# **Original Research Article**

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# Study of thyroid hormone status in severely malnourished children

# Nimilika Meena, R. L. Suman\*, Jitin Topia, Mahendra Yadav

Department of Pediatrics, RNT Medical College, Udaipur, Rajasthan, India

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\*Correspondence: Dr. R. L. Suman,

E-mail: sumanrl@yahoo.co.in

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## **ABSTRACT**

**Background:** In 2022 globally, nearly half of deaths among children under 5 years of age are linked to undernutrition particularly in low- and middle-income countries. Reductive adaptation, the body's physiological response to energy deficiency, can significantly impact various metabolic processes, including thyroid function immaturity. The present study has been conducted to study thyroid dysfunction in severe acute malnutrition (SAM); and its correlation with plasma protein levels.

**Methods:** This prospective cross-sectional study at RNT medical college, Udaipur, involved 100 children (group A) with SAM and 100 non-SAM children (group B). Demographic, clinical, and anthropometric data were collected. Serum levels of thyroid hormones (FT3, FT4 and TSH) and total protein were measured and analyzed for correlations and differences.

**Results:** Mean age of presentation of malnourished children was 16.14±9.16 months with male to female ratio 1.17:1. The mean value of FT3, FT4 and TSH in the group A was 2.39±1.50 pg/ml, 0.83±0.57ng/dl and 1.57±1.93 mIU/ml while of the group B was 4.55±1.88 pg/ml, 1.26±0.66 ng/dl and 2.12±1.17 mIU/ml respectively. The mean serum total protein was 5.58±0.93 g/dl in group A and 6.63±0.75 g/dl in group B. A significant correlation was found between FT3, FT4, and TSH levels with serum total protein levels.

**Conclusions:** In our study, we found that children with SAM exhibited lower levels of thyroid hormone compared to children with non-SAM. Significant correlation (p<0.05) was noted between thyroid hormone levels and serum total protein levels.

**Keywords:** Severe acute malnutrition, FT3, FT4, TSH, Serum total protein

### INTRODUCTION

India is considered as a major global economy and a country in epidemiological transition, but growth faltering rates are much above critical levels of 20 percent, and need immediate attention to achieve the sustainable development goals (SDGs).<sup>1</sup>

The national family health survey (NFHS-5), India stated that 36% of children <5 years of age are stunted, 20% are wasted, and 32% are underweight.<sup>2</sup>

The world health organization (WHO) defines malnutrition as "the cellular imbalance between the supply of nutrients and energy and body's demand for them to ensure growth, maintenance and specific function".<sup>3</sup> SAM is defined as severe wasting and/or bilateral pedal oedema. In malnutrition, as the supply of protein and energy is limited, the body tries to use them more economically by decreasing the basal caloric expenditure. When a child's intake is insufficient to meet daily needs, physiologic and metabolic changes take place in an orderly progression to conserve energy and prolong life. This process is called "reductive adaptation".<sup>4</sup>

Thyroid hormone is required for normal growth and maturation and is essential in regulating lipid and carbohydrate metabolism. The altered thyroid status in children has been known to contribute to growth retardation in conjunction with malnutrition.<sup>5</sup> As we know malnutrition leads to morbidities and high risk of complications which is not uncommon, however thyroid dysfunction is one of the complications in malnutrition, which is easily preventable and treatable.

In previous studies, it has been observed that prevalence of severe malnutrition in children under 5 years. of age is high in Rajasthan as compared to national average for most of the nutritional indicators (Underweight, Wasting.).<sup>6</sup>

There are limited studies available related to free triiodothyronine (FT3) and free thyroxine (FT4) levels in children with SAM compared to NON-SAM children. The present study has been conducted to study of effect of malnutrition on thyroid hormones and serum protein levels.

#### **METHODS**

A prospective cross-sectional study was carried out in 2024 at malnutrition treatment centre of Bal Chikitsalaya, Udaipur after obtaining approval from Department Review Committee and institutional ethical committee. According to study Lazarus et al sample size was calculated as: serum TSH levels of study group was  $1.93\pm1.2$  and that of control group was  $2.2\pm1.1.7$  Difference of standard deviation was 0.1, detectable mean difference of 20 % between two groups = 0.054. Using p value a statistician tool app sample size calculated as 54. Taking 10 % of non-responders sample size is rounded off to 60 cases and 60 controls.

The study was conducted on 100 malnourished children (1 month-59 months of age) and equal number of age and sex matched non-SAM children. A written informed consent from parents was obtained at the time of admission. The study involved analyzing data from children, categorizing their nutritional status based on severity using anthropometric measurements, including weight, height/length, weight for height, and mid-upper arm circumference. A detailed clinical assessment was performed, and the results were recorded in a predesigned proforma. Cases were classified as SAM according to WHO criteria.

SAM is defined by weight for height<-3SD of WHO standards and/or, mid upper arm circumference (MUAC) <11.5 cm, (in 6-59 months of age) and/or bilateral oedema.<sup>8</sup>

The assessment of malnourished children involved measuring weight with a digital scale, height for those over two years with a stadiometer, and length for less than two years using an infantometer. Mid-upper arm circumference (MUAC) was measured on the left arm with a non-stretchable tape. Weight-for-height was calculated using the IAP growth calculation app. Bilateral

pedal edema was diagnosed by pressing on the tops of the feet; a pit remaining after 10 seconds indicated edema.

#### Inclusion criteria

All severely acute malnourished children (1 to 59 months) fulfilling the WHO criteria and admitted in the department of pediatrics at MTC, children whose parents given the written consent for the same and non-SAM children of similar age groups admitted in pediatric wards were taken as controls were included.

#### Exclusion criteria

Children suffering from chronic infections (i. e., tuberculosis, UTI etc.), malabsorption syndromes (coeliac disease), protein losing enteropathy, nephrotic syndrome, major congenital anomalies and chronic liver and kidney diseases were excluded.

Under aseptic precautions, 3ml of venous blood was collected and was kept in red top vacutainer and test tube. The blood sample was then centrifuged at 5000 rpm (rotation per minute) for 5 minutes; serum thus obtained was used to estimate FT3, FT4, TSH by using (Immulite1000 immunoassay system-Siemens machine). FT3, FT4, TSH levels was estimated by electro chemiluminescence method. Serum total proteins level estimated by Biuret method, serum albumin estimated by Bromocresol green (BCG dye) method.

### Statistical analysis

Microsoft word and excel (2007) was used to generate figures and tables. The data of study was analyzed with the help of SPSS V 17 software for windows. Statistical analysis of categorical variables was compared between groups using the chi square test. Quantitative data was analyzed using student t test. All means were expressed as mean±SD and the proportion in percentage (%). P<0.05 was considered significant.

# RESULTS

A total of 200 children in age group between 1-59 months of age were included in the study. 100 children were severely malnourished (group A) and 100 children were non-SAM (group B). Fifty four percent children were males in group A compared to 61% in group B and 46% were females in group A compared to 39% in group B. The mean age of group A was 16.1 months and the mean age of group B was 18.3 months. The statistically significant difference was not present (p>0.05) (Table 1).

Severely malnourished children in group A were distributed based on their WHO criteria of SAM (Figure 1).

Eighty six percent children were belonged to lower socioeconomic status in group A, whereas in 46%

children in group B. Notably, 35% of group A children were incompletely immunized, compared to 16% in group B, with a statistically significant difference (p<0.05). Additionally, 27% of children over six months in group A were exclusively breastfed, compared to 8% in group B.

Table 1: Age wise distribution of children in group A and group B.

Comorbidity	Group A		Group B	
	N	%	N	%
Anaemia	93	93	77	77
Acute gastroenteritis	43	43	33	33
Pneumonia	25	25	12	12
Pyrexia	12	12	15	15
Sepsis	12	12	8	8
UTI	9	9	17	17
GDD	6	6	1	1
URI	4	4	7	7

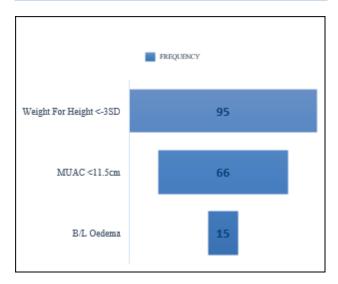


Figure 1: Funnel chart showing distribution of severely malnourished children according to WHO criteria of SAM.

The distribution of comorbidities among children revealed that anemia was the most common, affecting 93% of group A and 77% of group B (Table 2).

Table 2: Distribution of patients according to their comorbidities.

Age (in months)	N (%)		
	(Group A)	(Group B)	
Below 6	1	0	
6-24	86	81	
25-59	13	19	
Total	100	100	
Mean age (months)±SD	16.14±9.16	18.39±8.88	
P value	0.501		

Group A had a mean serum total protein level of 5.58±0.93 g/dl, significantly lower than group B 6.63±0.75 g/dl (p<0.05). The mean value of FT3, FT4 and TSH in the group A was 2.39±1.50 pg/ml, 0.83±0.57 ng/dl and 1.57±1.93 mIU/ml while of the group B was 4.55±1.88 pg/ml, 1.26±0.66 ng/dl and 2.12±1.17 mIU/ml respectively. The mean value of FT3, FT4 and TSH of the group A were significantly lower than the group B and was statistically significant (p<0.05) (Table 3).

Children with total protein levels below 4 g/dL had significantly lower FT3 (1.95±1.29 pg/ml) and FT4 levels (0.47±0.33 ng/dl) compared to the 4-7 gm/dL (FT3: 2.42±1.53 pg/ml; FT4: 0.86±0.58 ng/dl) with significant p<0.05. TSH levels were significantly higher in the total protein below 4 g/dL (3.47±2.40 mIU/ml) compared to the 4-7 gm/dL (1.82±1.45 mIU/ml), with significant difference (p<0.05) (Table 4).

Table 3: Laboratory parameters of group A and group B.

Parameters	Mean±SD, (group A)	Mean±SD, (group B)	T test	P value
Total protein (g/dl)	5.58±0.93	6.63±0.75	3.87	0.021
Albumin (g/dl)	3.09±0.73	3.35±0.68	1.76	0.07
FT3 (pg/ml)	2.39±1.50	4.55±1.88	3.88	0.001
FT4 (ng/dl)	0.83±0.57	1.26±0.66	2.78	0.014
TSH (mIU/ml)	1.57±1.93	2.12±1.17	3.99	0.02

Table 4: Correlation between serum total protein levels and thyroid hormones in group A.

Serum total protein levels	<4 gm/dl, (n=7)	4-7 gm/dl, (n=92)	>7 gm/dl, (n=1)	P value
FT3 (pg/ml)	1.95±1.29	2.42±1.53	2.3	0.026
FT4 (ng/dl)	0.47±0.33	0.86±0.58	1.21	0.032
TSH (mIU/ml)	3.47±2.40	1.82±1.45	1.03	0.001

#### **DISCUSSION**

Malnutrition in children during the first 1,000 days-from conception to 24 months-is a critical global health issue. This period is vital for physical and cognitive development, and poor nutrition can lead to lasting consequences, including poor health, cognitive impairment, academic challenges, and reduced economic productivity later in life.<sup>4</sup> Majority (87%) of SAM

children in our study were between 6-24 months of age, which is Similar to Saini et al, Rajkumar et al and Gupta et al.<sup>5,10,11</sup> The age distribution of patients can fluctuate based on regional differences in healthcare accessibility and infrastructure.<sup>9</sup>

We observed that 54% of cases were males. This could be due to some cultural belief by which boys may receive more resources, leading to better growth and development opportunities. Similar findings were noted by Khan et al, Surewad et al and Bhuyan but Najar et al observed that incidence of malnutrition was higher in females as compared to that in males with ratio 1.38:1.9,12-14 Socioeconomic status is a basic determinant of optimum nutritional status. <sup>15</sup> We found that 86% of children in our study belonged to lower socioeconomic status corresponding to Mehta et al and Nagar et al and Varma et al. <sup>15-17</sup>

Anaemia was most common comorbidity among both the groups (93% in group A and 77% in group B). Out of 93%, 18% children had severe anaemia. Since the majority of children in our study belonged to lower socioeconomic backgrounds, which is a key determinant of food access, their nutritional outcomes may have been influenced by these socioeconomic factors. The findings from Gupta et al highlight that nearly one-third of patients experienced both anaemia and diarrhoea. In contrast, Suman et al reported that two-thirds of their patients were anaemic, with one-third suffering from diarrhoea. 11,18 These discrepancies may be attributed to geographical differences and variations in dietary habits, which can significantly influence nutritional status and health outcomes. In our study, 35% malnourished children were incompletely immunized. Similar study conducted by Saini et al found that 23% children were incompletely immunized. 10

It is well established that exclusive breastfeeding for the first six months, followed by timely and adequate complementary feeding, promotes better growth and development in children. However, practices such as the use of prelacteal feeds, delayed initiation of complementary foods, and unhealthy weaning practices contribute significantly to malnutrition. Me observed that 27% malnourished children of >6 months of age were still on exclusive breastfeeding. Singh et al conducted a study on infant feeding and weaning practices in the rural communities in Rajasthan and observed that only 23% of mothers-initiated breast feeding within 24 hours of delivery and most mothers breast feed for at least 2 years. Description of the strength of the stren

In SAM, serum protein levels are significantly affected due to inadequate or unbalanced dietary intake. The body's energy conservation mechanisms are activated, leading to reduced protein biosynthesis in the liver. In our study we found that malnourished children exhibited a greater decrease in serum proteins levels compared to their non-malnourished counterparts, with a statistically

significant p=0.021. This aligns with studies by Dhanjal et al and Lazarus et al.<sup>7.21</sup>

In malnutrition, the body undergoes reductive adaptation, decreasing the basal metabolic rate (BMR) to conserve prolong survival.<sup>3</sup> energy and This adaptation significantly affects thyroid function, leading to altered thyroid hormone levels. Malnourished children often experience decreased thyroxine (T4) secretion and lower free T3 (FT3) levels due to impaired conversion of T4 to T3, primarily caused by reduced thyroxine monodeiodination in the liver and diminished levels of proteins like albumin and prealbumin.<sup>21</sup> In our study, the mean FT3 level in group A was significantly lower at 2.39±1.50 pmol/L compared to group B at 4.55±1.88 pmol/L (p=0.001). These findings were consistent with those of Dhanjal et al, Shaheen et al, and Shahjadi et al.<sup>21-23</sup> Similarly, the mean FT4 level in group A (0.83±0.57 ng/dl) was lower than in group B (1.26±0.66 ng/dl), with a statistically significant p value less than 0.05. This aligns with studies by Valinjkar et al, Surewad et al, Dhanjal et al and Shaheen et al. 13,21-23 Malnutrition can also disrupt the hypothalamic-pituitary-thyroid (HPT) axis. Reduced circulating nutrient levels can lower stimulation of the thyroid gland by thyroid-stimulating hormone (TSH), leading to decreased T4 production.<sup>21</sup> In our study, the mean TSH level in group A (1.57±1.93 mIU/L) was lower than in group B (2.12±1.17 mIU/L), with a statistically significant difference (p<0.05). This result is similar to that of Shaheen et al who reported a mean TSH of 1.30±0.41 mIU/L in cases versus 1.69±0.062 mIU/L in controls (p<0.05).22 The low TSH levels observed in group A may indicate central unresponsiveness to low FT3 levels, possibly due to low intracellular receptor capacity.<sup>25</sup>

Our study found that children with total protein levels below 4 g/dL had significantly lower mean FT3 (1.95±1.29 pmol/L) and FT4 (0.47±0.33 pmol/L) levels compared to those with protein levels between 4-7 g/dL (FT3: 2.42±1.53 pmol/L, FT4: 0.86±0.58 pmol/L), with p=0.026 and 0.032, respectively. Additionally, TSH levels were significantly higher in the low protein group (3.47±2.40  $\mu$ IU/mL), indicating disrupted thyroid status. These findings are consistent with research by Lazarus et al and Surewad et al underscoring the importance of adequate protein intake for maintaining thyroid function.  $^{7,13}$ 

In our study, some children had elevated TSH levels with normal thyroid hormone levels (subclinical hypothyroidism). This may be due to an exaggerated response to thyrotropin-releasing hormone or impaired breakdown of TSH because of SAM. <sup>16</sup>

We found that 3% of the patients had low FT3 levels along with high TSH but did not have clinical features of hypothyroidism, suggesting these changes might be an adaptive response to malnutrition. Since we did not give thyroid medications and monitor these patients until they

recovered, this could affect their growth and development.

The limitations of our study were serum thyroid binding globulin, thyroid binding prealbumin and antithyroglobulin antibodies were not estimated and malnourished children with altered thyroid hormone levels did not undergo follow-up assessments to evaluate their thyroid hormone status after nutritional recovery.

#### **CONCLUSION**

Our study revealed a low levels of thyroid hormone levels (FT3, FT4) in cases as compared to controls and had a significant correlation between thyroid hormone levels and serum total protein levels. Although 3% of the children in our study diagnosed with hypothyroidism, they did not exhibit clinical features of the condition. Continuous monitoring of these children is necessary to assess the clinical progression of hypothyroidism, determine the need for treatment, and evaluate their growth and development over time.

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Institutional Ethics Committee

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