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Serum Thyroid Hormone ProfileCorrelation With Critically Ill

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Abstract

These thyroid hormone changes may be mediated in part by cytokines or other inflammatory mediators, acting at the level of the hypothalamus and pituitary, the thyroid gland, and the hepatic deiodinase system, as well as on binding of thyroxine to thyroid binding globulin.[15]

Introduction

Under normal circumstances 100% of thyroxine and 10-20% of tri- iodothyronine are secreted directly by the thyroid gland. Monodeiodination of T4 contributing to 80-90% of T3 is caused by 5` deiodinase in the periphery and it also increases the clearance of the inactive isomer reverse T3 (rT3) (which is formed by the action of type III 5` deiodinase on T4).[9] Critical illness decreases the activity of 5`deiodinase, thereby, decreasing conversion of T4 to T3 and clearance of rT3.[6] Increased metabolic clearance of T4 in critical illness further diverts T4 to form the inactive isomer rT3.[8,16].Thus, in critical illness T3 reduces and rT3 increases.[7]

So far, most studies on thyroid function and its association with prognosis or illness severity have been carried out on adults, especially surgical patients.[28-29] , and there are only a few studies on critically ill children. Therefore, this study was performed to evaluate thyroid function in critically ill children and to assess the correlation of thyroid hormone levels with the disease outcome.

Objectives

1. To evaluate the thyroid hormone profile of critically ill children admittedin 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.

Review of Literature

The thyroid gland is divided into two lobes that are connected by the isthmus, which crosses the midline of the upper trachea at the second and third tracheal rings. In its anatomic position, the thyroid gland lies posterior to the sternothyroid and sternohyoid muscles, wrapping around the cricoid cartilage and tracheal rings. It is located inferior to the laryngeal thyroid cartilage,typically corresponding to the vertebral levels C5-T1.[32]

The thyroid attaches to the trachea via a consolidation of connective tissue, referred to as the lateral suspensory ligament or Berry‟s ligament. This ligament connects each of the thyroid lobes to the trachea. The thyroid gland, along with the oesophagus, pharynx, and trachea, is found within the visceral compartment of the neck which is bound by pretracheal fascia.

The "normal" thyroid gland has lateral lobes that are symmetrical with a well- marked centrally located isthmus. The thyroid gland typically contains a pyramidal extension on the posterior-most aspect of each lobe, referred to as the tubercle of Zuckerkandl.

Thyroid Hormone Production by TG Molecule Hydrolysis

Internalized vesicles containing TG-thyroid hormone complex fuse with lysosomes, resulting in complex breakdown and thyroid hormone release. This also produces iodotyrosines (monoiodotyrosine and diiodotyrosine). TG is further degraded to produce amino acids. Iodotyrosines are deiodinated by iodotyrosine dehalogenase to produce free iodine and are recycled in the follicular epithelial cells.

Secretion of Thyroid Hormone

After TG degradation, thyroid hormone (mainly T4) is secreted into the bloodstream at the basal membrane. Although the precise mechanisms of thyroid hormone secretion have not yet been completely clarified, thyroid hormone transporters, particularly monocarboxylate transporter (MCT) 8, may play a major role in secretion [37]. MCT8 comprises 539 amino acids in humans and 4 Molecular Mechanisms of Thyroid Hormone Synthesis and Secretion 77 contains 12 transmembrane domains. It promotes the uptake and secretion of thyroid hormone. However, MCT8 disruption cannot completely inhibit thyroid hormone secretion, indicating that additional mechanisms may be involved.

Effect of TSH on Thyroid Hormone Synthesis

TSH, a glycoprotein hormone, is secreted from the anterior pituitary. It comprises an α-subunit, which is common to other glycoprotein hormones such as luteinizing hormone and follicle-stimulating hormone, and a β-subunit,which is unique to TSH. It binds to the TSH receptor (TSHR), a G-protein- coupled receptor. It is translated into a protein comprising

764 amino acids, followed by cleavage of a 352–366- amino acid peptide, resulting in the formation of extracellular A and B subunits containing seven transmembrane domains [(38)]. TSHR activates both the Gs-adenyl cyclase-cAMP and Gq/11- phospholipase C-β signalling pathways[(39)]. The cAMP pathway regulates many steps in the synthesis and secretion of thyroid hormone, such as the expression of NIS, TG, and TPO, iodide uptake, and hormone secretion, whereas Gq/11-phospholipase C-β pathway activates iodine organification (activation of H2O2 production, see above) by stimulating intracellular calcium mobilization and iodide efflux from the apical membrane. TSH also stimulates follicular epithelial cell proliferation.

Release of T4 and T3 from thyroid gland

Thyroid epithelial cells ingest colloid by endocytosis from their apical membrane. Colloid contains thyroglobulin molecules that consist of MIT, DIT, T3 and T4. Colloid-laden endosomes fuse with lysosomes, which contain proteolytic enzymes that digest TG, thereby liberating THs. Free THs apparently diffuse out of lysosomes, through the basal plasma membrane of the cell into blood where they bind to carrier proteins for transport to target cells. Proteolysis also results in the liberation of MIT and DIT that are usually degraded within thyroid follicular cells and their iodine is retained and re- utilized. A small amount of thyroglobulin also reaches the bloodstream. The major product of the thyroid gland is T4. T3 is produced 10 times less but most T3 is derived from T4 by deiodination in peripheral tissues, liver, kidneys and muscle, catalysed by deiodinases. T3 is 3-4 times more potent than T4. In tissues, most of the effect of T4 results from this conversation to T3, so that T4 is a prohormone. Deiodination can also produce rT3, which is physiologically inactive. The majority of the activation of the prohormone T4 to the T3 occurs through non-thyroidal deiodination. Three deiodinase families are recognized and are termed as isoforms type I, II and III. Type I deiodinase is the major enzyme in the liver and kidneys. Type II enzyme is found in the heart, skeletal muscle, central nervous system, fat and thyroid. Type III deiodinase isoform is found in foetal tissue and placenta. Further degradation of rT3 and T3 results in the formation of several distinct diiodothyroxines (T2). The metabolic role of the T2 isomers is poorly understood and is unclear in humans. When T4 is released from the thyroid, it is primarily in a bound form with thyroxine-binding globulin (TBG), with lesser amounts bound to thyroxine-binding prealbumin (TBPA) and albumin. Only 0.03-0.05% of T4 within the circulatory system is in a free (unbound) form (fT4). In peripheral tissues, T4 is either converted to T3 or rT3, or eliminated. The half-life of T4 is 5-7 days. T3 is considered to be the most metabolically

active thyroid hormone. Although some T3 is produced in the thyroid, approximately 80% is generated outside the gland, primarily by conversion of T4 in the liver and kidneys. The nervous system is capable of converting T4 to T3. Majority of circulating T3 is in a bound form. TBPA and albumin, not TBG, are the binding proteins with high affinity for T3. Approximately 0.2% of T3 is in unbound or free form (fT3) in normal subjects. The half-life of T3 is 1-2 days. The normal plasma concentrations of T4 and T3 are 60-150nmol/L and 1.0-2.9nmol/L, respectively. Both hormones are extensively protein bound, some 99.98% of T4 and 99.66% of T3 are bound principally to a specific TBG and, to a lesser extent, to prealbumin and albumin.

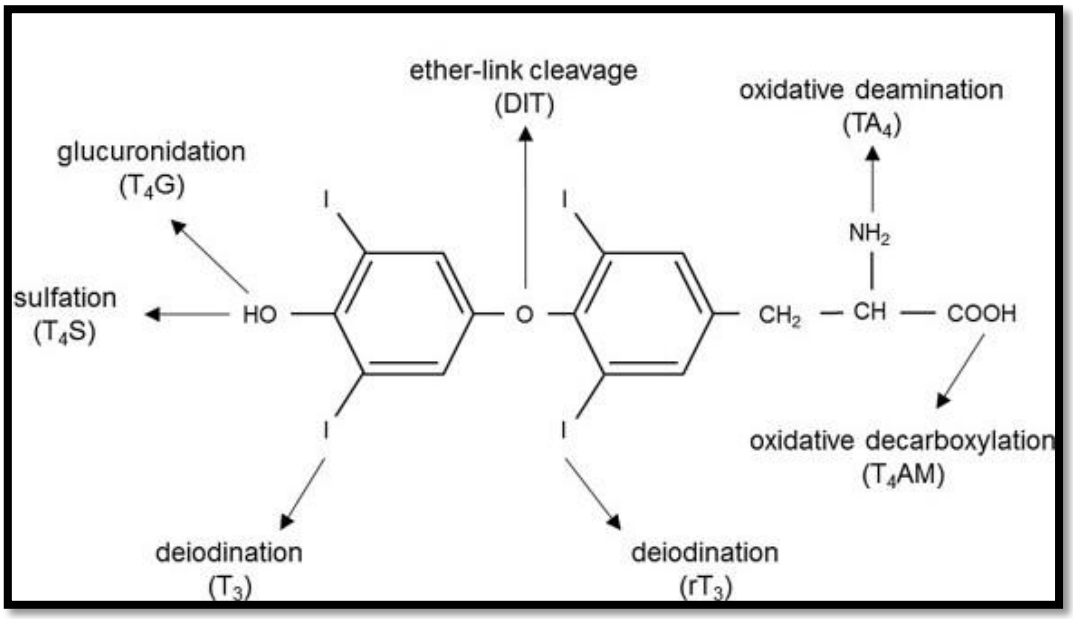
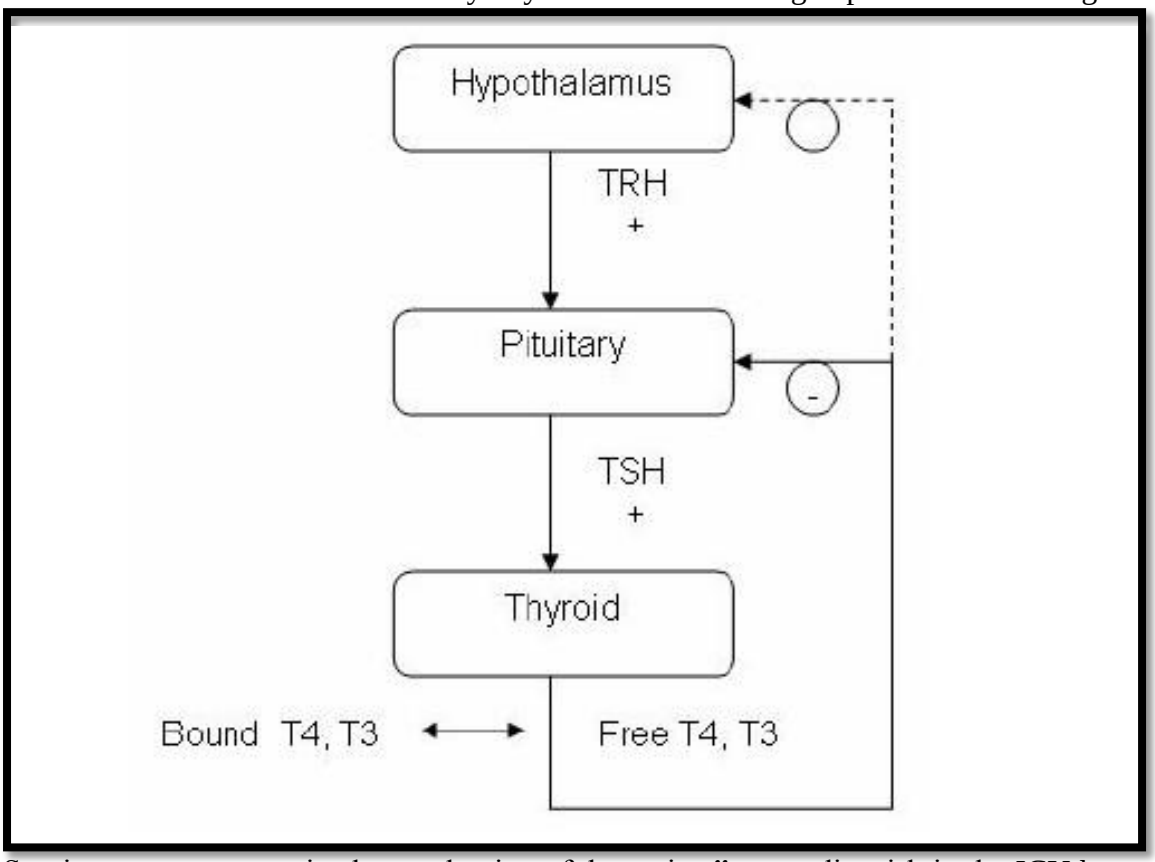


Figure 1: Pathways of thyroid hormone metabolism

Control of Thyroid Hormone Synthesis And Secretion

The most important regulator of thyroid homeostasis is thyroid-stimulating hormone[(47)] (thyrotrophin; TSH). The secretion of TSH is controlled by negative feedback by the THs hormones, which modulate the response of the pituitary to the hypothalamic hormone, thyrotrophin-releasing hormone (TRH, thyroliberin). The feedback mechanisms result in maintain of steady plasma concentrations of THs. TSH is glycoprotein hormone composed of alpha and beta subunits which are non-covalently bound to one another. Free alpha and beta subunits have essentially no biological activity. TSH is secreted from cells called thyrotrophs in the anterior pituitary gland. TRH is major controller of TSH secretion. TRH is secreted by hypothalamic neurons into hypothalamic-hypophyseal portal blood and through its receptors on thyrotrophs stimulates secretion of TSH. Secretion either TRH or TSH

hormones is inhibited by high blood concentrations of free THs in a classical negative feedback loop. The basic mechanisms for control in this system are: hypothalamus neurons secrete TRH which stimulates pituitary gland to secrete TSH; TSH stimulates thyroid gland to secrete THs; when blood levels of THs increase above a certain threshold TRH secretion is inhibited; inhibition of TRH secretion leads to inhibition of TSH secretion; inhibition of TSH secretion leads to inhibition of THs secretion in blood. Binding of TSH to receptors on thyroid epithelial cells (TSHR) seems to enhance all of the processes necessary for synthesis of THs, including synthesis of iodide transporter, thyroid peroxidase and thyroglobulin. High concentrations of TSH lead to faster rates of endocytosis and THs release into the blood. Conversely, when TSH levels are low, rates of thyroid hormone synthesis and release are diminished. TSH modifies THs synthesis by binding to a specific TSHR on the basal membrane of the thyrocyte. TSHR is a single protein with a large



Scoring systems are arrived at evaluation of the patient‟s mortality risk in the ICU by assigning a score to patient and predicting the outcome. However, patient‟s mortality is not only affected by ICU performance but also depends on many other factors such as demographic and clinical characteristic of population, infrastructure and non-medical factors (management and organization), case mix and admission practice[77]. The ideal probability model or scoring system would be institution independent and

population independent.

Paediatric Risk Of Mortality (PRISM)

Paediatric risk of mortality (PRISM) score allows for mortality risk assessment in the paediatric ICU. PRISM was developed from Physiologic Stability Index (PSI) to reduce the number of variables from 34 to 14 and number of ranges from 75 to 23 without losing the predictive power. It is institution independent and can be used within limits to compare different intensive care units [78]

In 1996 physiological variables and their ranges as well as diagnostic and other risk variables reflective of mortality risk were re-evaluated by Pollack MM et al to update and improve the performance of second-generation PRISM score. Thus, PRISM III was developed[(79)].

PRISM III

This was based upon a sample of 11,165 consecutive admissions to 32paediatric ICUs (10% of PICUs of USA) representing a wide diversity oforganizational and structural characteristics [(79)]. The variables that were most predictive of mortality as indicated by the highest PRISM scores were systolic BP, abnormal pupillary reflexes and stupor/coma were retained from PRISM score. Variables in the original PRISM that were not included in PRISM III are diastolic BP, respiratory rate, PaCO2/F1O2, serum bilirubin and calcium concentration. PRISM III has 17 physiologic variables subdivided into 26 ranges and is population independent

Age Group	**Age Range**
neonate	0 to < 1 month
infant	1 to 12 months
child	> 12 to 144 months (12 years)
adolescent	> 144 months (> 12 years)

Sub scores:

(1) Cardiovascular and neurologic vital signs: 5 measures

(2) Acid-base and blood gas: 5 measures

(3) Chemistry tests: 4 measures

(4) Haematology tests: 3 measures (with PT and PTT counted as one) Grading variables:

- Use the highest and/or lowest values for scoring.

Cardiovascular and Neurologic Vital Signs	**Findings**	**Points**
Systolic blood pressure	neonate AND > 55 mm Hg	0
	neonate AND 40 -55 mm Hg	3
	neonate AND < 40 mm Hg	7
	infant AND > 65 mm Hg	0
	infant AND 45 -65 mm	3
	Hg infant AND < 45 mm Hg	7
	child AND > 75 mm Hg	0
	child AND 55 -75 mm Hg	3
	child AND < 55 mm Hg	7
	adolescent AND > 85 mm Hg	0
	adolescent AND 65 -85 mm Hg	3
	adolescent AND < 65 mm Hg	7
Heart rate	neonate AND < 215 beats/minute	0
	neonate AND 215 - 225 bpm	3
	neonate AND > 225 beats/minute	4
	infant AND < 215 beats/minute	0
	infant AND 215 - 225 bpm	3
	infant AND > 225 beats/minute	4
	child AND < 185 beats/minute	0
	child AND 185 - 205 bpm	3
	child AND > 205 beats/minute	4
	adolescent AND < 145 bpm	0
	adolescent AND 145 - 155 bpm	3
	adolescent AND > 155 bpm	4
Temperature	< 33°C	3
	33 - 40°C	0
	> 40°C	3
Mental status	Glasgow coma score >= 8	0
	Glasgow coma score < 8	5
Pupillary response	both reactive	0
	1 reactive AND (1 fixed AND > 3mm)	7
	both fixed AND both > 3 mm	11

where:

- The heart rate should not be monitored during crying or iatrogenic agitation.
- Pupillary size should not be assessed after iatrogenic dilatation.
- Body temperature may be rectal, oral, axillary or blood.
- Mental status should not be scored within 2 hours of sedation, paralysis or anaesthesia.

If sedation, paralysis or anaesthesia is continuous, score-based status prior to sedation, paralysis or anaesthesia

Acid-Base and Blood Gases	**Findings**	**Points**
Acidosis	pH > 7.28 AND total CO2 >= 17 mEq/L	0
	(pH 7.0 - 7.28) OR (total CO2 5 - 16.9 mEq/L)	2
	pH < 7.0 OR total CO2 < 5	6
Ph	< 7.48	0
	7.48 - 7.55	2
	> 7.55	3
PCO_2	< 50 mm Hg	0
	50 - 75 mm Hg	1
	> 75 mm Hg	3
Total CO_2	<= 34 mEq/L	0
	> 34 mEq/L	4
PaO_2	>= 50 mm Hg	0
	42.0 - 49.9 mm Hg 3	3
	< 42 mm Hg	6

where:

- PaO2 requires arterial blood.
- PCO2 can be measured from arterial, venous or capillary specimens

Chemistry tests	**Findings**	**Points**
Glucose	<= 200 mg/dL	0
	> 200 mg/dL	2
Potassium	<= 6.9 mEq/L	0
	> 6.9 mEq/L	3
Creatinine	neonate AND <= 0.85 mg/dL	0
	neonate AND > 0.85 mg/dL	2
	infant AND <= 0.90 mg/dL	0
	infant AND > 0.90 mg/dL	2
	child AND <= 0.90 mg/dL	0
	child AND > 0.90 mg/dL	2
	adolescent AND <= 1.30mg/dL	0
	adolescent AND > 1.30 mg/dL	2
BUN	neonate AND <= 11.9 mg/dL	0
	neonate AND > 11.9 mg/dL	3
	not neonate AND <= 14.9 mg/dL	0
	not neonate AND > 14.9 mg/dL	3

where:

• Whole blood measurements for glucose are increased 10% over serum; for potassium 0.4 mEq/L.

Hematologi ctests	**Finding s**	**Point s**
white blood cell count	>= 3,000 per µL < 3,000 per µL	0 4
platelet count	> 200,000 per µL	0
	100,000 - 200,000 per µL	2
	50,000 - 99,999 per µL 4	4
	< 50,000 per µL	5
PT and PTT	neonate AND PT <= 22 seconds AND PTT <= 85 s	0
	neonate AND (PT > 22 seconds OR neonate and PTT > 85 seconds)	3
	not neonate AND PT <= 22 seconds AND PTT <= 57 seconds	0
	not neonate AND (PT > 22 seconds OR PTT > 57 seconds)	3

where:

• The upper limit of the normal reference ranges for PT and PTT are notgiven.

Other factors to document:

(1) Non operative cardiovascular disease

(2) Chromosomal anomaly

(3) Cancer

(4) Previous ICU admission during current admissio

(5) Pre-ICU CPR during current admission

(6) Post-operative (not including catheterizations) during past 24 hours

(7) Acute diabetes with ketoacidosis or other severe complication

(8) Admission from inpatient unit (do not count if in ICU for < 2 hours or if transferred from surgical recovery room)

- Cardiovascular and Neurologic sub score = (points for systolicpressure) + (points for temperature) + (points for mental status)
  +(points for heart rate) + (points for pupillary reflex)
- Acid-base and blood gas sub score = (points for acidosis) + (points forpH) + (points for PaCO2) + (points for total CO2) + (points for PaO2)
- Chemistry sub score = (points for glucose) + (points for potassium) +(points for creatinine) + (points for blood urea nitrogen)
- Haematology sub score = (points for WBC count) + (points for plateletcount) + (points for PT and PTT testing)

Total PRISM III score = (Cardiovascular and Neurologic sub score) + (Acid base and blood gas sub score) + (Chemistry sub score) + (Haematology sub score)

Interpretation:

- Minimum sub score and total score: 0
- Maximum cardiovascular and neurologic sub score: 30
- Maximum acid-base and blood gas sub score: 22
- Maximum chemistry sub score: 10
- Maximum haematology sub score: 12
- Maximum total PRISM III score: 74
- The higher the total score, the worse the prognosis.
- A rising score indicates deterioration.
- If performed during the first 12 hours in the ICU, the score is designated PRISM-1
- If performed during the first 24 hours in the ICU, it is designated PRISM- 24.
- Predictive equations:

- Predictive equations for prognosis are available for the 12 hour and 24- hour scores

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.

Observation and Results

The present study was performed to evaluate the thyroid hormone profile in critically ill children and to determine the correlation between the thyroid hormone profile, disease severity and the clinical outcome. The data obtained was subjected to statistical analysis.

The total number of study objects were 50 who fulfilled the inclusion criteria and were admitted in the PICU

Table 1: Distribution according to age groups

Age groups	**No. of patients (n)**	**Percentage (%)**
Below 1 year	07	14
1-5 years	19	38
6-10 years	13	26
11-15 years	11	22
Total	50	100

In our study, youngest patient was of 2 months old while oldest one was 14 years old. Majority of patients (38%, 19 patients) belonged to age group 1-5 years followed by age group 6-10 years Mean age of patients was found to be

5.74 years old with a standard deviation of ± 4.61.

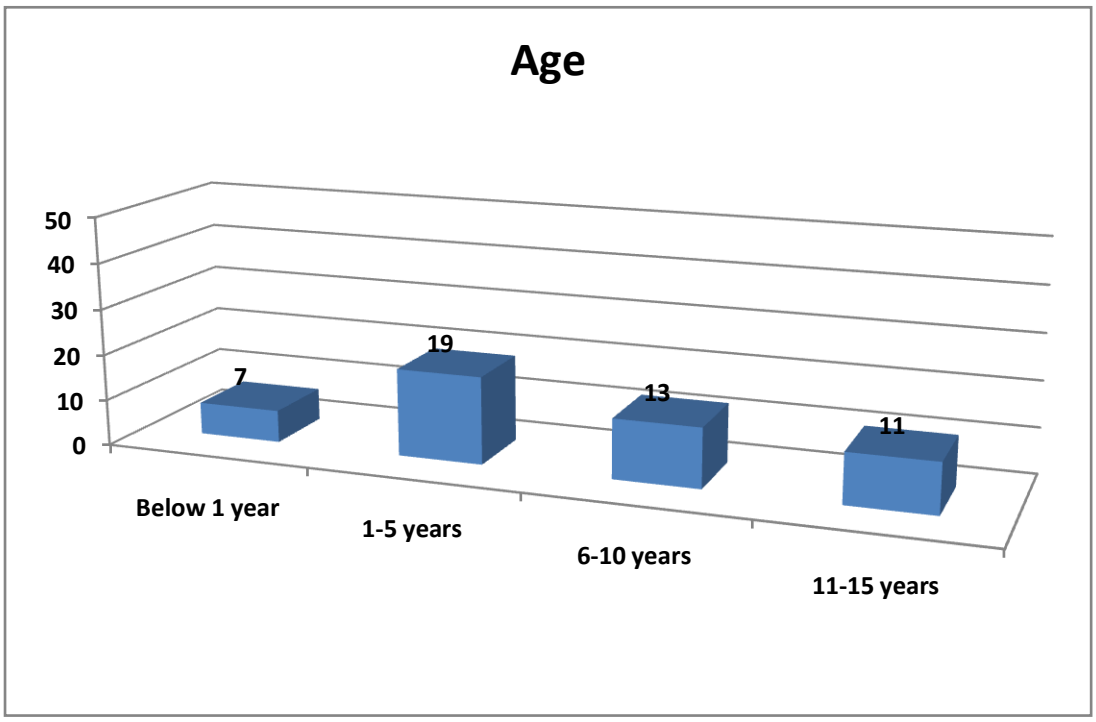


Figure.1: Distribution according to age groups.

Table 2: Distribution according to gender

Gender	**No. of patients (n)**	**Percentage (%)**
Males	29	58
Females	21	42
Total	50	100

Majority of patients (58%, 29 patients) were males while 42% (21 patients) were females.

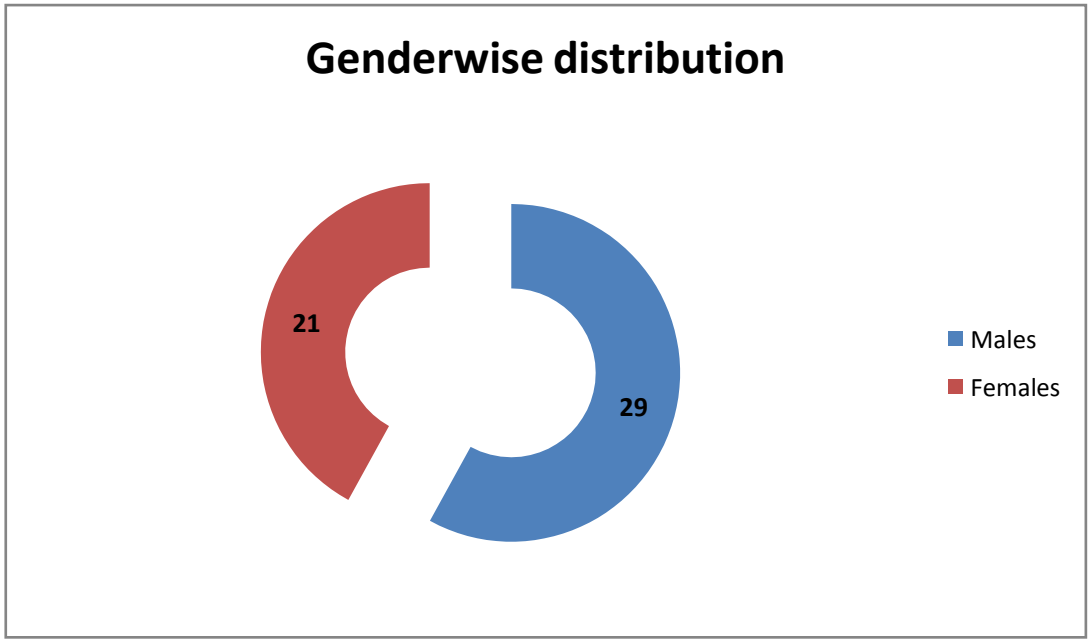


Figure 2: Distribution according to gender.

Table 3: Distribution according to hospital stay (Days)

Hospital stay (days)	**No. of patients (n)**	**Percentage (%)**
<15	34	68
15-30	10	20
>30	06	12
Total	50	100

Considering number of days of admission, most of the patients (68%, 34 patients) stayed at hospital for less than 15 days followed by 15 to 30 days (20%, 10 patients). Shortest duration of stay was for 3 days while longest stay was for 45 days. Mean of number of days of admission was 14.38 days with a standard deviation of ±11.42.

Table 4: Distribution of systems involved

Systems involved	No. of patients (n)	Percentage (%)
Single system	29	58
Multiple system	21	42
Total	50	100

Different systems like hematopoietic, endocrine, central nervous system, gastro-intestinal tract, etc. in body were found to be involved. Majority of the patients (16%, 8 patients) had respiratory system involvement followed by hematopoietic, infectious diseases and central nervous system related disorders.

Table 5: Distribution according to outcome

Outcome	No. of patients (n)	Percentage (%)
Discharged	42	84
Expired	08	16
Total	50	100

8 out of 50 patients (16%) expired during treatment and 42 (84%) patients were discharged after giving treatment.

Table 6: Distribution according to inclusion criteria

Inclusion criteria	No. of patients (n)	Percentage(%)
Creatinine	13	26
Mechanical ventilation	12	24
Mechanical ventilation + Creatinine	4	8
Mechanical ventilation + Creatinine + Platelet	2	4
Mechanical ventilation + Dopamine	2	4
Mechanical ventilation + Dopamine + Creatinine	1	2
Mechanical ventilation + Dopamine+ Creatinine +Urine output	2	4
Mechanical ventilation + Platelet	1	2
Platelet count	7	14
Platelet count + Creatinine	2	4
Platelet count + Creatinine + Dopamine	1	2
Platelet count + Dopamine	1	2
Urine output +Creatinine	2	4
Total	50	100

50 critically ill children admitted to the PICU with malfunction of one or more organs or systems were selected for the present study. Mechanical or pharmacological aids which were used as inclusion criteria are mechanical ventilation, dopamine >5mcg/kg /min, any

dose of adrenaline, serum creatinine >1mg/dl, platelet count < 1 lakh/mm3, and urine output< 1ml/kg/hr.

Table 7: Correlation of PRISM SCORE GROUPS after 24 hours of admission with the outcome

OUTCOME	PRISM SCORE <25	PRISM SCORE 25-40	PRISM SCORE >40	P value
DISCHARGED	42 (87.5%)	00	00	<0.001
EXPIRED	6 (12.5%)	02(100%)	00	0.03
TOTAL	48	02	00	

Out of 50 patients studied, 48 patients had prism score <25 after 24 hours of admission, of these 87.5% (42 patients) got discharged and 12.5% (6 patients) got expired; and the remaining 2 patients had prism score between 25-40, of these 100% (2 patients) got expired. This shows that lesser the prism score, better is the outcome and shows significant correlation between prism score groups after 24 hours of admission and the outcome with p value of <0.05.

Table 8: Correlation of outcome with PRISM score on arrival

Outcome	PRISM score (Mean±SD)	p-value
Discharged (n=42)	9.47±6.36	<0.001×
Expired (n=08)	20±12.60	<0.001×

The mean PRISM score on admission is significantly higher among expired patients in comparison to discharged patients (p <0.001×). Therefore, PRISM score shows significant correlation with the outcome i.e the mortality increases with the increase of PRISM III score

Table 9: Distribution and comparison of PRISM score with outcome

Outcome		PRISM score Mean ±SD	p-value
Discharged	**At the time of admission**	9.47±6.36	<0.001×
	At 24 hours of admission	5.95±2.35	
Expired	**At the time of admission**	20±12.60	0.3617
	At 24 hours of admission	18.12±10.85	

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 10.85, pvalue- 0.361).

Discussion

This is a hospital based prospective observational study which was conducted with the aim of evaluating the thyroid hormone profile in critically ill children admitted in PICU of KRISHNA HOSPITAL, Karad and to correlate between the thyroid hormone profile, PRISM SCORE and clinical outcome of the patients.

Euthyroid sick syndrome (ESS) is used to describe thyroid hormonal changes in critically ill patients in the setting of non thyroid illness (NTI). Low tri-iodo- thyronine is the earliest finding which is followed by low thyroxine levels and finally low thyroid stimulating hormone levels, indicating continuum of changes in the disease spectrum.[107] A similar study involving PICU patients concluded that the low T3 is a good predictor of mortality and the risk is increased 30 times when it is associated with low T4.[105

Thyroid Hormone Profile In Discharged And Expired Patients

Out of the total 50 cases, 8 patients (16%) expired during treatment and rest 42 (84%) patients were discharged. On comparing thyroid profile between discharged and expired patients, T3 levels at discharge/death and T4 both at admission and at the time of discharge /death were found to be significantly lower among expired patients. T3 at admission was found to be lower among expired patients as compared to discharged patients but it was not significant with p value>0.05. No significant change was observed in levels of TSH bothat admission and at the time of discharge/death. In this study, the serum T4 levels done on admission has been considered as the best baseline parameter for the discrimination between discharged and expired patients, which can be used for the prognosis of the clinical status of the critically ill patients. In the study conducted by **Sayarifard F et al.[(88)] in 2018**, T3 at admission and T4 on third day of admission was significantly lower among expired patients in comparison to discharged patients. In the study by **Patki VK et al.[(98)] in 2014**,on admission T3 level was significantly (p-0.001) lower in non survivors than survivors but there was no significant difference in T4 and TSH levels. Similarly, in the study by **Kumar KH et al.[(100)] in 2013**, it was concluded that expired patients (49.1 ± 32.7) had low T3 when comparedwith discharged patients (66.2 ± 30.1) with a pvalue = 0.004 and no significant difference was seen between those who survived and those who expired with respect to T4, TSH, HbA1c, and prolactin. In the study by **Suvarna et al.[(105)] in 2009**, mean T3 levels were significantly lower in expired patients , both at the time of admission and at the time of death and mean T4 levels in the second sample were significantly lower in expired patients as compared to patients who were discharged but there was no significant difference in mean TSH levels between discharged and expired patients.

Summary

1. 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).
2. No significant correlation was found between the duration of hospital stay and the

PRISM score groups.

3. A significant correlation was observed between the PRISM score measured at baseline and T3, T4 and TSH levels at baseline and with T3 and TSH levels at discharge or death. No significant correlation was observed between the PRISM score at baseline and T4 levels at discharge or death.
4. A significant correlation was observed between the PRISM score at 24 hours and T3 and TSH levels both at the baseline and at the time of discharge or death. No significant correlation was observed between the PRISM score at 24 hours and T4 levels both at the baseline and at the time of discharge or death.
5. Area under ROC curve shows that PRISM score at 24 hours have a significant diagnostic accuracy to predict the outcome in critically ill children with a cut off value >9, having sensitivity and specificity of 87.5% and 90.4% respectively.
6. Area under ROC curve shows that the T3 and T4 levels at discharge or death have a significant diagnostic accuracy to predict the outcome in critically ill children with a cut off value of <55 and <6.7 respectively, having sensitivity and specificity of 100%, 97.2% and 100%, 88.1 % respectively.
7. On logistic regression analysis, we observed that PRISM score at 24 hours, T3 and T4 levels at discharge or death were the 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.

Conclusion

The Sick Euthyroid Syndrome occurs in the majority of critically ill children andprogressive reduction in T3, T4 and TSH levels is related to bad prognosis.

In this study it has been demonstrated that baseline T4 levels are lesser in children who will eventually die and therefore this may be used as an indicatorof patient‟s clinical status on arrival and warrants more aggressive treatmentin such children.

There is improvement in T3, T4 and TSH levels in the patients who eventually got discharged and reduction in T3, T4 and TSH levels from the baseline values in the patients who succumbed to death.

This is suggestive of, if thyroid hormone profile is repeated after few days of admission to PICU, may help in identifying the patients at risk of mortality as they will show reduction in

T3, T4 or TSH levels in comparison to baseline levels which would reflect patients clinical status and no improvement would spell bad prognosis.

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