

## “Clinical Outcomes of Critically Ill Children and Correlation with Serum Thyroid Hormone Profile”

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### ABSTRACT

Sick euthyroid syndrome (SES), is the most common endocrine disorder in critically ill patients.<sup>(5)</sup> This syndrome is defined as low levels of tri-iodothyronine (T3), low or normal levels of thyroxine (T4) and normal levels of thyroid stimulating hormones (TSH) in the serum.<sup>(6)</sup> In critically ill patients, the most common disorder in thyroid hormones is low T3 levels.<sup>(7)</sup> Additionally, T4 level also decreases with disease severity<sup>(8-10)</sup> and it has been shown that low T4 level is associated with prognosis.<sup>(10-13)</sup>

### Introduction

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.<sup>(11)</sup> In adults, in different studies significant correlation of serum T3 and T4 levels and patient's prognosis has been shown and mortality is significantly higher in patients of NTI with low T4 and progressively declining T3 levels. However, in children and especially in infants no definite correlation has yet been found.<sup>(25-27)</sup> If the correlation can be established, children with a poor prognosis (low T3 T4 levels) could be identified earlier and this may allow for closer observation and therapeutic intervention.

### 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

1. To evaluate the thyroid hormone profile of critically ill children admitted in PICU.
2. To assess the clinical outcome of the patients using PRISM score.
3. To correlate the thyroid hormone levels with the PRISM SCORE and clinical outcome among the cases.

## THYROID HORMONE SYNTHESIS AND PHYSIOLOGY

### Chemical structure of thyroid hormones

Thyroid hormones play a major role in the development and functional maintenance of many organs<sup>(33)</sup>. They are a group of hormones synthesized and secreted from the thyroid gland, which is located in front of the trachea, below the thyroid cartilage. In general, two compounds, thyroxine (3,5,3',5'-tetra-iodo-L-thyronine, T4) and triiodothyronine (3,5,3'-tri-iodo-L-thyronine, T3), are considered thyroid hormones. In addition, another compound called reverse T3 (3,3',5'-tri-iodo-L-thyronine, rT3) is secreted from the thyroid gland.

The essential molecular structure comprises two iodinated benzene rings connected by ether linkage. T4 is the major hormone secreted from the thyroid gland, whereas the other hormones are mainly generated by the deiodination of T4 in extrathyroidal tissues. The ratio of the secretion of T4:T3:rT3 from the thyroid gland is approximately 100:5:2.5. T3, a bioactive thyroid hormone, is mainly produced by the deiodination of T4 in thyroid hormone target tissues.

### **Thyroid Hormone Metabolism**

In healthy human subjects with an adequate iodine intake, the thyroid gland produces predominantly the prohormone T4 and a small amount of the bioactive thyroid hormone T3. Roughly 80% of T3 is produced by outer ring deiodination (ORD) of T4 in peripheral tissues. The relative contribution of T3 secretion increases in iodine deficiency and other conditions where the thyroid gland is stimulated by TSH or TSH receptor antibodies, since this is associated with increased de novo T3 synthesis and thyroïdal expression of both D1 and D2, and thus increased intra-thyroidal T4 to T3 conversion. Nevertheless, there is good agreement that about 1/3 of T4 daily produced (~130 nmol) in normal humans is converted to T3, which corresponds to about 40 nmol and thus 80% of the estimated total daily T3 production of 50 nmol.

That most plasma T3 is derived from peripheral conversion of T4 is supported by the fact that normal plasma T3 levels are obtained in athyreotic patients treated with sufficient T4 to achieve high-normal plasma (F)T4 levels. Administration of T4 to hypothyroid rats to achieve normal plasma T4 levels results in subnormal plasma T3 levels not only because of the lack of T3 secretion but also because of a decreased T3 production by D1 in peripheral tissues, since this enzyme is under positive control of T3 itself<sup>(40)</sup>.

Besides ORD to T3, T4 is converted by inner ring deiodination (IRD) to the metabolite rT3, which accounts for about 40% of T4 turnover, while thyroïdal secretion of rT3 is negligible. T3 and rT3 undergo further deiodination, predominantly to the common metabolite 3,3'-diiodothyronine (3,3'T2), which is generated by IRD of T3 and by ORD of rT3<sup>(35-39)</sup>. Thus, ORD is an activating pathway by which the prohormone T4 is converted to active T3, whereas IRD is an inactivating pathway by which T4 and T3 are converted to the metabolites rT3 and 3,3' T2, respectively.

### **SUMMARY**

The process of THs synthesis, storage and secretion requires a series of highly regulated steps:

- Uptake of iodide: iodide from plasma is actively transported by a sodium- iodine symporter on basal membrane of thyrocytes.
- Oxidation of iodide to iodine: this occurs on the luminal side of the apical membrane and requires thyroid peroxidase (TPO) and hydrogen peroxide, which is generated by a calcium-dependent flavoprotein enzyme system situated at the apical membrane.
- Organification: incorporation of iodine into tyrosyl residues on thyroglobulin. MIT and DIT are formed through action of TPO.
- Coupling of MIT and DIT: If two DIT molecules couple together, the result is the formation of T<sub>4</sub>; If a MIT and a DIT are coupled together, the result is the formation neither T<sub>3</sub> or rT<sub>3</sub>. T<sub>4</sub>, T<sub>3</sub> and rT<sub>3</sub> remain linked to thyroglobulin.
- Internalization: when there is demand for THs, Tg is internalized by pinocytosis and appears as colloid droplets that fuse with lysosomes and undergo proteolytic degradation to release: T<sub>4</sub>, T<sub>3</sub>, MIT and DIT; any MIT and DIT is deiodinated and the iodine conserved.
- Delivery of T<sub>4</sub> and T<sub>3</sub> into the circulation.
- TSH appears to stimulate each of the above processes.

PRISM III is a widely accepted and is a standard against which other scores are compared. However there some problems with the use of PRISM III: - A lot of information is needed to calculate it and many units do not calculate it routinely. Worst reading of 12/ 24 hours is used and a lot of deaths occur (in one study over 40%) within first 24 hours, so the score may be diagnosing death rather predicting it. There may be blurring of differences of 2 units as patient in a good unit may recover rapidly and score may be lower and the same patient in a bad unit might have had higher score due to poor management and high mortality of bad unit may be interpreted as due to sicker patients. The time spent in the hospital before coming to ICU could improve the PRISM score and predict lower than actual mortality (lead time bias)<sup>(80)</sup>.

Uses of models of mortality prediction including PRISM III: - These models including PRISM III are most applicable to groups of patients (e.g. to assess institutional performance). These models help us to investigate best ways of organizing PICU by comparing different units.<sup>(81)</sup> They also help us to monitor effect of change in practice by observing trends within the unit over a time.<sup>(80)</sup> They can also be used for controlling severity of illness for various clinical trials.<sup>(79)</sup> They can be applied for resource utilization (rationing intensive care).

PRISM III takes 24 hours to complete and can't be used in regulating admission to PICU.<sup>(82)</sup> They have been used to assess relation between severity of illness and length of stay or cost.

**Yanni GN et al<sup>(83)</sup> in 2019**, conducted a study to evaluate thyroid hormone profile in children with sepsis as well as to assess the association between thyroid level and sepsis outcome. An observational cohort study was conducted in 80 children. T<sub>3</sub> and T<sub>4</sub> level were measured on day 1 and after > 72 hours of sepsis being diagnosed. They recorded length of stay in PICU, patient outcome and analysed the relationship with the chi-square

test. Level of T3 and T4 were decreased on day 1 in paediatric sepsis. Of 80 subjects, 57 (71.2%) with low-level T3 and 41 (51.2%) with low T4 were found. The relationship between T3 and T4 level on day 1 with the length of stay were not found ( $P = 0.500$ ;  $P = 0.987$ ). There was a significant relationship between level of T3 and T4 with outcome ( $P = 0.0001$ ; OR 24.706;  $P = 0.014$ ; OR 3.086). They concluded that the Euthyroid Sick Syndrome in children with sepsis does exist. There was a significant relationship between T3 and T4 level on day 1 with patient outcome.

**El-Ella SS, El-Mekkawy MS, El-Dihemey MA<sup>(84)</sup>** conducted a study in **2019** to assess the prevalence and prognostic value of non-thyroidal illness syndrome (NTIS) among critically ill children. A prospective observational study was conducted on 70 critically ill children admitted into paediatric intensive care unit (PICU). Free triiodothyronine (FT3), free thyroxine (FT4), and thyroid stimulating hormone (TSH) were measured within 24 h of PICU admission. Primary outcome was 30-day mortality. They found that NTIS occurred in 62.9% of patients but it took several forms. The commonest pattern was low FT3 with normal FT4 and TSH (25.7% of patients). Combined decrease in FT3, FT4, and TSH levels occurred in 7.1% of patients. An unusual finding of elevated TSH was noted in three patients, which might be related to the disease severity. Low FT4 was significantly more prevalent among non-survivors compared with survivors. NTIS independently predicted mortality. Concomitant decrease in FT3, FT4, and TSH was the best independent predictor of mortality. TSH negatively correlated with length of PICU stay. FT3 level was significantly lower among patients who received dopamine infusion compared with those who did not receive it. They suggested that larger studies were needed to better evaluate the prognostic value of NTIS in critically ill children

**Kumar KH et al<sup>(100)</sup>** in **2013** studied the thyroid hormone profile, prolactin and, glycosylated haemoglobin (HbA1c) at admission and analysed their correlation with mortality. A single centre, prospective, observational study, was conducted on 100 consecutive patients admitted to medical ICU irrespective of diagnosis. Patients with previous thyroid disorders and drugs affecting thyroid function were excluded. All participants underwent complete physical examination and a single fasting blood sample obtained at admission was analysed for total triiodothyronine (T3), total thyroxine (T4), thyroid stimulating hormone (TSH), HbA1c, and prolactin. The patients were divided into two groups: Group 1 — survivors (discharged from the hospital) and Group 2 — non-survivors (patients succumbed to their illness inside the hospital). The data were analysed by appropriate statistical methods and a P-value of  $<0.05$  was considered significant. A total of 64 patients survived, whereas remaining 36 succumbed to their illness. The baseline demographic profile was comparable between survivors and non-survivors. Non-survivors had low T3 when compared with survivors ( $49.1 \pm 32.7$  vs.  $66.2 \pm 30.1$ ,  $P = 0.0044$ ). There was no significant difference observed between survivors and non-survivors with respect to T4, TSH, HbA1c, and prolactin. They concluded that low T3 is an important marker of mortality in critically ill patients and that admission HbA1c, prolactin, T4, and TSH did not vary between survivors and non-survivors.

**Khajeh A et al<sup>(101)</sup>** in **2013**, performed a study to evaluate the efficacy of PRISM score in prediction of mortality rate in PICU. In this cohort study, 221 children admitted during an 18-month period to PICU, were enrolled. PRISM score and mortality risk were calculated. Follow up was noted as death or discharge. Results were analysed by Kaplan-Meier curve, ROC curve, Log Rank (Mantel-Cox), Logistic regression model using SPSS 15. Forty-

seven patients died during the study period. The PRISM score was 0-10 in 71%, 11- 20 in 20.4% and 21-30 in 8.6%. PRISM score showed an increase of mortality from 10.2% in 0-10 score patients to 73.8% in 21-30 score ones. The survival time significantly decreased as PRISM score increased ( $P \leq 0.001$ ). A 7.2-fold mortality risk was present in patients with score 21-30 compared with score 0-10. ROC curve analysis for mortality according to PRISM score showed an under-curve area of 80.3%. They concluded that PRISM score was a good predictor for evaluation of mortality risk in PICU.

**Tognini S et al<sup>(104)</sup> in 2010**, conducted a study to evaluate the prevalence of NTIS, its impact on patients' survival and the possible pathogenic role of systemic inflammation. An observational cross-sectional study was done on three hundred and one acutely ill older patients consecutively admitted to a primary care unit. Serum FT3, FT4 and thyrotropin levels as well as acute inflammation indexes were evaluated. The NTIS prevalence (specifically low T3 syndrome) was 31.9%. A significant association was found between NTIS and acute renal failure ( $P = 0.006$ ), New York Heart Association classification (NYHA) IV heart failure ( $P = 0.003$ ) and metastasised cancer disease ( $P = 0.0002$ ). Serum FT(3) values correlated inversely with serum C-reactive protein ( $P < 0.0001$ ), lactate dehydrogenase ( $P = 0.0004$ ), fibrinogen ( $P = 0.03$ ) and erythrocyte sedimentation rate ( $P < 0.0001$ ) values, and progressively decreased with increasing percentiles of age ( $P = 0.0004$ ). The mortality rate was significantly higher ( $P = 0.0002$ ) among patients with low T3 syndrome, which emerged as the sole predictive factor of death (odds ratio 4.3; 95% confidence interval 1.7-10.5). They concluded that low T3 syndrome is very common in the hospitalised older population, emerging as the most sensitive independent predictor of short-term survival. They also strongly felt that serum FT3 determination should be included in the assessment of short- term prognosis of acutely ill older patients.

### Material and Methods

**Study Design:** Hospital Based Prospective, Observational Study

**Study Duration:** 22 months from DECEMBER 2017 to SEPTEMBER 2019.

**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 total sample 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  $>5\text{mcg/kg /min}$ ,
2. Any dose of adrenaline,

3. Mechanical ventilation,
4. Serum creatinine >1 mg/dl,
5. Platelet count < 1,00,000/mm<sup>3</sup>
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 dysfunction.
3. Patients on any thyroid medications.
4. Patients who expired within 24 hours of admission.

#### Study Methodology

The critically ill patients admitted in PICU of Krishna hospital, fulfilling the inclusion criteria were selected for the study and written informed consent was taken from the parents. After taking complete history, detailed clinical examination was done and relevant investigations were sent for all the patients enrolled for the study.

PRISM III score (Pediatric Risk of Mortality scores) was used to predict the severity of disease and clinical outcome. It consists of 17 parameters: Systolic blood pressure, temperature, heart rate, pH, acidosis, total CO<sub>2</sub>, PaO<sub>2</sub>, PaCO<sub>2</sub>, Glasgow coma scale score, pupillary reflex, prothrombin time and partial thromboplastin time, serum creatinine, serum potassium, glucose, blood urea nitrogen, platelet count, and total leucocyte count. PRISM III score was calculated on admission and at 24 hours of admission. For this 8ml of venous sample was collected which was divided into 3ml of plain sample, 3ml of sodium citrate sample and 2ml of EDTA sample. Along with this 1ml of arterial blood sample was also collected.

Thyroid hormone profile was evaluated for all the patients enrolled for the study and was correlated with the PRISM score and the outcome of the patient. For this 5ml of plain sample was collected twice, first at the time of admission and second sample at discharge or at the time of resuscitation depending on the outcome of the patient.

The PRISM score was divided into 3 groups- group 1- score <25, group 2- score 25-40, group 3 — score >40. Outcome of the disease was correlated with PRISM score groups.

Patients were also divided on the basis of total number of admission days into three groups- group 1- <15 days, group 2- 15-30 days and group 3- >30 days and correlated with the disease severity.



TT3 KITS

T4 KITS

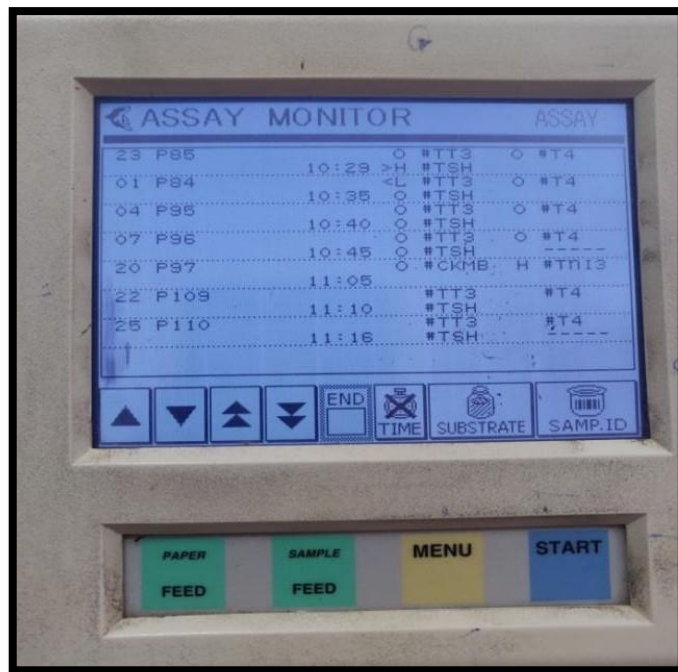


Figure 1- THYROID ASSAY MONITOR



Figure 2 - CBC AUTOANALYSER



Figure 3 - PT/INR ANALYSER



### Statistical Analysis

Data were described statistically in terms of frequencies (number of cases), percentages and mean ( $\pm$  SD) when appropriate. Comparison of quantitative variables between discharged and expired patients was done using Paired and Unpaired Student- t test or ANOVA test for independent samples if they are normally distributed. For comparison of categorical data, Chi square test was performed. A probability value (pvalue) of  $< 0.05$  was considered statistically significant. Area under ROC curve was evaluated to find the diagnostic accuracy of thyroid function tests and PRISM score as screening tests for predicting outcome. Correlation between PRISM score and thyroid profile was computed by using Pearson-correlation coefficient. Logistic regression analysis was also performed to find the significant predictors of outcome by taking outcome as dependent variable and thyroid function and PRISM score as independent variable by Forward Stepwise Wald Method. All statistical calculations were done using SPSS (Statistical Package for the Social Science) version 20.

**Table 1: Distribution based on vitals examined on arrival and after 24hours (parameters used to calculate PRISM score)**

Parameters	On arrival (Mean $\pm$ SD)	After 24 hours (Mean $\pm$ SD)	p-value
SBP (mmHg)	97.68 $\pm$ 27.04	104.3 $\pm$ 15.62	0.02926
HR (/min)	125.2 $\pm$ 30.87	112.9 $\pm$ 28.93	0.00253**
Temperature (°C)	100.49 $\pm$ 1.48	99.59 $\pm$ 1.37	$<0.001^*$
Acidosis	1.2 $\pm$ 1.85	0.6 $\pm$ 1.16	0.00294**
pH	7.24 $\pm$ 0.18	7.32 $\pm$ 0.115	$<0.001^*$
Total CO2	18.79 $\pm$ 6.25	21.23 $\pm$ 6.20	$<0.001^*$
PO2	100.10 $\pm$ 40.87	118.82 $\pm$ 32.76	$<0.001^*$
PCO2	38.37 $\pm$ 24.73	35.6 $\pm$ 15.11	0.26873
GCS	11.84 $\pm$ 3.34	12.38 $\pm$ 2.93	0.00447**
PT	20.56 $\pm$ 11.86	19.64 $\pm$ 9.27	0.0724
Creatinine	1.098 $\pm$ 0.49	0.948 $\pm$ 0.247	0.00502**
BUN	42.86 $\pm$ 36.47	33.86 $\pm$ 21.62	0.00442**
Potassium	4.018 $\pm$ 0.84	3.974 $\pm$ 0.758	0.45065
Glucose	112.38 $\pm$ 60.10	117.86 $\pm$ 39.74	0.30219
TLC	13816 $\pm$ 8283.77	13261 $\pm$ 7885.64	0.21978
Platelets	217360 $\pm$ 152694.4	216500 $\pm$ 158408.1	0.89846

Various parameters; systolic BP, heart rate, temperature, acidosis, pH, CO<sub>2</sub>, PO<sub>2</sub>, PCO<sub>2</sub>, Glasgow coma scale, prothrombin time, serum creatinine, BUN, serum potassium, serum glucose, TLC, and platelet count were studied on admission and after 24 hours of admission. Out of all the parameters, temperature, pH, total CO<sub>2</sub>, and PO<sub>2</sub> 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 PCO<sub>2</sub>, 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.

**Table 2: Correlation of thyroid profile done on arrival and at the time of discharge/death**

Thyroid parameter	On admission (Mean ± SD)	At the time of discharge/death (Mean ± SD)	p-value
<b>T3</b>	76.74±33.30	101±37.58	<0.001*
<b>T4</b>	7.24±2.54	8.57±3.07	<0.001*
<b>TSH</b>	2.81±1.54	3.67±1.55	<0.001*

Thyroid profile tests were done twice. First sample was taken at the time of admission and second at discharge or at the time of resuscitation depending on the outcome of the patient. On correlating the thyroid hormone profile of all the patients irrespective of the outcome, we found statistically significant increase in the levels of mean T3, T4 and TSH at the time of discharge or death (pvalue <0.001).

**Table 3: Distribution of PRISM score (after 24 hours) and its correlation with thyroid parameters**

Thyroid parameter	r-value	p-value
<b>On arrival</b>		
<b>T3</b>	-0.233	<0.001*
<b>T4</b>	-0.367	0.5519
<b>TSH</b>	-0.426	<0.001*
<b>At discharge/death</b>		
<b>T3</b>	-0.396	<0.001*
<b>T4</b>	-0.598	0.5826
<b>TSH</b>	-0.025	<0.001*

PRISM score studied at 24 hours of admission had significant negative correlation with T3 and TSH levels on admission which means higher the prism score at 24 hours, lesser will be T3 and TSH values on admission. This relationship was found to be significant with p value of <0.001. Similarly PRISM score at 24 hours of admission had negative correlation with T3 and TSH values on discharge/death with p value of <0.001. There is no significant correlation between prism score at 24 hours of admission and T4 levels on admission and at the time of discharge/death. (pvalue 0.55 and 0.58 respectively).

**Table 4: Area under ROC curve for the various variables used in the study to give the cut off values for prediction of clinical outcome**

Variables	AU- ROC	Cut off value	Sensitivity	95% CI	Specificity	95% CI
PRISM on admission with Outcome (expired) as classification variable	0.805	>11	62.50	24.5-91.5	76.19	60.5-87.9
PRISM at 24 hrs with Outcome (expired) as classification variable	0.896	>9	87.50	47.3-99.7	90.48	77.4-97.3
T3 ng/dl on admission with Outcome (expired) as classification variable	0.698	≤82	62.50	24.5-91.5	57.14	41.0-72.3
T4 mcg/dl on admission with Outcome (expired) as classification variable	0.765	≤8.8	75.00	34.9-96.8	38.10	23.6-54.4
TSH μU/ml on admission with Outcome (expired) as classification variable	0.625	>2.7	37.5	8.5-75.5	57.14	41.0-72.3
T3 ng/dl on discharge/death with Outcome (expired) as classification variable	0.997	≤55	100	63.1-100	97.62	87.4-99.9
T4 mcg/dl on discharge/ death with Outcome (expired) as classification variable	0.975	≤6.7	100	63.1-100	88.10	74.4-96.0
TSH μU/ml on discharge/ death with Outcome (expired) as classification variable	0.738	≤4.84	75.0	34.9-96.8	23.81	12.1-39.5

### Prism Score and Survival

Pediatric Risk of Mortality Score or PRISM scores are generally used to predict survival in sick neonates, infants, children, or adolescents. In this study, significant correlation was

found between PRISM score groups at admission as well as at 24 hours and the outcome with pvalue of  $<0.05$ , which is suggestive of lesser the PRISM score, better is the outcome. Mean PRISM score among discharged patients showed significant improvement at 24 hours of admission from the baseline values (5.9 vs 9.4, pvalue- 0.00018). While no significant change was observed in the mean PRISM score among the expired patients at 24 hours of admission from the baseline values (18.1 vs 20, pvalue- 0.361). The mean PRISM score on admission was significantly higher among expired patients in comparison to discharged patients ( $p < 0.001^*$ ). Therefore, PRISM score shows significant correlation with the outcome i.e higher the PRISM score worse is the prognosis and lesser chances of survival. No significant correlation was found between the duration of hospital stay and the PRISM score groups.

Area under ROC curve showed that PRISM score at 24 hours have a significant diagnostic accuracy to predict the outcome in critically ill children (AUROC- 0.896) with a cut off value  $>9$ , having sensitivity and specificity of 87.5% and 90.4% respectively. We also observed that PRISM score at 24 hours is the true predictor of outcome in critically ill children on logistic regression analysis i.e. more the PRISM score at 24 hours, lesser are the chances of survival.

**Bora R<sup>(85)</sup> in 2019**, undertook a study to evaluate the efficacy of PRISM III score in prediction of mortality, it was observed that as PRISM III score increases, mortality also increases approaching almost 100% with a score of more than or equal to 25 and suggested that PRISM III score with AUROC of 0.866 offered a good discriminative power. In a study by **Patel S et al.<sup>(86)</sup> in 2019**, PRISM III score on admission was higher among those who subsequently expired and concluded that since mortality rises with increase in PRISM III score at admission, therefore, PRISM III score could be considered as an indicator of the illness severity initially at the time of admission. In the study by **Popli V and Kumar A<sup>(91)</sup> in 2018**, it was observed that as PRISM III score increases, mortality also increases approaching almost 100% with a score of more than or equal to 19. Duration of PICU stay increases with increasing PRISM III score up to score of 14 and thereafter duration of stay gradually decreases with increasing score. The overall performance of the PRISM III score was good with AUROC of 0.871 (good discrimination). Similar findings were observed in the study by **Mukhtar FR et al.<sup>(92)</sup> in 2018**. In the study by **Suvarna et al.<sup>(105)</sup> in 2009**, PRISM score at 24 hours was concluded to be significant predictor of survival.

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. On comparing thyroid profile between discharged and expired patients, T3 at discharge/death and T4 both at admission and at the time of discharge/death were found to be significantly lower among expired patients. No significant change was observed in levels of TSH both at admission and at the time of discharge/death.
2. 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.

3. 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.
4. Significant correlation was found between PRISM score groups at admission as well as at 24 hours and the outcome with p value of <0.05, which is suggestive of lesser the PRISM score, better is the outcome.
5. The mean PRISM score on admission was significantly higher among expired patients in comparison to discharged patients ( $p < 0.001^*$ ). Therefore, PRISM score shows significant correlation with the outcome i.e. higher the PRISM score worse is the prognosis more chances of mortality.

## CONCLUSION

PRISM score at 24 hours, T3 and T4 levels at the time of discharge/death are true predictors of outcome in critically ill children i.e. more the PRISM score at 24 hours and less the T3 and T4 levels at discharge/death, lesser are the chances of survival. Thyroid hormone profile can be used as a predictor of mortality which is easy to evaluate and as a substitute of PRISM score which consist of 17 parameters and is more cumbersome to calculate.

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