, resulting in an accompanying increase of reverse triiodothyronine (rT3). Affected patients may display different types of NTIS, with NTIS Low fT3 presenting with an isolated decrease of free triiodothyronine (fT3) alone, and NTIS Low fT3 fT4 presenting with decrease in both, fT3 and free tetraiodothyronine (fT4) respectively. Initially, in critically ill, NTIS Low fT3 is the predominant entity, whereas prolonged critical illness results in NTIS Low fT3 fT4 [(3)].

The association between NTIS and sepsis, multiple organ failure, acute kidney injury and acute liver failure has been described previously [(2, 4)].

Interestingly, some studies suggest a potential role of TH levels to predict mortality in hospitalized patients since T3 levels are lower in non-survivors than in survivors in different clinical settings. Considering that most studies are underpowered and not primarily designed with this objective, whether NTIS may influence the outcome of critically ill patients admitted to ICU is still a matter of debate [(3)].

This study aimed to investigate the role of NTIS in prediction of mortality in ICU Patients.

Patients & Methods

This prospective cohort study was carried out on 50 ICU patients at the Department of Intensive Care Unit in Benha University Hospitals. The present study was carried out in the duration between December 2023 and July 2024.

The study was conducted after approval of Research Ethics Committee of Benha University, Egypt. Approval Code: MS 31-9-2023 Informed written consent was obtained from all patients prior to enrolment.

Inclusion criteria for the study include patients who are 18 years of age or older, of both sexes, and those who have an ICU length of stay (ICU-LOS) greater than 24 hours.

Exclusion criteria for the study include any history of thyroidal or pituitary disease, the use of medications affecting the thyrotrophic axis (such as thyroid hormone replacement or thyrostatic therapy), subjects on any hormonal therapy except for insulin, with TSH levels greater than 20 mIU/mL, a previous history of neck irradiation, and individuals who are pregnant or in the post-partum stage.

All patients were subjected to the following:

A. Full history taking:

- Personal history (personal data as name and age, gender and severity of disease.)
- Any complaint.
- Present history.
- Past History (chronic medical disorders).
- Family history.

B. Examination:

- General and Abdominal examination for any underlying medical disorders:

a) Complete general examination: including vital signs (blood pressure, temperature, heart rate)
b) Chest, cardiac, lower limbs and upper limbs.

C. Laboratory investigations:

- Routine laboratory investigations (CBC, Random Blood Glucose level, and urine analysis).
- Coagulation profile.
- Liver and renal functions tests.
- The thyroid function tests (Free T3, free T4, TSH, and total T4).

D. Patients screened for the following complications:

- Sepsis.
- Pneumonia.
- Acute respiratory distress syndrome.
- Acute liver failure.
- Acute kidney injury (AKI).
- The need for renal replacement therapy.
- The need for mechanical ventilation.

Methods

SAPS III was used to estimate the probability of mortality for ICU patients on admission and predicts hospital mortality upon ICU admission by using patient characteristics, induction for ICU admission, and physiologic derangement upon ICU admission. Factors associated with ICU mortality such as aged > 65 years, Acute physiology and chromic health Evaluation II (APACHE II) score, nosocomial infection, and acute kidney injury was documented [(5)].

During the initial assessment, APACHE II score was measured within 24 h of admission, which is the current standard to prognosticate mortality and morbidity across different populations with a maximum score of 71. APACHE II uses a point score based upon initial values of 12 routine physiologic measurements, age, and previous health status to provide a general measure of severity of disease. An increasing score (range 0 to 71) [(6)]. When APACHE II scores are combined with an accurate description of disease, they can prognostically stratify acutely ill patients and assist investigators comparing the success of new or differing forms of therapy. This scoring index can be used to evaluate the use of hospital resources and compare the efficacy of intensive care in different hospitals or over time.

Measurement of TSH, FT4, FT3, rT3: Fasting venous blood samples was collected on the morning of admission for the following thyroid functions tests- total T3, total T4, TSH, free T3, and free T4. Determination of serum-free T3, T3, T4 and TSH was with direct immunoassay test and its normal values were based also on patient's age. Assay reference ranges were as follows:

- Free T3 (2.3-4.2 pg/ml).
- Free T4 (0.93-1.7 ng/dl).
- Total T3 (0.6-2.1 ng/dl)
- Total T4 (5-12 ug/dl).
- Serum TSH (0.3-5.0 mU/L) [(7)].

A ratio of free T3/free T4 was calculated. NTIS was diagnosed when fT3 and/or Ft4 levels decrease, with normal or decrease levels of TSH. After diagnosis of NTIS patients was categorized into two groups:

- Normal group.
- NITS.

Serum creatinine and albumin levels were also measured using the Hitachi 7600-120 analyzer. We calculated the estimated glomerular filtration rate (eGFR) by using the abbreviated Modification of Diet in Renal Disease study equation. Serum CRP levels were measured using the QuikRead CRP test kit . Intra-assay coefficients of variation ranged from 2% at 140 mg/L to 15% at 9 mg/L. The NT-proBNP level was determined using the Elecsys electrochemiluminescence assay. The reported total coefficients of variation are 4.4% at mean concentrations 248.9 ng/L and 3.91% at 5,449 ng/L, respectively [(8)].

Study outcome

- Primary outcome: prediction of ICU mortality.

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- Secondary outcome: Length of stay in ICU and hospital stay and In-hospital mortality

Statistical analysis

Data was collected, coded then entered as a spread sheet using Microsoft Excel 2016 for Windows, of the Microsoft Office bundle; 2016 of Microsoft Corporation, United States. Data was analyzed using IBM Statistical Package for Social Sciences software (SPSS), (IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). The Kolmogorov-Smirnov test was used to verify the normality of distribution. Continuous data was expressed as mean ± standard deviation, median & IQR while categorical data as numbers and percentage. A statistical value <0.05 was considered as significant.

Analytic statistics

- **Chi-square test**; used to study the association between two qualitative variables.
- **Logistic Regression:** To measures the relationship between the categorical target variable and one or more independent variables. It is useful for situations in which the outcome for a target variable can have only two possible types
- **The ROC Curve (receiver operating characteristic)** provides a useful way to evaluate the Sensitivity and specificity for quantitative Diagnostic measures that categorize cases into one of two groups

Results

This table shows that platelet count, CRP, ALT, direct bilirubin, PT and INR are significant predictors of NTIS. A high statistically significant decrease in TSH, free T3 and free T4 levels among studied cases with NTIS Table 1.

This table shows a high statistically significant increase of both SAPS III and APACH II scores among studied cases with NTIS. This table also shows a high statistically significant increase in prevalence of sepsis, pneumonia, ARDS, need for mechanical ventilation, liver cell failure and AKI among studied cases with NTIS. A statistically significant increase in prevalence of ICU or hospital mortality among studied cases with NTIS. With increased both hospital and ICU LOS Table 2.

This table shows that after applying regression analysis for significant predictors of NTIS, ALT, SAPS III, APACH II, sepsis, ARDs, mechanical ventilation, LCF and ICU LOS still significant predictors**.** This table also shows that after applying regression analysis for significant predictors of in hospital mortality, WBCs count, albumin, ALT, NTIS, APACH score, ARDs, need for mechanical ventilation, LCF and ICU LOS still significant predictors Table 3.

This table shows that sensitivity of free T_3 (<2 pmol\l) as a predictor of hospital mortality is 90.8% with the ability to exclude 81.3% of negative cases and 86.7% accuracy, it was a statistically significant predictors. This table also shows that sensitivity of free T_4 (<10 pmol\l) as a predictor of hospital mortality is 90.9% with the ability to exclude 85.2% of negative cases and 86.7% accuracy, it was a statistically significant predictor Table 4.

Table 1: Relation between NTIS occurrence and laboratory data and thyroid functions on admission and prognostic scores among studied group.

	Non-NTIS N=36	**NTIS N=14**	**t-test MW#**	**P value**
Hb (g/dL)	13.38 ± 1.46	12.92 ± 1.49	0.985	0.324
Platelets (10^3/cmm)	372.19 ± 77.13	273.54 ± 80.1	**4.01**	**<0.001****
WBCs (10^3/cmm)	6.86 ± 1.55	6.27 ± 1.46	1.83	0.07
CRP (mg/L)	14.8 ± 15.1	31.2 ± 16.59	**2.81**	**0.002***
ESR (mm/h)	27.8 ± 10.5	22.7 ± 16.9	1.86#	0.205
AST (U/L)	38.17 ± 18.97	42.9 ± 19.77	1.02#	0.382
ALT (U/L)	38.96 ± 19.55	54.13 ± 25.05	**2.83#**	**0.005****
Total bilirubin (mg/dL)	0.93 ± 0.29	1.19 ± 0.75	1.71	0.09
Direct bilirubin (mg/dL)	0.1 04 ± 0.07	0.37 ± 0.67	**2.09#**	**0.02***
Albumin (g/dL)	4.31 ± 0.65	4.32 ± 0.59	0.051#	0.959
PT	12.02 ± 1.29	14.48 ± 2.68	**5.6**	**<0.001****
INR	1.11 ± 0.073	1.32 ± 0.24	**5.69**	**<0.001****
TSH (mU\l)	3.65 ± 0.85 1.55-4.88	0.45 ± 0.53 0.25-1.65	**3.22**	**<0.001****
fT3 (pmol\l)	3.59 ± 1.16 3.15-4.65	2.11 ± 0.95 1.55-2.53	**4.16**	**<0.001****
fT_4 (pmol\l)	16.3 ± 4.31 13.2-19.5	10.5 ± 0.67 9.12-11.8	**3.65**	**<0.001****

*P-value<0.05 is significant **P-value<0.001 is high significant MW: Mann-Whitny test of significance

Table 2: Relation between NTIS and complications, mortality and LOS among studied group.

		Non-NTIS N=36	**NTIS N=14**	**X^2 MW#**	**P**
SAPS III	**Mean ± SD**	29.6 ± 11.15	45.4 ± 13.2	4.72	**<0.001***
	Range	20-38	33-58		
APACH II	**Mean ± SD**	35.3 ± 10.4	53.7 ± 11.5	4.55	**<0.001***
	Range	33-44	46-70		
Sepsis		3 (8.3%)	5 (35.7%)	5.62	**0.02***
Pneumonia		4 (11.1%)	6 (42.9%)	6.34	**0.01***
ARDs		1 (2.8%)	3 (21.4%)	4.77	**0.03***
Mechanical ventilation		12 (33.3%)	11 (78.6%)	8.31	**0.004***
Duration of MV (hours)					**<0.001****
Median (Range)		56 (10-131)	159 (38-356)	3.65#	
Liver cell failure		1 (2.8%)	3 (21.4%)	4.77	**0.03***
AKI		4 (11.1%)	5 (35.7%)	4.14	**0.04***
ICU mortality		4 (11.1%)	5 (35.7%)	4.22	**0.04***
Hospital mortality		4 (11.1%)	6 (42.9%)	6.34	**0.01***
ICU LOS (d)				3.65#	**<0.001****
Median (Range)		7 (4-13)	29 (10-36)		
Hospital LOS (d)					
Median (Range)		26 (11-31)	35 (15-56)	3.65#	**<0.001****

**P-value<0.001 is high significant MW: Mann-Whitny test of significance

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Table 3: Multivariate regression for significant predictors of NTIS and in hospital mortality.

		predictors of NTIS				
		B	**S.E**	**Odd`s ratio**	**95% CI**	**P value**
Platelet count		-0.213	0.112	1.22	0.564-1.87	0.213
CRP		-0.144	0.105	1.88	0.985-2.11	0.170
ALT		0.501	0.301	4.08	2.33-5.22	0.04*
Direct bilirubin		-0.155	0.008	0.027	0.004-0.13	0.811
PT		-0.006	0.007	0.932	0.211-0.99	0.502
INR		-0.113	0.122	0.324	0.123-0.657	0.321
SAPS III		1.21	0.321	4.27	1.32-6.12	0.002*
APACH II		1.55	0.422	4.56	1.56-5.23	0.003*
Sepsis		0.654	0.422	1.77	0.98-2.44	0.03*
Pneumonia		0.231	0.256	1.13	0.95-2.33	0.074
ARDs		0.555	0.388	1.34	0.872-3.25	0.02*
Mechanical ventilation		0.875	0.445	3.54	1.32-7.42	0.001*
LCF		1.04	0.466	2.13	1.55-6.23	0.005*
AKI		0.243	0.286	1.21	0.768-3.22	0.067
ICU LOS		0.244	0.155	2.54	1.67-4.34	0.004*
Hospital LOS		-0.324	0.261	1.04	0.777-3.14	0.084
		predictors of in hospital mortality				
		B	**S.E**	**Odd`s ratio**	**95% CI**	**P value**
Platelet count	0.003	-0.213	0.112	1.22	0.564-1.87	0.213
WBCs count	0.004	0.233	0.307	1.35	0.876-3.22	0.03*
Albumin	<0.001	0.344	0.445	1.18	0.985-2.11	0.04*
ALT	<0.001	0.501	0.301	4.08	2.33-5.22	0.04*
Direct bilirubin	0.04	-0.055	0.018	0.237	0.114-0.73	0.321
PT	0.002	0.206	0.307	1.32	0.713-1.99	0.552
INR	0.002	0.313	0.422	1.14	0.23-1.57	0.461
NTIS	<0.001	0.266	0.387	2.13	1.55-4.23	0.03*
SAPS III	<0.001	0.211	0.221	1.71	1.12-3.22	0.222
APACH II	<0.001	1.55	0.422	4.56	1.56-5.23	0.003*
Sepsis	0.005	0.654	0.422	1.77	0.98-2.44	0.322
Pneumonia	0.003	-0.231	0.256	1.13	0.95-2.33	0.074
ARDs	0.002	0.555	0.388	1.34	0.872-3.25	0.02*
Mechanical ventilation	0.004	0.778	0.565	2.74	1.12-5.32	<0.001*
LCF	0.003	1.34	0.666	2.15	1.25-4.33	0.001*
AKI	<0.001	0.243	0.286	1.21	0.768-3.22	0.213
ICU LOS	<0.001	-0.144	0.256	1.24	0.637-3.46	0.002*

Table 4: Clinical performance of fT_3 and fT_4 as predictor of in hospital mortality (ROC curve analysis)

			fT_3				
Cut-off	**AUC**	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Accuracy**	**P**
>2	0.811	90.8%	81.3%	76.9%	94.1%	86.7%	0.005
			fT_4				
Cut-off	**AUC**	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Accuracy**	**P**
<10	0.883	90.9%	85.2%	76.9%	94.1%	86.7%	0.001

Discussion

Our study found that 28% of the studied cases developed NTIS. [9] reported the prevalence of NTIS as 71.5% in critically ill ICU patients, spread across age groups of 18–94 years. The slightly lower prevalence in our study might be due to differences in patient populations or the criteria used for NTIS diagnosis. A prospective observational study by [10] aimed to investigate the correlation between the severity of shock and thyroid hormone derangement. They reported that, NTI patterns were observed in 70% of patients.

In our study, patients with NTIS showed significant differences in several laboratory parameters compared to non-NTIS patients. Notably, platelet count, CRP, ALT, direct bilirubin, PT, and INR were significant predictors of NTIS. These findings suggest that NTIS is associated with a more severe systemic inflammatory response and liver dysfunction.

In our study, the association between NTIS and elevated CRP levels (31.2 ± 16.59 vs. 14.8 ± 15.1, p=0.002) is consistent with the findings of [11], who reported NTI severity is significantly associated with higher CRP levels in critically ill patients. This supports the hypothesis that NTIS is closely linked to the systemic inflammatory response in critical illness.

CRP rises in response to infectious and inflammatory diseases and shows greater elevations in serious bacterial infections [12]. It has been shown to be elevated in adult patients with a higher mortality risk [13].

As expected, patients with NTIS showed significantly lower levels of TSH, fT3, and fT4 compared to non-NTIS patients in our study.

This is consistent with the classic pattern of NTIS described in the literature, characterized by low T3, low or normal T4, and normal or low TSH levels [1].

Low FT3 level in our study, match the results reported by [14], who proposed several mechanisms that may explain how acute critical illness causes lower levels of FT3, a defect in the enzyme 5 deiodinase that converts thyroxin to FT3, a reduction in the number of thyroid receptors mediated by interleukin 1b and the presence of a thyroid protein binding inhibitor.

Our study demonstrated a strong association between NTIS and higher SAPS III and APACHE II scores. This aligns with the findings of [15], who reported that low T3 levels were associated with higher APACHE II scores in critically ill patients. These results suggest that NTIS may be a marker of disease severity and could potentially enhance the prognostic value of existing scoring systems in the ICU setting.

In a retrospective study, [3] aimed to enlighten the possible associations between patients' characteristics, severity of critical disease and NTIS in a large cohort of critically ill patients. They also showed significant differences between patients with and without NTIS in severity of critical disease.

As NTIS is primarily associated with critical illness, higher SAPS II scores and an increased number of organ failures (ARDS, acute kidney injury, acute liver failure) may be expected in patients with NTIS [16].

Our results agree with [9] who reported that, APACHE II score was higher in the NTIS group (14.88 ± 7.56) than in the euthyroid group (11.57 ± 10.28).

Our study results are in concordance with the study by [17] where the APACHE II scores were higher in patients with NTIS than in normal thyroids function.

In our study, patients with NTIS had a significantly higher prevalence of various complications, including sepsis, pneumonia, ARDS, need for mechanical ventilation, liver cell failure, and acute kidney injury. These findings are consistent with those of [2], who reported associations between low T3 levels and increased risk of organ failure in ICU patients. In accordance, [18] reported that,

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almost two-third of older patients with pneumonia had a diagnosis of NTIS. In harmony, [3] showed a significant increase in a multitude of co-morbidities in NTIS Low fT3 fT4 patients compared to non-NTIS patients.

[9] found in-hospital complications of acute kidney injury and rate of re-admissions significantly correlated with lower TT3 and FT3. Lower freeT3/freeT4 ratios were found to be associated with cardiac complications such as heart failure and cardiac arrest.

The notably higher rate of mechanical ventilation in NTIS patients (78.6% vs. 33.3%, p=0.004) and longer duration of ventilation in our study suggest that NTIS may be associated with more severe respiratory compromise. This could be due to the direct effects of thyroid hormone deficiency on respiratory muscle function or an indicator of overall disease severity.

Our study found significantly higher ICU and hospital mortality rates in patients with NTIS.

The increased length of stay in both ICU and hospital for NTIS patients aligns with the findings of [19], who reported longer ICU stays in patients with low T3 levels. This suggests that NTIS may be associated with prolonged recovery and increased healthcare resource utilization.

This also agrees with a systematic review and meta-analysis by [20] who reported that, NTIS was independently associated with increased risk of mortality in critically ill patients.

In harmony, [3] showed significant differences between patients with and without NTIS in ICU-LOS. They also showed a significant increase in an inferior outcome in NTIS Low fT3 fT4 patients compared to Non-NTIS patients.

Systematic reviews evaluating patients with acute neurologic events [21], cardiovascular disease [22], sepsis [23], and chronic renal failure [24] point to an incremental risk of unfavorable outcomes in patients with NTIS.

A recent meta-analysis showed that the mortality of COVID patients with NTIS was significantly higher than that of non-NTIS patients [25].

In our study, multivariate regression analysis identified ALT, SAPS III, APACHE II, sepsis, ARDS, mechanical ventilation, liver cell failure, and ICU length of stay as significant independent predictors of NTIS. These findings highlight the complex interplay between thyroid dysfunction, systemic inflammation, and multi-organ failure in critical illness.

For in-hospital mortality, WBC count, albumin, ALT, NTIS, APACHE II score, ARDS, need for mechanical ventilation, liver cell failure, and ICU length of stay were identified as significant predictors. The inclusion of NTIS in this model suggests that thyroid dysfunction provides prognostic information independent of traditional risk factors and severity scores.

[26] performed a univariate logistic regression between different variate of mortality predictors for this type of patient as APACHE score, CRP and albumin to compare them with thyroid function as a main mortality predictor in the study. They found that the increased APACHE II score could significantly predict the increased risk of mortality while decrease FT3 and FT4 could significantly predict the increased risk of mortality.

[8] found that the increased APACHE II score could significantly predict the increased risk of mortality while decrease any of the thyroid hormones including TT3, TT4, FT3, FT4 or TSH could significantly predict the increased risk of mortality.

[27] reported that, a multiple regression analysis revealed that a FT4 lower than 16.6 pmol/L (OR: 4.92 (1.60–18.19), $p = 0.009$) and having NTIS (OR: 6.04 (1.45–27.93), $p = 0.016$) could predict a high risk of mortality.

Our ROC curve analysis demonstrated that both fT3 and fT4 levels have good diagnostic performance in predicting in-

hospital mortality. A cut-off value of fT3 < 2 pmol/L showed 90.8% sensitivity and 81.3% specificity, while fT4 < 10 pmol/L demonstrated 90.9% sensitivity and 85.2% specificity.

These results are comparable to those reported by [28], who found that low T3 levels had high sensitivity and specificity for predicting mortality in critically ill patients.

Free T3 was described as an independent predictor of mortality in two studies by [29] and another Chinese study [8].

[9] observed that the ratio of free T3 to free T4 significantly predicted mortality. With the AUC by ROC of 0.630, it showed poor diagnostic performance.

Similar observations were made by [30] who showed that decreased FT3/FT4 ratio, an indirect marker of peripheral thyroxin deiodination, was an independent risk factor for frailty and increased mortality in hospitalized older patients.

[20] reported that, in univariate analysis, free T3 (FT3) and FT4 levels in non-survivors were relatively lower than that of survivors.

These results of our study are matching with many studies that have reported an association between the thyroid hormone levels and the prediction of mortality in intensive care patients like [31].

[26] reported that, levels of FT3 and FT4 were significantly lower in non-survivors than in survivors. The levels of FT3 were most sensitive in the prediction of the prognosis of critical illness when compared to its level between survivors and non-survivor patients of the study with P-value > 0.05 followed by FT4 level. Regarding the FT3, 5.04 was the cut off value with 63.2% sensitivity, 50.8% specificity, 69.2% negative predictive value, and 44.0% positive predictive value. It showed 55.5% accuracy & the area under the curve (AUC) was 0.610. Regarding the FT4, 15.0 was the cut off value with 61.8% sensitivity, 50.0% specificity, 68.1% negative predictive value, and 43.1% positive predictive value. It showed 54.5% accuracy & the area under the curve (AUC) was 0.601. From results, FT3 is the most sensitive thyroid function in predicting prognosis and mortality of critically ill patients in ICU.

[27] reported that, a FT4 value lower than 16.6 pmol/L showed an area under the curve (AUC) of 0.655 (0.56–0.78, $p = 0.02$), with 76% sensitivity and 61.5% specificity to detect a high risk of mortality.

On the contrary, [32] found that levels of TSH were higher in nonsurvivors than in survivors. This can be attributed to hormonal changes in critical illness that may result in mild physiological hypothyroidism, thereby limiting muscle breakdown and oxygen consumption. Increased TSH concentration would be consistent with this transient hypothyroidism.

Conclusion

In conclusion, our study demonstrates that NTIS is common among ICU patients and is associated with increased disease severity, higher complication rates, and increased mortality. The strong predictive value of fT3 and fT4 levels for in-hospital mortality suggests that thyroid function tests could be valuable additions to prognostic models in the ICU setting.

Conflict of interest

None of the contributors declared any conflict of interest.

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