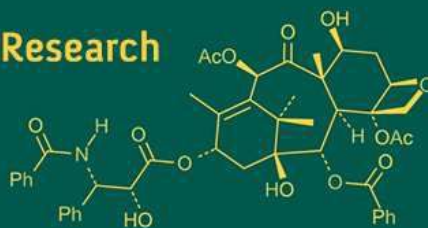
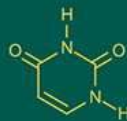


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Serum Thyroid Hormone Status in Children with Severe Acute Malnutrition

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Abstract

Severe acute malnutrition (SAM) is a medicosocial disorder characterized by a range of pathological conditions arising from a deficiency of protein and energy and is commonly associated with infections. To assess the serum thyroid hormone status in children with severe acute malnutrition. A Cross-sectional descriptive study was carried out at Department of Biochemistry in collaboration with the Department of Pediatrics, Sylhet MAG Osmani Medical College, Sylhet, Bangladesh from January, 2022 – December, 2022. Total 35 children were taken in this study. All children with severe acute malnutrition (SAM), attending the Department of Pediatrics, Sylhet MAG Osmani Medical College Hospital, during the study period was the study population. Among them who fulfilled the eligibility criteria for enrollment in the study were selected as sample. The mean age of total 35 children was 14.45 ± 10.03 months, with maximum age 38 months and minimum age 6 months. Among them, 68.6% of SAM children were male ($n=24$) and 31.4% were female ($n=11$). Male to female ratio was 2.2:1. Most of the children were from urban area (74.3%) in the study population. On the other hand, according to monthly family income, majority were in low monthly income group (54.3%). Mean height and weight of SAM children were 49.97 ± 6.56 cm and 2.89 ± 1.19 kg respectively. However, mean value of MUAC and WHZ score was below the cut-off point (113.28 ± 2.04 mm and -2.49 ± 1.19 SD respectively). The mean FT3, FT4, and TSH levels were 2.90 ± 0.79 pg/ml, 1.09 ± 0.32 ng/dl, 5.53 ± 1.67 μ IU/ml respectively in the study participants. The mean TSH values in 6-12, 13-24 and 25-48 months group was 5.19 ± 1.81 , 6.58 ± 0.49 , and 5.28 ± 1.21 μ IU/ml respectively and the range of TSH was 1.78-7.72, 5.66-7.01, and 3.01-7.05 μ IU/ml respectively. The difference of mean serum FT3, FT4 and TSH values were not statistically significant among the different age groups of study subjects (p value > 0.05), as mean values were quite similar in all groups. Among the study participants, 15(42.9%) respondents had increased TSH levels and remaining 20(57.1%) had normal TSH levels according to the cut-off point (0.7-6.4 μ IU/ml). Range of serum TSH in SAM children was 1.78-7.72 (μ IU/ml). About 28.6% of respondents had reduced FT4 level and remaining 71.4% had normal FT4 level according to the cut-off point (0.8-2.0 ng/dl). Range of serum FT4 level in children was (0.58-1.72) ng/dl. Serum FT3, FT4, and TSH levels were found within normal reference range. Based on the results of this study, it can be concluded that there was no change in thyroid hormone status in children with severe acute malnutrition.

Keywords: Serum Thyroid Hormone, Children, Acute Malnutrition

Introduction

Severe acute malnutrition (SAM) is a medicosocial disorder characterized by a range of pathological conditions arising from a deficiency of protein and energy and is commonly associated with infections [1]. SAM is diagnosed when the child has any one of the following criteria: 1) Weight-for-height Z score < -3 SD from the median of the reference population 2) Mid-upper-arm circumference (MUAC) < 115 mm, 3) Bipedal edema [2]. Malnutrition in children is the consequence of a range of factors which are often related to poor food quality, insufficient food intake, and severe and repeated infectious diseases; frequently, it involves some combination of the three [3]. According to malnutrition is synonymous with protein energy malnutrition (PEM), signifying an imbalance between the supply of protein and energy and the body's demand for them to ensure optimal growth and function. This imbalance of protein and energy intake leads to malnutrition in the form of stunting, wasting and underweight. Malnutrition in children is widely prevalent in developing countries. It is one of the leading causes of morbidity and mortality in children throughout the world.

The World Health Organization (WHO) reported that malnutrition is the leading cause of 60% deaths in developing countries in children aged less than five years [4]. About twenty million children under the age of 5 years suffer from severe acute malnutrition globally and one million of them die each year. Six countries in Asia together have more than twelve million children suffering from severe acute malnutrition; 6 lacs in Afghanistan, 6 lacs in Bangladesh, 4 lacs in Pakistan, 6 lacs in Yemen, 1.2 million in Indonesia and 8 million in India. The World Health Assembly's aim of lowering and maintaining the prevalence of SAM below 5% by 2025 is not being yet met for children with SAM. Still, SAM is a life-threatening condition in Bangladesh [5]. SAM causes a wide range of endocrine alterations. In SAM, concentrations of all three thyroid hormone binding proteins (Thyroxine-binding globulin, thyroxine-binding pre-albumin and albumin) are found low and the serum T₄ and T₃ levels decline abruptly, often into a clearly hypothyroid range. However, the serum TSH concentration was found unchanged [6]. Low T₃ levels is probably due to low binding proteins, impaired thyroxine mono deiodination in liver which leads to decreased peripheral conversion of T₄ to T₃ (Acts by inhibiting 5' deiodinase system) [7]. Several studies have been done to estimate the serum FT₃, FT₄ and TSH levels. Most of the studies concluded that hypothyroidism existed were based on the findings of low BMR values and decreased level of peripheral binding protein or total thyroxine levels. But, there was limited data and studies available regarding the concentration of these hormones in SAM. So, this study was designed to assess the thyroid hormone level in children with SAM.

Methodology

Study design: Cross-sectional descriptive study.

Place of study

Department of Biochemistry in collaboration with the Department of Pediatrics, Sylhet MAG Osmani Medical College, Sylhet, Bangladesh.

Period of study: January, 2022 – December, 2022.

Study population

All children with severe acute malnutrition (SAM), attending the Department of Pediatrics, Sylhet MAG Osmani Medical College Hospital, during the study period was the study population. Among them who fulfilled the eligibility criteria for enrollment in the study were selected as sample.

Sample size

Considering 2% prevalence of SAM (BDHS, 2017-18), with 5% significance level and 5% marginal error, sample size was calculated by using Guilford and Frutchers formula. The formula was: $n = z^2pq/d^2$. Hence, the required sample size was 31. Total 35 children were taken in this study.

Inclusion criteria

- Children with severe acute malnutrition between the age group from 6 to 59 months.

Exclusion criteria

- History of chronic disease like chronic kidney disease, chronic liver disease etc.
- History of thyroid disorder.
- Any kind of congenital anomaly.
- Malabsorption syndrome.
- Known Malignancy.
- Endocrinopathies.
- Chronic medication.

Method of data collection

Both qualitative and quantitative data was collected by using a semi-structured questionnaire designed for the study. The questionnaire was prepared by reviewing literature and by consulting with Guide, Co-guide and experts.

Procedure of data collection

All children aged 6 months to 59 months admitted in the Department of Pediatrics, Sylhet MAG Osmani Medical College Hospital during the study period were assessed for severe acute malnutrition. A detailed history was taken from the parents or caregivers regarding the complaints, birth history, socio-economic condition, developmental history, immunization status, feeding including exclusive breastfeeding and faulty feeding practices etc. Then, a thorough physical examination was performed in all subjects. Anthropometric measurements such as weight, height/length, weight for height/length Z score, mid-upper arm circumference and bipedal edema were recorded. In case of children aged less than 2 years old (Or less than 87 cm if the age was not available), recumbent length was measured. On the other hand, in case of 2 years or older children (or 87 cm or more if the age was not available) and able to stand, their standing height was measured with the help of a stadiometer. The stadiometer was placed on a level floor. Shoes and socks were removed before measurement. The length/height of the child was measured to the nearest cm. Weight was taken on a weighing scale. Weight was recorded to the nearest 100 gm. The mid-upper-arm circumference (MUAC) was taken over the left triceps, with the arm hanging by the side, and a non-stretchable tape around the midpoint of the left arm, midway between the acromion process and olecranon process. To locate the correct point for measurement of MUAC, the child was asked to flex their elbow to 90°. A measuring tape was used to find the midpoint between the end of the shoulder (Acromion) and the tip of the elbow (olecranon). That midpoint was marked. Then the arm was allowed to hang freely, palm towards the thigh, and the measuring tape was placed around the arm at the midpoint mark. MUAC was measured to the nearest mm. Children were assessed for the presence of pitting edema. Thumb pressure was applied gently on top of the feet for few seconds and pitting edema was judged.

Blood sample collection procedure

Blood samples were drawn from an antecubital vein under aseptic precautions from each subject in a sterile tube without any anticoagulant for biochemical tests. Serum was separated and biochemical test was done in the Department of Biochemistry, Sylhet MAG Osmani Medical College, Sylhet.

Biochemical Analysis

Serum thyroid hormone (TSH, FT3, FT4) concentration was estimated by ADVIA Centaur CP immunoassay system using direct chemiluminescent technology. 5 Ready Pack (Primary reagent packs containing ADVIA Centaur Lite Reagent and Solid Phase) was used for this purpose.

Statistical analysis

Collected data was checked and edited first. Then, it was processed and analyzed with the help of Statistical Package for Social Science (SPSS) Version 24.0. Quantitative data was expressed as mean $\pm$ SD (standard deviation). Qualitative data was expressed as frequency and percentage. The p-value of <0.05 was considered statistically significant.

Results

A total of 35 children enrolled in this study having severe acute malnutrition (SAM). The mean age of total 35 children was 14.45 $\pm$ 10.03 months, with maximum age 38 months and minimum age 6 months. Among the study subjects, 20(57.1%) children were between to 6-12 months group, 08(22.9%) children were between 13-24 months group and 7(20%) children were between 25-48 months group. Most of the children with SAM were male in the study group. Among them, 68.6% of SAM children were male (n=24) and 31.4% were female (n=11). Male to female ratio was 2.2:1. Most of the children were from urban area (74.3%) in the study population. On the other hand, according to monthly family income, majority were in low monthly income group (54.3%).

Table 1: Demographic characteristics of the study participants (n=35)

Age (months)	Frequency (n)	Percentage (%)
6-12	20	57.1
13-24		
25-48	07	20.0
Total	35	100
Gender		
Male	24	68.6
Female	11	31.4
Total	35	100
Socio-economic status		
Residence		
Urban	26	74.3
Rural	9	25.7
Monthly family income		
Low	19	54.3
Middle	7	20
High	9	25.7

Distribution of participants according to anthropometry measurement

Mean height and weight of SAM children were 49.97 $\pm$ 6.56 cm and 2.89 $\pm$ 1.19 kg respectively. However, mean value of MUAC and WHZ score was below the cut-off point (113.28 $\pm$ 2.04 mm and -2.49 $\pm$ 1.19 SD respectively).

Table 2: Distribution of participants according to anthropometry measurement SAM (n=35)

Anthropometry	(mean $\pm$ SD)
Height (cm)	49.97 $\pm$ 6.56
Weight (kg)	2.89 $\pm$ 1.19
MUAC (mm)	113.28 $\pm$ 2.04
WHZ score	-2.49 $\pm$ 1.19

MUAC= mid-upper arm circumference, WHZ score= Weight-for-height Z score, SD= Standard deviation.

Different thyroid hormone values of the participants:

The mean FT3, FT4, and TSH levels were 2.90 $\pm$ 0.79 pg/ml, 1.09 $\pm$ 0.32 ng/dl, 5.53 $\pm$ 1.67 μ IU/ml respectively in the study participants. Though, all the values were within the reference range.

Table 3: Mean Serum FT3, FT4 and TSH values of the participants SAM (n=35)

Thyroid hormone	(mean $\pm$ SD)
FT3 (pg/ml)	2.90 $\pm$ 0.79
FT4 (ng/dl)	1.09 $\pm$ 0.32
TSH (μ IU/ml)	5.53 $\pm$ 1.67

SD = Standard deviation

Age wise serum FT3 level in study subjects

The mean FT3 values were within the reference range. The mean FT3 values in 6-12, 13-24 and 25-48 months group was 2.93 $\pm$ 0.84, 2.56 $\pm$ 0.09 and 2.80 $\pm$ 0.78 pg/ml respectively and range of serum FT3 was 2.03-3.98, 1.89-3.95, 2.05-3.92 pg/ml respectively.

Table 4: Age wise serum FT3 level in study subjects, SAM (n=35)

Age groups (months)	Frequency (n)	Mean $\pm$ SD	Range (pg/ml)
6-12	20	2.93 $\pm$ 0.84	2.03-3.98
13-24	8	2.56 $\pm$ 0.09	1.89-3.95
25-48	7	2.80 $\pm$ 0.78	2.05-3.92
Total	35	2.90 $\pm$ 0.79	1.89-3.98

SD: Standard deviation, SAM: Severe acute malnutrition

Age wise serum FT4 level in study subjects: The mean FT4 values were not quite similar in all groups, though they were within the reference range. The mean FT4 values in 6-12, 13-24 and 25-48 months group were 1.15 $\pm$ 0.28, 0.93 $\pm$ 0.38 and 1.08 $\pm$ 0.38 (ng/dl) respectively and the range of FT4 was 0.62-1.59, 0.58-1.72, and 0.62-1.59 ng/dl respectively.

Table 5: Age wise serum FT4 level in study subjects, SAM (n=35)

Age groups (Months)	Number (n)	Mean $\pm$ SD	Range (ng/dl)
6-12	20	1.15 $\pm$ 0.28	0.62-1.59
13-24	8	0.93 $\pm$ 0.38	0.58-1.72
25-48	7	1.08 $\pm$ 0.38	0.62-1.59
Total	35	1.09 $\pm$ 0.32	0.58-1.72

SD: Standard deviation, SAM: Severe acute malnutrition

Age wise serum TSH level in study subjects: The mean TSH values were not quite similar in all groups, though they were within the reference range. The mean TSH values in 6-12, 13-24 and 25-48 months group was 5.19 $\pm$ 1.81, 6.58 $\pm$ 0.49, and 5.28 $\pm$ 1.21 μ IU/ml respectively and the range of TSH was 1.78-7.72, 5.66-7.01, and 3.01-7.05 μ IU/ml respectively.

Table 6: Age wise serum TSH level in study subjects, SAM (n=35)

Age groups (Months)	Number (n)	Mean $\pm$ SD	Range (μ IU/ml)
6-12	20	5.19 $\pm$ 1.81	1.78-7.72
13-24	8	6.58 $\pm$ 0.49	5.66-7.01
25-48	7	5.28 $\pm$ 1.21	3.01-7.05
Total	35	5.53 $\pm$ 1.67	1.78-7.72

Comparison of mean FT3, FT4, and TSH levels among different age groups of the study subjects: The difference of mean serum FT3, FT4 and TSH values were not statistically significant among the different age groups of study subjects (p value > 0.05), as mean values were quite similar in all groups.

Table 7: Comparison of mean FT3, FT4 and TSH levels among different age groups of the study subjects, SAM (n=35)

Parameter (Mean $\pm$ SD)	Study subjects			p value
	(6-12) month	(13-24) month	(25-48) month	
FT3 (pg/ml)	2.93 $\pm$ 0.84	2.56 $\pm$ 0.09	2.80 $\pm$ 0.78	0.546
FT4 (ng/dl)	1.15 $\pm$ 0.28	0.93 $\pm$ 0.38	1.08 $\pm$ 0.38	0.295
TSH (μ IU/ml)	5.19 $\pm$ 1.81	6.58 $\pm$ 0.49	5.28 $\pm$ 1.21	0.124

Statistical analysis were done by one way ANOVA

Distribution of participants according to serum TSH level

Among the study participants, 15(42.9%) respondents had increased TSH levels and remaining 20(57.1%) had normal TSH levels according to the cut-off point (0.7-6.4 μ IU/ml). Range of serum TSH in SAM children was 1.78-7.72 (μ IU/ml).

Table 8: Distribution of participants by serum TSH level, SAM (n=35)

Serum TSH level	Frequency (n)	Percentage (%)
Increased TSH level	15	42.9
Normal TSH level	20	57.1

SD: Standard deviation, SAM: Severe acute malnutrition

Distribution of participants according to serum FT4 level: About 28.6% of respondents had reduced FT4 level and remaining 71.4% had normal FT4 level according to the cut-off point (0.8-2.0 ng/dl). Range of serum FT4 level in children was (0.58-1.72) ng/dl.

Table 9: Distribution of participants according to serum FT4 level, SAM (n=35)

Serum FT4 level	Frequency (n)	Percentage (%)
Reduced FT4 level	10	28.6
Normal FT4 level	25	71.4

SAM: Severe acute malnutrition

Discussion

Malnourished children suffer from numerous complications including deficiencies of vitamin, minerals, and trace elements [1]. Severe acute malnutrition (SAM) affects every organ system and as it progresses, organ dysfunction develops, one of those is marked changes in secretion and metabolism of thyroid hormones and in the structure of the thyroid gland [8]. This cross-sectional descriptive study was focused to evaluate the status of serum thyroid hormone in children with severe acute malnutrition. Total 35 children with severe acute malnutrition (SAM) were enrolled in this study. Mean age of SAM children was 14.45 $\pm$ 10.03 months, with maximum age 38 months and minimum age 6 months. Highest percentage of children with SAM were belonged to 06-12 months (n=20/35, 57%). Male were predominantly high (n=24, 68.6%) and male to female ratio was 2.2:1 in this study. In a similar study showed, malnourished children were more (86.25%) in the age group above 2 years where 52.5% of malnourished children were males and 47.5% of children were females [9]. In this study, most of the children

were from urban area (74.3%) and mostly were poor (54.3%) according to monthly family income. Findings were alike another study as a higher percentage of children were from urban municipalities (59.3%) and nearly three-quarters of children belonged to low-income households in children with SAM (45.83%) [10]. Mid upper arm circumference (MUAC) is regarded as a cost effective and easiest method to detect SAM in children with minimal risk. Anthropometry measurement had significant relation with SAM [11]. The mean value of MUAC (113.28 $\pm$ 2.04 mm) and WHZ score (-2.49 $\pm$ 1.19) were low in children according to the cut-off point (MUAC<115 mm, WHZ <-2SD). In this present study, the mean ($\pm$ SD) FT3 value in children with SAM (2.90 $\pm$ 0.79pg/ml) was within the reference range which was quite similar to the study of Osman et al. [12]. They found no significant decreases in T₃. On the other hand, reduced FT4 level was observed in some children but the mean ($\pm$ SD) value of FT4 was within the reference range (1.09 $\pm$ 0.32ng/dl) in this study. According to Chandrashekaraiyah, Ratageri & Kamath [1] TT3 and TT4 levels were low in 22% and 28% children respectively. This was also seen in Surewad et al. [13], where mean FT4 value in children with SAM was less than children with MAM and statistically highly significant ($p<0.001$). Low T₄ levels in children with SAM may be due to fall in thyroid secretion rate, depletion of reserves and failure of the adaptive mechanism. Also in this study, increased TSH levels were observed in children with SAM (n=15, 42.9%), though the mean TSH value was within the reference range (5.53 $\pm$ 1.67 μ IU/ml), which agreed with the study of Abubaker, Mohammed and Salih [14]. Similarly in another study, higher mean value of TSH was found in SAM children [4]. In another study, Chandrashekaraiyah, Ratageri & Kamath [1] showed only 04(8%) children out of 50 had increased TSH level according to the cut-off point. In contrast, study conducted by Gupta and Chaurasiya [15] showed that the mean TSH levels in children were not increased significantly. Again this study showed that the mean FT3, FT4, and TSH values were not significantly differ among the different age group of children with SAM (p value >0.05). Increased TSH levels in some studies could be probably due to an exaggerated response to stimulation by thyrotropin-releasing hormone (TRH) or may be impaired catabolism of TSH due to SAM. The altered thyroid hormone status in children with SAM is perhaps a defense mechanism against excessive metabolic stimulation and energy consumption and protects the malnourished child with low-calorie reserve from an early death [15]. Altogether, this study illustrated the thyroid status in children with SAM and the mean serum FT3, FT4, and TSH levels were found within normal reference range. The findings might be due to small sample size. Further study with age and sex-matched healthy comparative group could potentially add additional insights to this study.

Conclusion

Serum FT3, FT4, and TSH levels were found within normal reference range. Based on the results of this study, it can be concluded that there was no change in thyroid hormone status in children with severe acute malnutrition.

Limitations

- All samples were collected from a single tertiary care centre. Therefore, it may not reflect the regional variations of the country.
- There was a lack of detailed information on dietary intake, serum albumin levels, and nutritional intervention, which could potentially add additional insights to this study.

Recommendations

A multicenter study involving a larger sample size with longitudinal follow-up may be conducted to reach a more reliable conclusion.

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