ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

THYROID PROFILE IN CRITICALLY ILL CHILDREN ADMITTED IN PICU AT CHELUVAMBA HOSPITAL

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Received Date: 18/08/2024 Acceptance Date: 05/09/2024

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Abstract

Background: Thyroid hormones are essential for normal growth, development, and metabolic regulation. Their levels are often altered in critically ill children, a condition referred to as euthyroid sick syndrome or non-thyroidal illness. These changes are associated with poor outcomes, including organ failure and death, especially in severe cases of sepsis, trauma, and malnutrition. Monitoring thyroid hormone levels in pediatric intensive care settings is critical for managing critically ill children effectively. The objective of this study was to assess thyroid hormone profile in critically ill children admitted to the Pediatric Intensive Care Unit (PICU) at Cheluvamba Hospital and to correlate these hormonal changes with clinical outcomes. **Methods:** A prospective observational study was conducted over six months in Cheluvamba Hospital, Mysore. The study included 60 children (aged 2 months to 18 years), with 30 critically ill children in the experimental group and 30 relatively healthy children in the control group. Thyroid hormone levels, including T3, T4, TSH, FT3, and FT4, were measured and compared between the two groups. Statistical analyses were performed using the Chi-Square test, with a significance level set at $p < 0.05$. **Results:** The study found that 76.7% of the critically ill children had low FT3 levels compared to 20.0% in the control group ($p < 0.001$). Similarly, 76.7% of the critically ill children had low T3 levels compared to 13.3% in the control group ($p = 0.052$). No significant differences in FT4 and T4 levels were observed. Mortality was higher in the experimental group (16.7%) compared to the control group (0.0%) ($p = 0.02$). **Conclusion:** The study underscores the importance of monitoring thyroid hormone levels, particularly FT3 and T3, in critically ill children. Early therapeutic interventions aimed at correcting thyroid dysfunction may improve clinical outcomes and reduce mortality in pediatric intensive care settings.

Keywords: Thyroid hormone profile; critically ill children; Non-thyroidal illness

Introduction

Thyroid hormones are necessary for normal growth and development in children. They have tight control of metabolic rate and as a result their levels become altered during time of stress and critical illness like sepsis, trauma, renal failure, severe malnutrition and following cardiopulmonary bypass.[1] The most typical alterations are low total and free T3, elevated rT3 and normal T4 levels although T4 and TSH suppression may occur in more severe or chronic illness. These alterations in thyroid hormone levels are referred to as euthyroid sick syndrome or non-thyroidal illness. The changes in thyroid hormone levels are seen as a result of

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cytokines and inflammatory mediators released in patients with non-thyroidal illness. Mechanism of changes during critical illness include;

1. Release of cytokines particularly IL1, IL6, TNF-alpha and interferon beta.
2. Impaired peripheral de-iodination of T4 to T3
3. Decreased clearance of rT3
4. Inhibition of thyroid hormone binding to hormone binding proteins and tissues.

Changes in thyroid hormone levels will later result in disruption of oxygen consumption, cardiovascular, sympathetic nerves, respiration, digestive and hematopoeisis which in turn will lead to organ system failure and death.[2] Hence, it is very important to know the changes in thyroid hormone levels during critical illness and this study aims to assess the hormonal changes in children admitted in PICU of Cheluvamba hospital.

Objectives

- To assess the thyroid hormone profile in critically ill children admitted in PICU at Cheluvamba hospital.
- To assess the correlation of thyroid hormone changes to final outcome.

Material And Methods

The study was a prospective observational investigation conducted at Cheluvamba Hospital, Mysore, over a period of six months. The target population consisted of children aged between 2 months and 18 years who were admitted to the Paediatric Intensive Care Unit (PICU) of the hospital, fulfilling both the inclusion and exclusion criteria.

Sample size was calculated using the following formula

$$n1 = \frac{(\sigma_1^2 + \sigma_2^2/\kappa)\,(Z_{1-\alpha/2} + Z_{1-\beta})^2}{\Delta^2}$$

$$n2 = \frac{(\kappa * \sigma_1^2 + \sigma_2^2)\,(Z_{1-\alpha/2} + Z_{1-\beta})^2}{\Delta^2}$$

Wherein

n1 and n2 are sample sizes in the two study groups

σ_1 = Standard deviation of group 1

σ_2 = Standard deviation of group 2

Δ = Difference in group mean

$Z_{1-\alpha/2}$ = 1.96 (From Z table) at type 1 error of 5% (confidence level of 95%)

$Z_{1-\beta}$ = 0.84 (From Z table) at 80% power

κ = ratio of n1/n2

Mean thyroid hormone levels was used from the study by Jyoti Suvarna *et al.* (2022)[3] to estimate the sample size. The ratio of n1 and n2 is taken as 1. At 95% confidence level and power of the study at 80% the minimum sample size was calculated to be 23 per group. However 30 subjects were included in each group during the study period.

The inclusion criteria stipulated that all children aged between 2 months and 18 years, who were admitted to the PICU with critical illness and had no previous history of thyroid illness, were eligible for inclusion. Critical illness was operationally defined as any condition that led to the malfunction of one or more organ systems requiring support to maintain vital functions, such as mechanical ventilation for more than 24 hours, ionotropic support, urine output less than 1 ml/kg/hr, and a platelet count of less than 1 lakh. Exclusion criteria

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included children with parental thyroid illness, any clinical evidence of thyroid dysfunction, or those who were syndromic.

The methodology of the study involved comparing thyroid function between two groups of children. Group A (Experimental group) consisted of 30 critically ill children admitted to the PICU, while Group B (Control group) comprised 30 comparatively healthy children admitted to the general wards of the hospital. Thyroid function tests, including levels of T3, T4, TSH, Ft3, and Ft4, were conducted for all participants after obtaining informed consent from their parents. The results of these tests were analysed using age-specific cut-offs as defined in the 21st edition of the Nelson Textbook of Paediatrics. The thyroid function tests of the critically ill children in Group A were compared with those of the relatively healthy children in Group B, who were of the same age and sex.

Data collection was performed meticulously, with all information being entered into Microsoft Excel (Windows 10; Version 2010). The analysis was carried out using the Statistical Package for Social Sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago). Descriptive statistics, such as mean and standard deviation (SD) for continuous variables, were calculated, along with frequencies and percentages for categorical variables. The association between variables was evaluated using the Chi-Square test for categorical variables, with the level of significance set at 0.05.

Results

Table 1: Age and Gender Distribution

		Group				**P value**
		Experimental Group		**Control Group**		
		Count	**%**	**Count**	**%**	
Age	<1 year	4	13.3%	5	16.7%	0.925
	1-5 years	12	40.0%	12	40.0%	
	6-10 years	6	20.0%	7	23.3%	
	>10 years	8	26.7%	6	20.0%	
Gender	Female	12	40.0%	11	36.7%	0.791
	Male	18	60.0%	19	63.3%	

Pearson Chi-Square Tests

In the present study, the majority of subjects in both the experimental and control groups were within the 1-5 years age group (40.0%). The distribution across other age categories was fairly consistent between the two groups, with 13.3% of subjects in the experimental group and 16.7% in the control group being less than 1 year old, while 26.7% and 20.0% of subjects, respectively, were above 10 years old. No significant difference in age distribution between the two groups was observed, as evidenced by the p-value of 0.925. Regarding gender, the experimental group had 40.0% female and 60.0% male subjects, compared to 36.7% female and 63.3% male subjects in the control group, with no significant difference between the two groups (p = 0.791).

Table 2: Thyroid profile among study groups

		Groups				**Total**	**P value**
		Experimental		**Control**			
		Frequency	**%**	**Frequency**	**%**		
FT3 levels	**Low**	23	76.7%	6	20.0%	29 (48.3%)	**<0.001***
	Normal	7	23.3%	24	80.0%	31 (51.7%)	
FT4	**Low**	5	16.7%	5	16.7%	10 (16.7%)	**1.000**

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levels	**Normal**	25	83.3%	25	83.3%	50 (83.3%)	
TSH Levels	**Low**	5	16.7%	0	0.0%	5 (8.3%)	**0.052**
	Normal	25	83.3%	30	100.0%	55 (91.7%)	
T3 levels	**Low**	23	76.7%	4	13.3%	27 (45.0%)	**0.052**
	Normal	7	23.3%	26	86.7%	33 (55.0%)	

Pearson Chi-Square Tests

In terms of thyroid profile, the results indicated a significant difference in FT3 levels between the two groups. A higher proportion of subjects in the experimental group had low FT3 levels (76.7%) compared to the control group (20.0%), with a p-value of <0.001, indicating a statistically significant difference. However, there was no significant difference in FT4 levels between the experimental and control groups, as both groups had 16.7% of subjects with low FT4 levels, and the remaining 83.3% had normal levels (p = 1.000). While there was a trend toward lower TSH levels in the experimental group (16.7% with low TSH compared to 0.0% in the control group), the difference was not statistically significant (p = 0.052). Similarly, the T3 levels showed a trend with 76.7% of the experimental group having low T3 compared to only 13.3% in the control group, though this difference approached but did not reach statistical significance (p = 0.052).

Table 3: Outcome among study groups

		Group				**P value**
		Experimental Group		**Control Group**		
		Count	**%**	**Count**	**%**	
Outcome	Death	5	16.7%	0	0.0%	0.02*
	Survived	25	83.3%	30	100.0%	

Pearson Chi-Square Tests

In the experimental group, 16.7% of subjects died, whereas no deaths were recorded in the control group. The difference was statistically significant with a p-value of 0.02. In contrast, 83.3% of subjects in the experimental group survived, compared to 100.0% in the control group, further reinforcing the significant outcome difference between the two groups.

Discussion

The present study examined the thyroid hormone levels among critically ill children and their impact on clinical outcomes. Thyroid hormones play a crucial role in metabolic regulation, and their alteration in critically ill patients, especially children, has been a topic of concern. The findings from this study are consistent with previous literature, which highlights the significance of thyroid hormone profiles in predicting and managing outcomes in pediatric intensive care units.

The significant difference in FT3 levels observed between the experimental and control groups aligns with previous research, emphasizing the importance of monitoring thyroid function in critically ill children. Monteiro (1) reported similar findings, noting that critically ill children often exhibit abnormal FT3 levels, which are indicative of disease severity. In this study, 76.7% of the experimental group had low FT3 levels compared to only 20.0% in the control group, with a p-value of <0.001, indicating a statistically significant difference. This suggests that the critical illness in the experimental group may have caused a significant alteration in thyroid function, contributing to poor outcomes. The low FT3 levels in the majority of the experimental group are consistent with the concept of non-thyroidal illness syndrome (NTIS), where FT3 levels drop significantly due to the body's metabolic response to severe illness (2).

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The findings also resonate with the work of Suvarna and Fande (3), who found that children in critical conditions often exhibit low FT3 levels, which are associated with poor prognosis. The low FT3 levels in the experimental group suggest that therapeutic interventions aimed at correcting thyroid dysfunction may be necessary to improve outcomes in critically ill children.

In contrast to FT3, FT4 levels did not show a significant difference between the experimental and control groups in this study, which is consistent with findings from Radman and Portman (4). They reported that FT4 levels tend to remain stable or show only minor changes in critically ill children, irrespective of illness severity or the interventions applied. In this study, both the experimental and control groups showed similar FT4 levels, with 83.3% of subjects in both groups maintaining normal FT4 levels ($p = 1.000$), suggesting that FT4 may not be as sensitive an indicator of illness severity or prognosis as FT3 in pediatric patients.

Furthermore, Zucker *et al.* (5) highlighted that while FT4 levels are essential for understanding overall thyroid function, they do not always correlate with clinical outcomes in critically ill children. This could explain why the critical condition in the experimental group did not significantly alter FT4 levels, indicating that FT4 might not be the primary target for therapeutic management in such cases.

The trend towards significance observed in TSH levels between the two groups points to the complex relationship between thyroid function and critical illness. This study revealed that 16.7% of the experimental group had low TSH levels, while none in the control group did ($p = 0.052$). Although this difference was not statistically significant, it suggests a potential impact of illness on TSH regulation, which warrants further investigation. Similar trends were observed by Anand *et al.* (8), who studied critically ill infants and found variations in TSH levels reflecting the body's response to stress and illness. The findings suggest that early interventions may help stabilize TSH levels in critically ill children, which could enhance recovery.

T3 levels, which are crucial for metabolic regulation, showed a near-significant difference between the experimental and control groups. In this study, 76.7% of the experimental group had low T3 levels compared to 13.3% in the control group ($p = 0.052$). The low T3 levels in the experimental group support the concept of low T3 syndrome, which is associated with poor outcomes in critically ill patients. This finding is important as T3 is the active form of thyroid hormone, and its regulation is critical for managing the metabolic needs of critically ill children. Sahana *et al.* (7) reported similar findings, noting that low T3 levels are common in critically ill children and are often linked to poor prognosis.

The outcome analysis revealed that 16.7% of the experimental group succumbed to their illness compared to 0.0% in the control group ($p = 0.02$). This finding highlights the potential link between thyroid hormone dysregulation and mortality in critically ill children. Zucker *et al.* (5) also found that low T3 and FT3 levels are closely associated with higher mortality rates in pediatric intensive care settings. The relatively high survival rate in this study suggests that better thyroid hormone regulation might contribute to improved outcomes.

These findings are consistent with those of Suvarna and Fande (3), who observed that thyroid dysfunction, particularly low T3 levels, is common in non-survivors among critically ill children. The results from the experimental group, showing poorer thyroid profiles and higher mortality rates, reinforce the importance of timely interventions targeting thyroid function in critical care settings.

The results of this study suggest that monitoring thyroid hormone levels, particularly FT3 and T3, is crucial for managing critically ill children. Early and targeted interventions aimed at correcting thyroid dysfunction could potentially improve survival rates and recovery. This

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aligns with the recommendations of Monteiro (1), who emphasized the importance of regular thyroid function monitoring in pediatric intensive care units.

Limitations and Future Research

While the findings of this study are significant, several limitations should be acknowledged. The sample size was relatively small, and the study was conducted at a single center, which may limit the generalizability of the results. Further, the study did not explore the long-term outcomes of thyroid hormone intervention, which could provide more insights into the management of thyroid dysfunction in critically ill children.

Future research should focus on larger, multicenter studies to validate these findings and explore the long-term benefits of thyroid hormone therapy in pediatric intensive care settings. Additionally, studies investigating the mechanisms underlying thyroid hormone dysregulation in critical illness could provide valuable insights into developing more effective therapeutic interventions.

Conclusion

This study highlights the significance of thyroid hormone levels in predicting and managing outcomes in critically ill children. Regular monitoring and timely therapeutic interventions targeting thyroid hormone dysregulation, particularly FT3, T3, and TSH levels, should be an integral part of pediatric intensive care management to improve prognosis and survival rates.

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