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Original Article

Free Thyroid Hormone Profile and Its Association with Nutritional Status in Children with Severe Acute Malnutrition: A Cross-Sectional Study

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ABSTRACT

Objective: To assess free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH) concentrations in children with severe acute malnutrition (SAM) and to evaluate their associations with anthropometric indices and biochemical markers of protein status.

Methods: In this cross-sectional study, 68 children aged 6–59 months with SAM admitted to the pediatric ward of Deen Dayal Upadhyay Hospital, New Delhi (February 2024–March 2025) were enrolled. Anthropometric measurements including weight-for-height (WFH) Z-score and mid-upper arm circumference (MUAC) were recorded. Serum FT3, FT4, TSH, total protein, and albumin were measured. Statistical analysis was performed using R (version 4.5.1), and correlations were assessed using Spearman's rank analysis.

Results: The median age was 18 months, with a male-to-female ratio of 0.75:1. The median WFH Z-score was −4.05, and the median MUAC was 113 mm, indicating severe wasting. Median FT3, FT4, and TSH concentrations were 312 pg/dL, 12 ng/L, and 2.39 mIU/L, respectively, within laboratory reference ranges. Mean total protein was 6.6 g/dL, while mean albumin was 3.26 g/dL. FT3 and FT4 showed significant positive correlations with MUAC, total protein, and albumin, whereas TSH demonstrated significant inverse correlations with free hormone levels and protein markers. WFH Z-score did not correlate significantly with biochemical parameters.

Conclusion: WFH Z-score and MUAC reflect different dimensions of the pathophysiology of SAM. The hypothalamic–pituitary–thyroid axis appears preserved in children with SAM. Free thyroid hormones (FT3 and FT4) rather than total thyroid hormones may provide a physiologically relevant evaluation of thyroid status in SAM children.

Keywords*: Severe acute malnutrition, free thyroid hormones, thyroid function, mid-upper arm circumference, pediatric malnutrition.*

INTRODUCTION

Severe Acute Malnutrition (SAM) is a life-threatening nutritional condition of childhood that contributes to significant pediatric mortality and morbidity [1]. According to a joint report by the WHO, UNICEF, and the World Bank in 2025, 42.8 million children are wasted, threatening the lives of 6.6% of children under the age of 5 years globally [2]. SAM is characterized by a complex interplay of wasting and undernutrition, giving rise to a spectrum of complications that significantly impact morbidity and mortality. The physiological consequences of SAM are profound, affecting virtually every organ system in the body [3], including the endocrine system and thyroid.

Multiple studies have revealed that children afflicted by Severe Acute Malnutrition (SAM) exhibit notable disruption in thyroid function, often characterized by reduced levels of thyroid hormones. Multiple studies [4–6] have shown that the Total T3 (TT3) and Total T4 (TT4) decrease in children with Severe Acute Malnutrition. This underscores the severity of

the impact of malnutrition on thyroid hormone production and regulation. While multiple studies have been conducted on TT3 and TT4, only a limited number of studies have been conducted on Free T3 (FT3) and Free T4 (FT4) in children with SAM.

The vast majority of thyroid hormone in circulation is bound to transport proteins; only a small amount of the hormone exists in a free, unbound state [7]. One of the key features of SAM is a decrease in the levels of total serum protein and serum albumin [8]. Whether this change in protein levels affects free thyroid hormone levels remains unclear. This study will assess FT3, FT4, and TSH levels in children with SAM, investigating the impact of nutritional status on these levels by comparing them against normal ranges. Furthermore, this study assessed the children's protein status via total protein and albumin levels to investigate the correlation between these nutritional markers and thyroid function.

METHODOLOGY

The sample size was determined based on the method described by Hulley et al. [9] for estimating a population mean with a 95% confidence interval and a precision of 0.5. Standard deviations for FT3 (0.84), FT4 (0.62), and TSH (2.1) were derived from a study by Surewad GV et al. [10] on patients with SAM. The calculated requirements for these parameters were 11, 6, and 68, respectively. To ensure adequate power for all outcomes, the study adopted the largest calculated value, resulting in a minimum required sample size of 68.

A cross-sectional study was conducted from February 2024 to March 2025. Sixty-eight children with Severe Acute Malnutrition (SAM) admitted to the pediatric ward of Deen Dayal Upadhyay Hospital, Delhi were included in the study. Children meeting the inclusion criteria were recruited using consecutive sampling. The children already suffering from thyroid disorders, children with chronic illnesses like tuberculosis and HIV, children with liver or kidney diseases and children suffering from malabsorption syndromes like celiac disease and protein-losing enteropathy were excluded from the study.

Prior approval from the Institutional Ethical Committee (IEC) and Scientific Research Committee (SRC) of the Deen Dayal Upadhyay Hospital was sought before the study was conducted. The anthropometric parameters were measured as described. A digital weighing scale was used to measure weight to the nearest gram by the taring method. The stadiometer was used to measure height for children above 2 years of age, and the infantometer was used for infants' length to the nearest 0.1cm. Mid upper arm circumference (MUAC) was measured on the left arm with a non-stretchable tape at the midpoint between the acromion and the olecranon process. MUAC was measured to the nearest mm. Z-scores for Weight for height/Length were calculated with the Anthrocalc App [11] which is based on the WHO growth charts [12].

Following aseptic precautions, 2 mL of blood was collected from the medial cubital vein and sent to the laboratory for the estimation of FT3, FT4, TSH, Total protein, and Albumin values. Serum FT3, FT4, and TSH estimation was done by the Chemiluminescence method on the immunoassay Analyzer Beckman Coulter Access 2, in the Department of Pathology & Lab Medicine of the Hospital. The cut-off values of FT3, FT4, and TSH, as per the standard reference, were followed [13]

The statistical analysis was performed using R (version 4.5.1), with a p-value < 0.05 considered statistically significant for all tests. Descriptive statistics were used to summarize the population's characteristics. Continuous variables (age, height, weight, MUAC, Z-score) were presented as mean ± standard deviation (SD), median, and range (minimum-maximum). Categorical variables (gender, edema) were reported as frequencies (n) and percentages (%).

Normality of all continuous data was assessed using the Shapiro-Wilk test. Biochemical profiles (Free T3, Free T4, TSH, protein, albumin) were summarized using the mean, standard error (SE), and 95% confidence intervals (CI). Finally, the relationships between key variables were analyzed using Spearman's rank correlation to determine the strength and direction of monotonic associations. The results were presented in a correlation matrix.

RESULTS

The descriptive summary of the anthropometric measures is shown in Table 1. The mean age of the study participants was 18.93 (±10.77 months). Among them, 42.65% (n = 29) were male and 57.35% (n = 39) were female, with a male-to-female ratio of around 0.75:1. Only 5.88% (n=4) had edema, indicating that the majority (94.1%, n=64) were cases of severe acute malnutrition (SAM) without edema.

Table 1. Descriptive summary of anthropometric measures (N=68)

Anthropometric measures	Mean	SD	Min	Max	Median	Skewness	Kurtosis
Age (in months)	18.93	10.77	6	48	18	+1.12	+3.68

Height (in cm)	75.38	9.40	53	106	75	+0.65	+4.03
Weight (in Kg)	6.72	1.69	3	11.9	6.46	+0.84	+4.31
MUAC (in mm)	114.7	6.13	102	128	113	+0.39	+2.44
Z score (WFH)	-4.05	0.84	-6.8	-3.06	-3.98	-0.95	+3.69

The thyroid profile of the study participants is shown in Table 2. The mean and median FT3, FT4, and TSH values were within laboratory reference ranges.

Table 2. Thyroid profile characteristics of the study participants(N=68)

Thyroid profile	Mean	SE	95% CI	Median	Reference range
Free T3(pg/dL)	323.97	5.02	313.96-333.99	312	240-560
Free T4(ng/L)	12.22	0.40	11.43-13.02	12	7-20
Serum (TSHmIU/L)	2.58	0.13	2.33-2.83	2.39	0.5-4.5

Table 3 shows the nutritional status of the study participants. While the average protein level falls within the normal range, the albumin level was found to be lower than the normal reference range, suggesting mild to moderate hypoalbuminemia in these children.

Table 3: Nutritional status of study participants (N=68)

Nutritional status	Mean	SE	95% CI	Median	Reference range
Protein(g/dL)	6.60	0.07	6.45-6.75	6.60	6-8
Albumin(g/dL)	3.26	0.06	3.14-3.39	3.4	3.5-5

Figure 1 shows the correlation among the different study parameters. Among the study participants (N=68), MUAC showed a statistically significant positive correlation with Free T3 (r = 0.35), Free T4 (r = 0.26), protein (r = 0.343), and albumin (r = 0.386), indicating that as MUAC increased, these biochemical parameters also tended to be higher. Free T3 demonstrated a significant positive correlation with MUAC (r = 0.35), Free T4 (r = 0.667), and protein (r = 0.27), suggesting a consistent association with both anthropometric and nutritional biomarkers. Free T4 was significantly and positively correlated with Free T3 (r = 0.667), MUAC (r = 0.26), protein (r = 0.312), and albumin (r = 0.251). TSH showed a significant negative correlation with Free T3 (r = -0.33), Free T4 (r = -0.308), protein (r = -0.408), and albumin (r = -0.434), indicating that higher TSH levels were associated with lower values of these variables. Protein levels were positively and significantly correlated with MUAC (r = 0.343), Free T3 (r = 0.27), Free T4 (r = 0.312), and albumin (r = 0.694), but negatively correlated with TSH (r = -0.408), underlining its relationship with both nutritional and endocrine parameters. Albumin also showed statistically significant positive correlations with MUAC (r = 0.386), Free T4 (r = 0.251), and protein (r = 0.694), and a significant negative correlation with TSH (r = -0.434). No statistically significant correlations were observed between the Z-score and any other variable in the correlation matrix. This may be due to lack of variance in the WFH Z-score (mean = -4.05) that severely reduces the statistical power to detect a correlation.

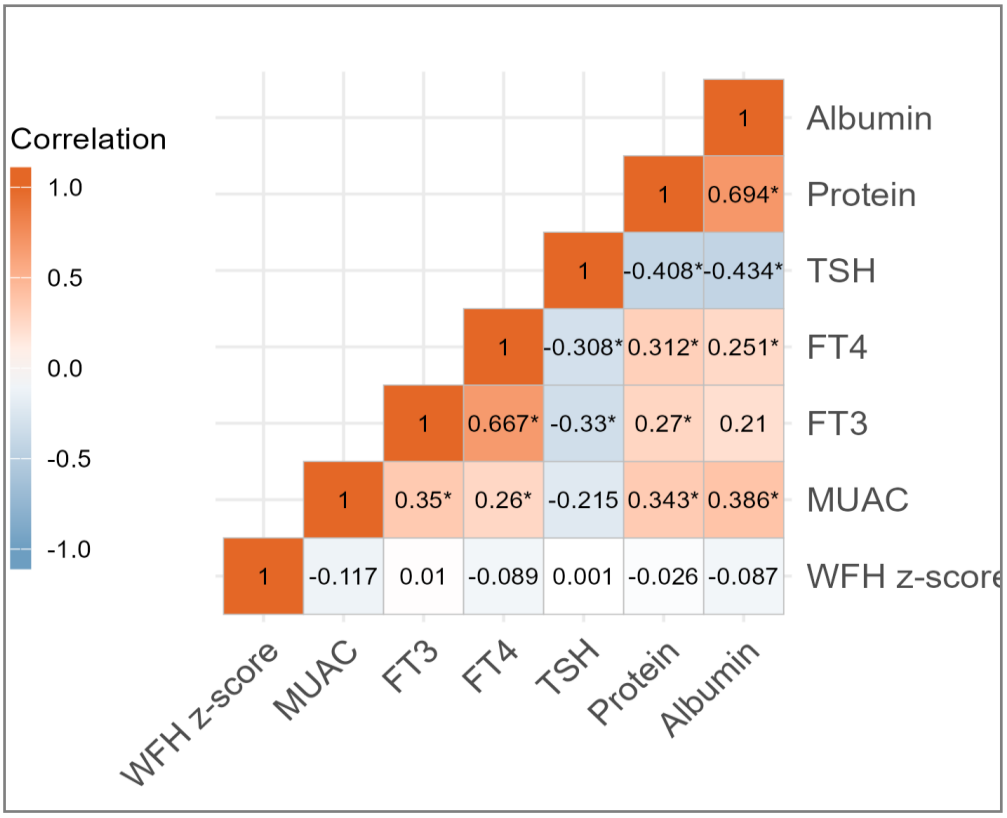

Figure 1: Spearman Correlation Matrix

DISCUSSION

The age profile of our study, with a mean age of 18.93 months (Table 1), is consistent with the literature, which identifies the period of weaning and early childhood as a window of high vulnerability for malnutrition. This finding aligns closely with studies by Chandrashekaraiah S et al.[14] (mean age 18 months) and Islam R et al.[15] (mean age 14.45 months). However, other studies report older cohorts, such as Mehta S et al.[5] (mean age 26.49 months) and Lazarus M et al.[4] (mostly >2 years), underscoring the variability in the age of presentation of SAM across different demographics.

The gender distribution in this study is predominantly female, with 42.65% males and 57.35% females (M:F ≈ 0.75:1) (Table 2). This is consistent with findings reported in a similar urban setting by Chandrashekaraiah S et al[14] (M:F ≈ 0.8:1). This pattern is inverted in rural settings where male predominance is reported by Islam R et al[15] (M:F ≈ 2.2:1), Gupta S and Chaurasiysa O[16] (M:F = 1.6:1) and Lazarus M et al[4] (M:F ≈ 1.1:1). This may be due to differential health-seeking behavior in rural and urban areas.

A low prevalence of edema, observed in only 5.88% of the cases (n=4), with the majority of the participants without edema (94.1%, n=64). This shows that the study population is overwhelmingly characterized by a non-edematous form of SAM, known as marasmus. The WFH Z-score data (mean -4.05, skewness = -0.95) is also consistent with the finding of severe wasting. Therefore, this study should be interpreted as primarily representative of children with marasmic SAM.

The thyroid profile of study participants showed mean of FT3 and FT4 to be 323.97 pg/dL (CI 313.96-333.99, p<0.001) and 12.22 ng/L (CI 11.43-13.02, p<0.001), respectively. Islam R et al[15] showed comparable mean for FT3 and FT4 of 290 pg/dL and 10.9 ng/L respectively. Surewad GV et al[10] also reported similar means for FT3(316 pg/dL) and FT4 (11.5 ng/L). The mean of TSH of the study participants was 2.58 mIU/L (CI 2.33-2.83, p<0.001). Multiple other studies found similar means for TSH, like Chandrashekaraiah S et al[14] (2.5 mIU/L), Mehta S[5] (2.51 mIU/L), Chatterjee R et al[17] (2.24 mIU/L).

The mean total protein and albumin of our study population were 6.60 (CI 6.45-6.75) and 3.26 (CI 3.14-3.39), respectively. Although total protein was within the normal range, albumin was low. Similar low levels of albumin were reported by Chandrashekaraiah S et al[14] who reported it as 2.97 g/dL, Saini A et al[18] who reported it as 3.05 g/dL, and Sah et al[19] who reported it as 2.24 g/dL. This is consistent with the WFH Z-scores, which showed severe wasting.

Despite the severe wasting noted in the study population, the principal and most significant finding of this study is the preservation of FT3, FT4, and TSH in the normal physiological range. Our observation, similar to that of Islam et al[15], stands in contrast to several studies that found altered thyroid function, when assessing Total T3 (TT3) and Total T4 (TT4).

For instance, Chandrashekaraiah S et al. reported low serum TT3 and TT4 in 22% and 28% respectively, and high TSH in 8% of their study population [14]. Gupta S and Chaurasiya O [16], Mehta S [5], Chatterjee R et al. [17] and Sah SP et al. [19] all noted reduction in TT3 and TT4 levels without a concomitant alteration in TSH levels[16]. Studies specifically evaluated FT3, FT4, and TSH, like Islam R et al[15] and our current investigation did not find this association, suggesting a distinction in the interpretation of free thyroid and total thyroid statuses in malnutrition.

A plausible hypothesis to explain these contrasting results lies in the role of thyroid transport proteins. Over 99% of circulating thyroid hormones are bound to transport proteins, primarily Thyroxine-Binding Globulin (TBG), transthyretin, and albumin. It is only a minuscule fraction of the 'unbound' or 'free' hormone that is biologically active and exerts its metabolic effects [7]. A cardinal feature of SAM is the profound depletion of protein resources due to inadequate protein intake and impaired hepatic synthesis. This results in a reduction of thyroid transport proteins. Consequently, the amount of Total thyroid hormones in the serum is reduced. Therefore, the lower TT3 and TT4 values noted by other researchers likely reflect decreased binding capacity, not true hormonal deficiency, while the biologically active FT3 and FT4 remain homeostatically preserved. This finding suggests that measurement of free thyroid hormones (FT3 and FT4), rather than total thyroid hormones (TT3 and TT4), may provide a more accurate assessment of thyroid status in children with SAM.

Further compelling evidence for a functional and preserved Hypothalamic Pituitary Thyroid (HPT) axis is provided by the correlational analysis. A statistically significant negative correlation is observed between TSH and FT3 ($r = -0.330$, $p<0.05$) and between TSH and FT4 ($r = -0.308$, $p<0.05$). This inverse relationship is characteristic of the HPT axis negative feedback loop.[20]

The correlation matrix demonstrates a series of physiologically coherent and statistically significant relationships between nutritional, anthropometric, and endocrine parameters. Significant positive correlations were found between markers of nutritional status and free thyroid hormone levels. For instance, FT4 was positively correlated with both total protein ($r=0.312$, $p<0.05$) and albumin ($r=0.251$, $p<0.05$), while FT3 showed a positive correlation with total protein ($r=0.270$, $p<0.05$). This suggests a direct relationship wherein higher protein levels are associated with higher circulating levels of free thyroid hormones.

Conversely, a significant negative correlation between TSH and the nutritional markers was detected: TSH vs. total protein ($r = -0.408$) and TSH vs. albumin ($r = -0.434$). This inverse relationship indicates that a decline in protein and albumin levels tends to correspond with higher TSH, even when it remains within the normal reference range. Given that free hormone levels are maintained, this pattern suggests a potential compensatory mechanism that, as the metabolic stress of malnutrition intensifies, the pituitary gland may be increasing its stimulatory effort (i.e., increased TSH secretion) to compel the thyroid to produce an adequate amount of hormone. This highlights a potential mechanism of pituitary compensation in the context of declining nutritional status.

The correlation matrix revealed a divergence in the correlational patterns of two primary Anthropometric indices for SAM, i.e., WFH Z-score and MUAC. Contrary to the established role in SAM diagnosis, the WFH Z-score showed a complete absence of significant correlation with any of the other parameters' measures. In contrast, MUAC showed a significant positive correlation with FT3($r=0.35$, $p<0.05$), FT4($r=0.26$, $p<0.05$), protein ($r=0.343$, $p<0.05$), and albumin ($r=0.386$, $p<0.05$). Also, WFH Z-score and MUAC reflect different dimensions of the pathophysiology of SAM[21]. The WFH Z-score is an index that is sensitive to the acute changes in body weight relative to the skeletal frame. MUAC, on the other hand, directly measures the composition of muscle and subcutaneous fat reserves.

One possible explanation for this lack of correlation is a "floor effect". Wasting (low WFH Z-score), while indicative of recent weight loss, can also persist as a chronic state.[22] Physiologically, such children have likely already undergone significant metabolic adaptation, causing biochemical markers like albumin and free thyroid hormones to stabilize at the minimum level (floor level) required for survival. Consequently, the minor variations in Z-score within this already extreme group are insufficient to elicit a detectable response from markers that have already reached a physiological plateau. In this context, MUAC serves as a more direct indicator of the body's total somatic protein and energy reserve than the WFH Z-score, which is depleted over a more prolonged period of nutritional deficit. Clinically, this implies that a low MUAC, even when Z-scores are similar among patients, signifies a more profound depletion of protein reserves. These children may be at a higher risk for metabolic complications and warrant closer monitoring. Further investigation is warranted to elucidate the distinct clinical and physiological information provided by each of these critical anthropometric measures.

CONCLUSION

In this cohort of predominantly non-edematous severe acute malnutrition, circulating FT3, FT4, and TSH concentrations were maintained within laboratory reference ranges despite marked anthropometric depletion and hypoalbuminemia. The preserved inverse relationship between TSH and free thyroid hormones supports functional basal feedback regulation of the hypothalamic–pituitary–thyroid axis.

Free thyroid hormone concentrations demonstrated modest but consistent associations with MUAC and biochemical markers of protein status, whereas WFH Z-score did not correlate with endocrine parameters. These findings suggest that peripheral somatic reserve, as reflected by MUAC, may more closely parallel endocrine-metabolic status than weight-for-height alone in children with marasmic SAM.

Overall, the data indicate that biochemical euthyroidism can be maintained in chronic non-edematous SAM at a single time point. Assessment of free thyroid hormones may therefore provide a more physiologically relevant evaluation of thyroid status in this population. Longitudinal studies incorporating comprehensive thyroid profiling during nutritional rehabilitation are warranted to further characterize endocrine adaptation in pediatric malnutrition.

Limitations

The following limitations are to be considered.

- This study employed a cross-sectional design, which is effective for identifying associations and correlations between variables, but cannot establish causality. A longitudinal study that follows children through nutritional rehabilitation would be required to understand the dynamic, causal relationships between the studied parameters.
- The study was done in a single urban center. Caution should be exercised when extrapolating these results to populations in different geographic areas, especially rural communities, which may present with different epidemiological patterns.
- The study population primarily consisted of non-edematous SAM (Marasmus). Therefore, our conclusions may not extend to children with edematous SAM (Kwashiorkor).
- The absence of a healthy control group limits direct comparison of thyroid hormone levels between malnourished and well-nourished children.

Declarations

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