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Correlation of Serum Thyroid Hormone Profile

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Abstract

Critical illness is any illness, sickness or a disease or a corrective measure or situation which is life threatening or potentially life threatening.

During critical illness, the state of stress results in increased energy expenditure, hypermetabolism, hyperglycemia and muscle loss.[1, 2]

The mechanisms of these successive adaptive changes are increasingly understood and are now gathered into a general theory of the metabolic response to stress.

Some of the specific endocrine changes which occur as a part of the stress response are as follows.[4]

- Sick euthyroid syndrome
- Relative adrenal insufficiency of critical illness
- Stress-induced hyperglycaemia
- Increased cortisol secretion and peripheral sensitivity
- Increased levels of Human Growth Hormone

In euthyroid patients with non-thyroidal illnesses, serum TSH alterations include transiently decreased or elevated basal TSH levels, blunted response of TSH to TRH, diminished or absent diurnal variations of TSH, and altered TSH glycosylation and bioactivity.[15,20]

Changes in the indices of thyroid function are very common but rarely isolated. They are often associated with alterations in other endocrine hormones such as reductions in serum gonadotropin and sex hormone concentrations and increase in serum adrenocorticotropic hormone and free cortisol levels.[21-22] Therefore, Sick Euthyroid Syndrome should not be considered as an isolated abnormal event but should be considered as a part of a generalized systemic endocrinal response to illness.

Whether SES promotes recovery and is adaptive or it is a direct result orcause of the illness and organ failure and therefore maladaptive is unclear.[6] On the other hand there is not enough information on the effectiveness of thyroid hormones replacement in critically ill patients [23] ·Interestingly, all the conditions in which sick euthyroid syndrome has been documented have nothing more in common than catabolic state. Therefore, it has been suggested that the decrease in thyroid hormone level may be a protective phenomenon to limit catabolism of protein and decrease energy requirements in non-thyroidal illness (NTI).[24]

Aims and Objectives

To study the thyroid hormone profile in critically ill children and to correlate between the

thyroid hormone levels, severity of disease and clinical outcome among the critically ill children.

Objectives

a. To evaluate the thyroid hormone profile of critically ill children admittedin PICU.
b. To assess the clinical outcome of the patients using PRISM score.

c. To correlate the thyroid hormone levels with the PRISM SCORE and clinical outcome among the cases.

Synthesis and Secretion of Thyroglobulin into the Follicular Lumen.

In the thyroid gland, thyroid hormone is synthesized within the unique structure called the thyroid follicle, which comprises a layer of follicular epithelial cells (also known as thyroid follicular cells or thyrocytes) surrounding a follicular lumen. Notably, the unique feature of the thyroid hormone synthetic pathway is that thyroid hormone is produced in the follicular lumen and not inside the follicular epithelial cells. No other hormone is produced outside the cell.

The follicular lumen is filled with a glycoprotein called thyroglobulin (TG) that is specific to the thyroid gland. Human TG is a large glycoprotein containing 2,748 amino acids. It is synthesized within follicular epithelial cells and secreted by exocytosis into the lumen, where it forms a homodimer. TG contains 123 tyrosine residues. Among these residues, those located close to the N- and C-termini are utilized to synthesize thyroid hormones. Although these residues play a major role in thyroid hormone synthesis, other residues may also be important to form an appropriate secondary structure for effective hormone synthesis.

Iodine Uptake into Follicular Epithelial Cells

The iodine concentration in follicular epithelial cells is 40-fold higher than that in plasma. Thus, iodine in plasma must be transported against a high concentration gradient. Iodine is transported as iodide (I^-) by secondary active transport. The transporter called Na^+/I^- symporter (NIS) is located on the basal membrane of thyroid epithelial cells[(34)]. Human NIS comprises 643 amino acids and has 13 transmembrane domains. NIS cotransports a single I^- molecule with two Na^+ molecules using a Na^+ electrochemical gradient generated by Na^+/K^+ATPase. Thyroid-stimulating hormone (TSH, thyrotropin) stimulates iodine uptake mainly by stimulating NIS transcription. In contrast, high dose of intracellular I^- transiently inhibits thyroid hormone synthesis through the inhibition of iodine organification (Wolff-Chaikoff effect).

Thyronamines (TAMs) are a novel class of iodothyronine-like endogenous signalling compounds [(45)]. Their structure differs from T4 and T3 only with regard to the absence of the carboxylate group of the alanine side chain. THs and TAMs are designated Tx and TxAM, respectively, with "x" indicating the number of iodine atoms per molecule, thus following the same rules for nomenclature. So far, only 3-iodothyronamine (3-T1AM) and thyronamine (T0AM) have been detected in vivo using liquid chromatography-tandem mass spectrometry (LC-MS/MS)[(45)]. 3T1AM and T0AM have been shown to exert acute and dramatic effects on heart rate, body temperature and physical activity, inducing a torpor-like state[(45)], but also more subtle effects on neurocognitive function [(46)].

Formation of THs within the TG molecule occurs at the cell-colloid interface bycoupling of

tyrosyl residues of TG with iodide. Iodination of tyrosines on TG, also known as "organification of iodide" is carried out by TPO. This reaction results in either MIT or DIT being incorporated into thyroglobulin. The other synthetic reaction is a coupling reaction where iodotyrosine molecules are coupled together. If two DIT molecules couple together, the result is the formation of T4. If MIT molecule and DIT molecule are coupled together, the result is the formation either T3 or rT3. THs accumulate in colloid, on the surface of the thyroid epithelial cells, still tied up in molecules of thyroglobulin. THs have to be liberated from the TG and secreted as a free hormone into the blood. There are several steps at the end of hormone synthesis. Thyroid epithelial cells ingest colloid that contains thyroglobulin molecules. Uptake of TG by thyrocytes occurs by micropinocytosis, which can be either nonspecific (fluid phase) or receptor mediated. Both forms of micropinocytosis, also called endocytosis or vascular internalization, involve the formation of small vesicles at the apical membrane, which invaginate to form intracellular vesicles that fuse with lysosomes. Nonspecific endocytosis is a constitutive process. In contrast, receptor-mediated endocytosis involves specific binding of certain substances to cell surface receptors, with high or low-affinity. Several receptors have been proposed on the apical surface, where they could mediate endocytosis, or on intracellular membranes, where they might influence intracellular trafficking. Megalin is a 600 kDa cell surface protein expressed on the apical surface of a restricted group of absorptive epithelial cells of the human body including the renal proximal tubule cells, epididymal cells, type II pneumocytes and thyroid epithelial cells. TG binds to megalin in solid-phase assay, with characteristics of high-affinity receptor-ligand interactions. This receptor probably has function in a process of endocytosis and transcytosis. A thyroid asialoglycoprotein receptor may internalize and recycle immature forms of TG back to the colloid. Finally, there are several principal intracellular pathways of TG after endocytosis by thyrocytes:

a) TG is internalized by fluid-phase nonspecific micropinocytosis and transported to lysosomes, where TG is degraded and THs are released;
b) TG is internalized by an unidentified low-affinity receptor and possibly transported to lysosomes;
c) TG is internalized by a receptor (possible the asialoglycoprotein receptor) and recycled back into the colloid;
d) TG is internalized by megalin and transported by transcytosis at the basolateral surface where TG is released by exocytosis into blood.

Thyroid Function In Critically Ill Children And New-Born

Many neuroendocrine changes are observed during critical illness. In adults, the neuroendocrine response to physiological stress has been described as occurring in at least two distinct stages:

- an acute phase, seen within the first hours or days of the illness, and a
- chronic phase, occurring 7 days or later after the onset of the illness.

During the acute phase, pituitary activity is essentially maintained; however, the anabolic pathways of these pituitary hormones are inactivated peripherally, presumably to adapt the body to illness and to delay anabolic processes.

On the contrary, during the chronic phase of illness, the pulsatile secretion of the anterior pituitary hormones is observed to be uniformly reduced, thereby causing decreased stimulation of anabolic metabolism at target organs. The decreased pulsatile activity of the pituitary gland is believed to be due to reduced hypothalamic stimulation, since infusion of hypothalamic releasing factors can restore pituitary function, including pulsatile secretion and appropriate feedback inhibition.[51,4] The changes in neuroendocrine function in critically ill children are not as well described in the literature but are thoughtto be similar to those of adults.

Thyroid hormone secretion is greatly suppressed in both children and adults with critical illness and after surgical procedures [52-55]. The changes in thyroid hormone levels observed during critical illness are well documented and are collectively referred to as euthyroid sick syndrome or nonthyroidal illness (NTI) syndrome. Previously, it was thought that the changes in thyroid hormone levels observed in the critically ill patient were not representative of true hypothyroidism (hence, the term „euthyroid sick syndrome"). However, there is accumulating evidence that these patients may in fact have acquired transient central hypothyroidism during critical illness.

Ruangnapa K et al[87] in 2018 conducted a study to compare the performance of a modified Paediatric Risk of Mortality (PRISM) III model with the original PRISM III in prediction of mortality risk in a Thailand paediatric intensive care unit (PICU). Children aged 1 month to 18 years who stayed in the PICU for more than 8 h during a period of three years were included in the study. The medical records of 1175 PICU patients were included in the analysis. The patients were randomly split into two equal groups: a development (n = 588) and a validation (n = 587) sample. A modified PRISMIII model was derived from the original PRISM III by omitting arterial blood gas parameters and adding selected clinical variables. The model was developed using a multiple logistic regression model on the development sample and assessed using the area under the curve (AUC) obtained from a receiver operating characteristic curve. The modified PRISM III scores were significantly higher in non-survivors (median = 9, interquartile range [IQR] = 4 — 13) compared to survivors (median = 2, IQR = 0 — 5). The modified PRISM III model had similar discriminative performances compared to the original PRISM III in predicting 2-day mortality (AUC: 0.874 vs. 0.873), 7-day mortality (AUC: 0.851 vs. 0.851) and overall mortality (AUC: 0.845 vs. 0.956). The modified PRISM III model was calibrated in the validation sample, and the standardized mortality ratios (SMRs) were similar. They concluded that the performance of a modified PRISM III model in predicting mortality risk was comparable to the original PRISM III. Both had similar discriminative performance and SMR for overall mortality prediction in a PICU.

Gutch M[89] and colleagues designed a study in **2018** to determine the correlation between changes in thyroid hormone levels and the prognosis of ICU-admitted patients. A total of 270 ICU-admitted patients without previous history of thyroid disorder were included in the study. The baseline characteristics, acute physiology and chronic health evaluation (APACHE-II) score, thyroid hormone levels, lactate, and other parameters were recorded on admission. ICU mortality was the primary outcome. They analysed the ability of each parameter to predict mortality in the participants. Further, they also evaluated whether the combination of thyroid hormone levels with APACHE-II score could improve the mortality

prediction. A total of 81 patients (30%) expired during their ICU treatment. Both FT3 and FT4 levels were lower in non-survivors compared to survivors. Among the thyroid hormones, FT3 had the highest predictive value for ICU mortality. Univariate logistic regression analysis showed that fT3 (β = 140.560) had the highest predictive potential for ICU mortality compared with APACHE-II score (β = 0.776), FT4(β = 17.62) and other parameters. Multivariate logistic regression analysis revealed that the combination of FT3 and APACHE-II (R2 = 0.652) was superior in predicting mortality than APACHE-II alone (R2 = 0.286). They concluded that FT3 was the strongest predictor of ICU mortality compared to all other parameters included in their study. Further, the combination of FT3 levels and APACHE-II scores provided for a higher probability for predicting mortality in ICU patients.

Hassan ZE, Quyoom I, Mushtaq I[(90)] in 2018 conducted a study to evaluate the validity of PRISM Score in predicting mortality in a tertiary care hospital in North India. A prospective observational study was conducted in a PICU which included 411 patients. They divided patients into two categories based on PRISM-III 24 score - Patients with PRISM score >8 and those with a score of ≤8. Three hundred twenty-three (323) patients had a PRISM score ≤8, and 38 patients died in this category (11.8% mortality). In contrast, 88 patients had a PRISM score >8, and 32 patients died in this category (36.4% mortality). They found that Prism score >8 was a significant predictor of mortality (chi- square value of 29.615 and a p-value of <0.001). The odds ratio for dying in the presence of PRISM score >8 was 9.28 (9 times more risk of dying compared to patients with a prism score >8) with a 95% CI of 2.47-7.43. Cox regression analysis showed that PRISM score >8 was an independent predictor of mortality. Further, they concluded that PRISM score was a significant predictor of mortality.

Popli V and Kumar A[(91)] in 2018, organised a study to validate PRISM III scoring system in predicting mortality outcome in the PICU of a tertiary care hospital. This study included 145 patients who met the inclusion criteria. The final outcome was recorded as death or discharge. It was observed that mortality increased with increasing PRISM III score approaching almost 100% by PRISM III score of 19 and more. Length of stay in PICU increased with increasing PRISM III score up to score of 14 thereafter length of stay decreased gradually with increasing score. In this study the predictive value of PRISM III score was good in their PICU setup. The overall performance of the PRISM III score was good with AUC of 0.871 (good discrimination) and reasonable agreement between observed and expected mortality across most mortality risk intervals (good calibration).They concluded that the mortality increases with the increase of PRISM III score i.e. higher the PRISM III score, higher the mortality.

Wang F et al[(102)] in 2012, conducted a study to assess the prognostic value of the complete thyroid indicators (free triiodothyronine, total triiodothyronine; free thyroxine, total thyroxine, thyroid-stimulating hormone and reverse triiodothyronine) in unselected ICU patients. A total of 480 consecutive patients without known thyroid diseases were screened for eligibility and followed up during their ICU stay. Each patient's baseline characteristics,including the Acute Physiology and Chronic Health Evaluation II (APACHE II) score and thyroid hormone, N-terminal pro-brain natriuretic peptide (NT- proBNP) and

C-reactive protein (CRP) levels were collected. The primary outcome was ICU mortality. Potential predictors were analysed for possible association with outcomes. They also evaluated the ability of thyroid hormones together with APACHE II score to predict ICU mortality by calculation of net reclassification improvement (NRI) and integrated discrimination improvement (IDI) indices. Among the thyroid hormone indicators, FT3 had the greatest power to predict ICU mortality, as suggested by the largest area under the curve (AUC) of 0.762 ± 0.028. Multiple regression analysis revealed that FT3 level (standardized $\beta = -0.600$, $P = 0.001$), APACHE II score (standardized $\beta = 0.912$, $P < 0.001$), NT-proBNP level (standardized $\beta = 0.459$, $P = 0.017$) and CRP level (standardized $\beta = 0.367$, $P = 0.030$) could independently predict primary outcome. They concluded that in unselected ICU patients, FT3 was the most powerful and only independent predictor of ICU mortality among the complete indicators. The addition of FT3 level to the APACHE II score could significantly improve the ability to predict ICU mortality.

Angelousi AG[(103)] in 2011 conducted a systemic review to find an association between thyroid function tests at baseline and the outcome of patients with sepsis or septic shock. They included nine studies that all had a prospective cohort design. Seven involved children or neonates, and two involved adults. Mortality was the outcome evaluated in eight studies, while the length of ICU stay was evaluated in the remaining study. In univariate analysis, six of the nine included studies showed that either, free or total, triiodothyronine or thyroxine was lower in the group of patients with sepsis or septic shock who had unfavourable outcome than in those who had favourable outcome. Two other studies showed higher TSH values in the group of patients with unfavourable outcome. No significant relevant findings were observed in the remaining study. Regarding the correlation of sepsis prognostic scoring systems with thyroid function tests, the three studies that provided specific relevant data showed variable findings.

Material and Methods

Study Design: Hospital Based Prospective, Observational Study

Study Duration: 22 months from DECEMBER 2017 to SEPTEMBER2019.

Study Area

This study was conducted on children admitted to PICU, Department of Pediatrics, Krishna Institute of Medical Sciences, Karad

Type of Study: OBSERVATIONAL study.

Sample Size:

Considering the retrospective records of patients admitted in PICU of Krishna Institute of Medical Sciences, Karad fulfilling the inclusion criteria, a totalsample size of 50 critically ill children was selected.

Sampling Technique

Consecutive type of non-probability sampling was followed.

Inclusion Criteria:

Children between 1 month to 15 years of age who were admitted to the PICU of Krishna

Hospital with malfunction of one or more organs or systems and requiring support to maintain vital function by any one or more of the below mentioned pharmacological or mechanical aids :

1. Dopamine >5mcg/kg /min,
2. Any dose of adrenaline,
3. Mechanical ventilation,
4. Serum creatinine >1mg/dl,
5. Platelet count < 1,00,000/mm3
6. Urine output< 1ml/kg/hr.

Exclusion Criteria:

1. Patients having family or maternal history of any thyroid illness.
2. Patients having clinical features of thyroid dysfuncton.
3. Patients on any thyroid medications.
4. Patients who expired within 24 hours of admission.

Table 1: Correlation of thyroid profile done on arrival and at the time of discharge/death and their outcome

Thyroid parameter	Outcome	No. of patients (n)	Mean ± SD	p-value
T3 (On arrival)	Discharged	42	80.33±33.53	0.0659
	Expired	08	57.87±26.31	
T3 (At the time of discharge/death)	Discharged	42	107.78±31.42	<0.001
	Expired	08	29.75±16.85	
T4 (On arrival)	Discharged	42	7.63±2.38	0.0255
	Expired	08	5.16±2.44	
T4 (At the time of discharge/death)	Discharged	42	9.56±2.11	<0.001
	Expired	08	3.41±1.89	

TSH (On arrival)	Discharged	42	2.61±1.19	0.2363
	Expired	08	3.83±2.63	
TSH (At the time of discharge/death)	Discharged	42	3.85±1.39	0.1662
	Expired	08	2.71±2.03	

p value is used for comparison between the thyroid parameters and the outcome (discharged/ expired).

Here, the correlation between thyroid hormone profile and outcome of admission is taken into consideration. T3, T4 and TSH samples taken both at the time of admission and at the time of discharge or death were correlated with outcome as discharged or expired. Mean serum T3 level at the time of discharge/death was found to be significantly lower among expired patients in comparison to discharged patients (pvalue <0.001). Similarly, mean serum T4 levels were significantly lower among expired patients in comparison to discharged patients both on admission and at the time of discharge/death (pvalue 0.02 and <0.01 respectively). While mean serum T3 level on admission and mean serum TSH levels both on admission and at the time of discharge/death were not found to have a significant correlation with the outcome i.e. discharged or expired (pvalue >0.05).

Table 2: Distribution of mean values of thyroid profile tests done among expired patients (n=8)

Thyroid parameter	On arrival (Mean ±SD)	At the time of death (Mean ±SD)	p-value
T3	57.87±26.31	29.75±16.85	0.04013
T4	5.16±2.44	3.41±1.89	0.001
TSH	3.83±2.63	2.71±2.03	0.0102

On correlating thyroid hormone profile among expired patients , it was found that mean T3, T4 and TSH values were significantly lower at the time of death in comparison to their values at the time of admission with a pvalue of 0.04,
0.001 and 0.01 respectively.

Table 3: Distribution of mean values of thyroid profile tests done among discharged patients (n=42)

Thyroid parameter	On arrival (Mean ±SD)	At the time of discharge (Mean ±SD)	p-value
T3	80.33±33.53	107.78±31.42	<0.001×

T4	7.63±2.38	9.56±2.11	<0.001×
TSH	2.61±1.19	3.85±1.39	<0.001×

On correlating thyroid hormone profile among discharged patients, the mean T3, T4 and TSH values were found to be significantly raised at the time of discharge as compared to their levels at the time of admission with pvalue <0.001. This is suggestive of improvement in the condition of patients.

Table 4: Distribution based on PRISM score grouping at the time ofadmission

PRISM score group	No. of patients (n)	Percentage (%)
<25	46	92
25-40	03	06
>40	01	02
Total	50	100

The Prism score was grouped into three groups as <25, 25-40 and >40. 46 (92%) patients were grouped into Prism score <25, 3 (6%) patients had Prism score between 25-40 and 1 (2%) patient had Prism score >40 at the time of admission.

Figure.1: Distribution based on PRISM score grouping at the time ofadmission.

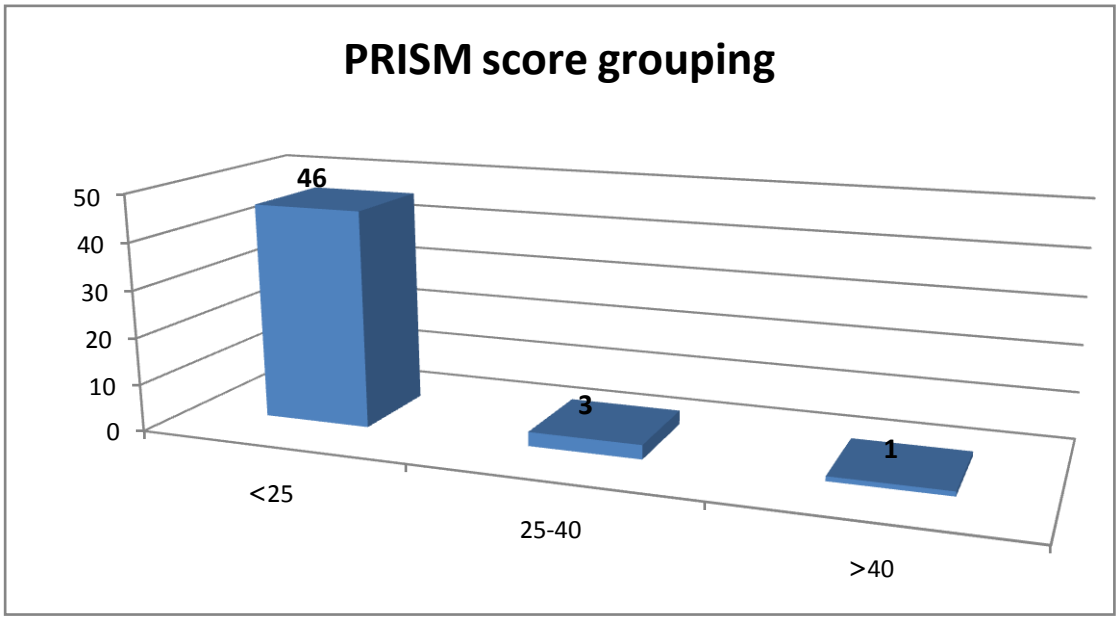

Table 5: Distribution based on PRISM score grouping after 24 hours

PRISM score group	No. of patients (n)	Percentage (%)
<25	48	96
25-40	02	04
>40	00	00
Total	50	100

48 (96%) patients had Prism score <25, 2 (4%) patients had Prism scorebetween 25-40 and none had Prism score >40 after 24 hours of admission.

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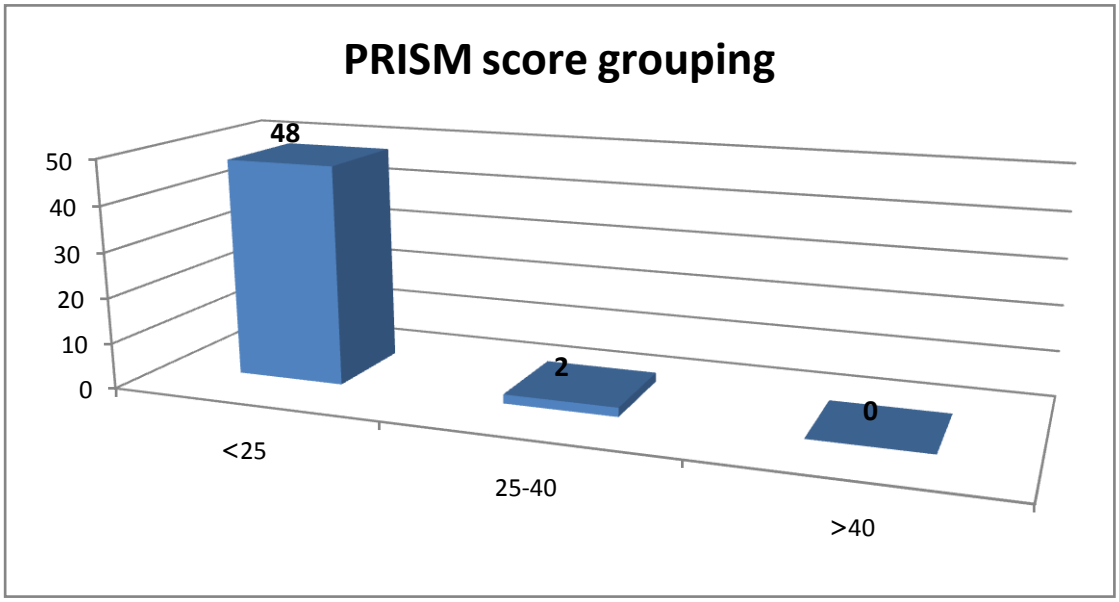

Figure.2: Distribution based on PRISM score grouping after 24 hours ofadmission

Table 6: Correlation of PRISM SCORE GROUPS on admission with theoutcome

OUTCOME	PRISM SCORE <25	PRISM SCORE 25-40	PRISM SCORE >40	P value
DISCHARGED	41 (87.2%)	01(50%)	00	<0.001
EXPIRED	6 (12.8%)	01(50%)	01 (100%)	0.044
TOTAL	47	02	01	

Out of 50 patients studied, 47 patients had prism score <25 on admission, of these 87.2% (41 patients) got discharged and 12.8% (6 patients) got expired; 2 patients had prism score between 25-40, of these 50% (1 patient) gotdischarged and 50% (1 patient) got expired and the remaining 1 patient had prism score >40 who got expired (100%). This shows that lesser the prism score, better is the outcome and shows significant correlation between prism score groups on admission and the outcome with p value of <0.05.

baseline values (18.1 vs 10.85, pvalue- 0.361).

Table 7: Distribution and correlation of PRISM score with systemsinvolved

System involved	PRISM score (Mean ±SD)	p-value
PRISM score on arrival		
Single system	9.17±5.57	<0.001×
Multiple system	13.90±10.89	<0.001×

PRISM score after 24 hours		
Single system	6.62±5.12	<0.001×
Multiple system	9.67±7.75	<0.001×

Patients with single system involvement had lower prism score on admission as well as at 24 hours of admission as compared to those with multiple system involvement. (p value <0.001) Prism score at the time of admissionand after 24 hours of admission was found to be highly significant when correlated with single and multiple organ system involvement.

Table 8: Distribution and correlation of PRISM score and hospital stay

Parameter	**Hospital stay (Days)**			**p-value**
PRISM score	**<15**	**15-30**	**>30**	0.258
<25	31	10	05	
25-40	02	00	01	
>40	01	00	00	

The duration of hospital stay did not show significant correlation with the Prism score groups with an insignificant statistical pvalue of 0.258.

Table 9: Distribution of PRISM score (at the time of admission) and itscorrelation with thyroid parameters

Thyroid parameter	**r-value**	**p-value**
On arrival		
T3	-0.129	<0.001×
T4	-0.256	0.0051
TSH	-0.281	<0.001×
At discharge/death		
T3	-0.125	<0.001×
T4	-0.374	0.0751
TSH	-0.183	<0.001×

PRISM score studied at the time of admission had negative correlation with T3, T4 and TSH levels on admission which means higher the PRISM score onadmission, lesser will be T3,T4 and TSH values. This relationship was found to be significant with p value of <0.001, 0.005 and <0.001 respectively. Similarly PRISM score on admission had significant negative correlation with T3 and TSH values on discharge/death with p value of <0.001 which means higher the PRISM score on admission, lesser will be the T3 and TSH levels in the second sample. There is no significant correlation between PRISM score on admission and T4 levels on discharge/death (pvalue 0.07).

The area under ROC curve for the various parameters such as thyroid hormone variables, PRISM score at admission and 24 hours, with outcome(expired) as classification variable, along with the sensitivity and specificity is listed in above table.

From above table it was concluded that, PRISM score at 24 hours, T3 and T4 values at death/ discharge had maximum area under roc curve and high sensitivity and specificity values. Thus, PRISM score at 24 hours and T3 ad T4 levels at the time of discharge/death have maximum diagnostic accuracyin predicting outcome in critically ill children.

Table 10: Multiple Logistic Regression between Outcome (Dependent Variable) and Prism Score at 24 hours, T3 and T4 at discharge/death (Independent Variables) by Forward Stepwise Wald Method.

Variables	Coefficient	SE	Wald	Df	P-value
PRISM SCORE at 24 hrs	0.49398	0.18080	7.4649	1	0.0063
T3 at death/discharge	-0.1275	0.0487	6.8439	1	0.0089
T4 at death/discharge	-1.00636	0.33094	9.2471	1	0.0024

PRISM score at 24 hours of admission, T3 and T4 levels in the second sample i.e. at the time of discharge/death were found to be significant predictors of survival statistically which means more the PRISM score at 24 hours and less the T3 and T4 levels at the time of discharge/death, lesser are the chances of survival.

Discussion

On comparing the thyroid profile among the expired patients, it was found that mean T3, T4 and TSH values were significantly lower at the time of death in comparison to their values at the time of admission. On comparing the thyroid profile among the discharged patients, the mean T3, T4 and TSH values were found to be significantly raised at the time of discharge as compared to their levels at the time of admission. In a study by **Suresh M et al.[(95)] in 2017**, it was found that serum T3 had a significant inverse relationship to the severityof critically ill patients whereas there was no relationship between T4 or TSH levels and severity of illness. In the study by **Patki VK et al.[(98)] in 2014**,it was observed that serum T3, T4 and TSH levels improved in those who survived but failed to improve in expired patients. Similarly, in the study by **Suvarna et al.[(105)] in 2009**, serum T3, T4 and TSH values improved in patients who survived unlike in those who expired.

In this study, both T3 and T4 in the second sample were found to be the true predictors of mortality, i.e. as the T3 and T4 decreases in the second sample, there are less chances of survival. In a study by **Sayarifard F et al.[(88)] in 2018**, they concluded that T3 on admission and T4 at third day of admission might be helpful in predicting disease outcome and patient‟s survival. In the study by **Patki VK et al.[(98)] in 2014**, T4 in second sample were

significant predictors of death. In the study by **Suvarna et al.[105] in 2009**, T4 levels taken at the time of discharge/death were significant predictors of survival.

In this study, it was concluded that T4 levels on admission reflected the patients clinical status and T3 and T4 levels are predictors of mortality. In the study by **Patki VK et al.[98] in 2014**, they concluded that in critically ill children T3 levels reflected the patient‟s clinical status and T4 levels could predict death. In the study by **Suvarna et al.[105] in 2009**, it was concluded that patient‟s clinical status is reflected by T3 while T4 levels could predict chances of survival of the patient.

These observations implies that serum T3 and T4 levels reflects the clinical status of the patients and persistently low serum T3 and T4 levels might reflect poor outcome of the patients. Therefore, it has been suggested that thereduction in thyroid hormone level may be a protective phenomenon to limit protein catabolism and lower energy requirements in non-thyroidal illness(NTI). The degree to which thyroid functions are affected by NTI is related to the severity of the illness and can serve as a useful, if relatively non-specific, prognostic indicator.

In this study, out of all the parameters used for the calculation of PRISM III score, temperature, pH, total CO2, and PO2 were found to be highly significant with p value <0.001×. Heart rate/min, acidosis, Glasgow coma scale, serum creatinine and BUN levels were also found to be statistically significant with p value <0.05. Of these PCO2, prothrombin time, serum potassium, serum glucose, total leucocyte count and platelet count were not found to be significant (pvalue - >0.05) for calculating PRISM III score and prediction of mortality. In the study by **Varma et al.[94] in 2017**, it was observed that among different parameters used for the estimation of PRISM III score, SBP, pupillary reaction to light, Glasgow coma score , acidic pH, total CO2, blood urea nitrogen, platelet count and Partial thromboplastin time showed highly significant association with the mortality and PCO2, PaO2, temperature, serum potassium and serum creatinine showed significant association with mortality. Parameters like Heart rate, serum Glucose, and total leucocyte count did not show significant association with the mortality.

This is suggestive of that PRISM III score on admission could be taken as an initial indicator of illness severity at the time of admission and PRISM III score at 24 hours is true predictor of mortality i.e higher the PRISM III score, higher is the mortality. Therefore, PRISM III score can be used to select critically ill children for admission to PICU and for optimizing the utilization of limited resources available in PICU.

Summary

A hospital based prospective observational study was conducted on patients admitted to the PICU of Department of Pediatrics, Krishna Institute Of Medical Sciences, Karad for duration of 22 months (From December 2017 to September 2019). The aim of the study was to evaluate the thyroid hormone profile in critically ill children and to correlate between the thyroid hormone profile, disease severity and clinical outcome. Total of 50 patients admitted to the PICU of KIMS, Karad fulfilling the eligibility criteria were selected after informed

consent from parents. A detailed systemic examination, relevant investigations and treatment for their disease was instituted and monitored. PRISM III score was calculated at admission and at 24 hours to predict the outcome of the patients. Thyroid evaluation was done twice in all patients, once at admission and second time at the time of discharge or at the time of resuscitation of the patient. Following observations were made during the study-

1. Mean age of patients was found to be 5.74 years old. Majority of patients (58%, 29 patients) were males while 42% (21 patients) were females. Mean of number of days of admission was 14.38 days.
2. Out of total 50 patients, 8 patients (16%) expired during treatment andrest 42 (84%) patients were discharged.
3. Majority of patients (16%, 8 patients) had respiratory system involvement followed by hematopoietic, infectious diseases and central nervous system related disorders.
4. Out of all the parameters used for the calculation of PRISM score, temperature, pH, total CO2, and PO2 were found to be highly significant with p value $<0.001^{\times}$. Heart rate/min, acidosis, Glasgow coma scale, serum creatinine and BUN levels were also found to be statistically significant with p value <0.05.

Conclusion

If thyroid hormone levels are measured early in the course of critical illness, which are considered as predictors of subsequent outcome in the patient, the clinical value of such laboratory assessment will be enhanced as there will be time available for intensive therapeutic intervention.

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