

## EFFECT OF PROTEIN-ENERGY MALNUTRITION (PEM) ON THYROID HORMONES AND PLASMA PROTEIN LEVELS BEFORE AND AFTER NUTRITIONAL REHABILITATION

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Received : 25/02/2023  
Received in revised form : 27/03/2023  
Accepted : 08/04/2023

**Keywords:**

Protein Energy Malnutrition;  
Thyroxine; Triiodothyronine, Thyroid stimulating hormone.

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DOI: 10.47009/jamp.2023.5.3.147

Source of Support: Nil,  
Conflict of Interest: None declared

*Int J Acad Med Pharm*  
2023; 5 (3); 716-720



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### Abstract

**Background:** Protein-energy malnutrition is one of the leading causes of death among children under five in India. These children undergo several endocrinological adaptive alterations. This study aimed to evaluate the effect of protein-energy malnutrition (PEM) on thyroid hormones and plasma protein levels before and after nutritional rehabilitation. **Materials and Methods:** This prospective observational study was conducted between June 2019 and May 2020, including fifty children aged between 6 months and 5 years with protein-energy malnutrition. Demographics, birth characteristics, nutritional history, and detailed anthropometric measurements were collected using a predesigned template. According to WHO classification, the cohorts were divided into moderate acute malnutrition (MAM) and severe acute malnutrition (SAM) groups. Free Triiodothyronine (FT3), free Thyroxine (FT4), Thyroid Stimulating Hormone (TSH), serum total protein (TP), and serum albumin were estimated in these groups before and after nutritional intervention. **Results:** No statistically significant difference was found between PEM, age, and gender of cases. However, a statistically significant difference was noted in serum albumin in both groups. Free T3 levels were low before nutritional rehabilitation and improved significantly afterward in the MAM group. Serum TSH did not show a significant variation in children of both groups. **Conclusion:** PEM is linked to a decrease in T3 and T4 levels without changing TSH levels. Therefore, it can be concluded that thyroid functions are adversely affected in severe PEM due to the adaptive response to chronic nutritional deprivation. Early intervention with a balanced diet containing essential nutrients is necessary to reduce undernutrition in children.

## INTRODUCTION

Malnutrition is a global problem that affects all geographical areas and age groups, without distinguishing between affluence or poverty and gender. Malnutrition is defined as a mismatch between the body's nutrient requirements and the amount of nutrients it receives, and it can manifest as undernutrition or obesity / overnutrition. Malnutrition in any form is linked to various health problems and carries a higher risk of death.<sup>[1-3]</sup>

According to the World Health Organization's definition of 2010, undernutrition is categorized into protein-energy malnutrition (PEM) or micronutrient deficiency. Acute malnutrition affects about 16 million children under five globally across all geographical spectrum. Undernutrition accounts for

approximately 45 percent of deaths among children under five, primarily in low and middle-income countries. Asia and Africa shoulder the heaviest burden of under-five malnutrition. The National Family Health Survey (NFHS-5), India stated that 34% of children ages less than 5 years are stunted, 20% are wasted, and 32% are underweight.<sup>[2,4-6]</sup>

Undernutrition can manifest in many ways like stunting, wasting, marasmus and kwashiorkor. The clinical spectrum ranges from increased vulnerability to infections, impaired growth and cognitive development, impaired hepatobiliary and thyroid function, reduced sensory-motor abilities and reproductive function, and diminished psychosocial functions.<sup>[7]</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>[8]</sup> Studies have been conducted to understand the relation between thyroid hormones and PEM. However, only a few studies have evaluated the correlation between the effect of malnutrition on thyroid hormones before and after nutritional rehabilitation in children with PEM. Therefore, this study was done to assess and research the changes in the levels of thyroid hormone and plasma protein levels before and after nutritional rehabilitation in PEM children.

## MATERIALS AND METHODS

The aim of this prospective hospital-based study was to evaluate the impact of protein-energy malnutrition (PEM) on thyroid hormone levels and plasma protein levels before and after nutritional rehabilitation. Severe acute malnutrition (SAM) children and moderate acute malnutrition (MAM) children aged 6 months to 5 years were assessed. They were evaluated at Nutritional Rehabilitation Centre (NRC), Institute of Child Health And Research Centre, Government Rajaji Hospital & Madurai Medical College, from June 2019 to May 2020. The study population consisted of fifty children, aged 6 months to 5 years, classified as having protein-energy malnutrition according to WHO criteria. Patients with nephrotic syndrome and chronic glomerulonephritis with an excessive loss of proteins were excluded from the study. Approval from the Institutional ethics committee was obtained before the start of the study. Full written informed parental consent was obtained for all participants. Demographic details such as gender, residence, type of family, and family size were recorded in the study proforma. Birth characteristics, including birth weight, birth order, place of birth, age gap between siblings, and congenital disorders, were also noted. Nutritional history, including breastfeeding practices (such as exclusive breastfeeding), age of weaning, and poor feeding practices, were also documented. Furthermore, the child's medical history, including past and recent illnesses, as well as parental age, education, and occupation, were collected. A detailed clinical assessment of the nutritional status was done. Anthropometric measurements like height, weight and Mid Upper Arm Circumference

(MUAC) were documented. As per WHO classification, children were categorized into moderate malnutrition (z-score between 2SD and 3SD) and severe malnutrition (z-score < -3 SD). To estimate FT3, FT4, TSH, total proteins and albumin, 3 ml of blood was collected under aseptic condition. Free T3, Free T4 and TSH estimation was done by MAGLUMI 600 by using the CLIA method. Biuret method was employed for serum total proteins level analysis and Bromocresol green dye method for serum albumin. After giving nutritional intervention at our NRC and adequate nutrition at home, a repeat measurement of TSH, Free T3, Free T4, Total proteins and albumin was done after 6 months. Initial values were compared with the values after nutritional rehabilitation. IBM Statistical Package for the Social Sciences (SPSS) Software was engaged for statistical analysis. Data were analyzed through the paired T-test, chi-square, and ANOVA tests. P-value <0.05 was considered statistically significant.

## RESULTS

A total of 62 children were enrolled at the start, of which 12 were lost to follow-up. Effectively of the 50 children evaluated, 27 children were categorized into Moderate Acute Malnutrition (MAM) group and 23 into Severe Acute Malnutrition (SAM) group, as per the WHO definition criteria. After giving nutritional intervention and adequate nutrition, they were followed up for 6 months. The highest numbers of cases were noted in the 12-23 month age group, followed by the 48-60 month group. The mean age was 30 months, and the median was 29 months. There was no statistically significant difference ( $p = 0.98$ ) in the age distribution between the PEM and non-PEM cases. The gender distribution is summarized in [Table 2]. Boys made up 52% ( $n=26$ ) of the study population, while 48% ( $n=24$ ) were girls. Sixty one percent ( $n=14$ ) were female and 39% ( $n=9$ ) were male, and 37% ( $n=10$ ) were female and 63% ( $n=17$ ) were male in SAM and MAM respectively. No statistical significance was noted between gender and PEM. The mean birth weight among SAM and MAM cases were 2.33 kg and 2.65 kg, respectively. More than two-thirds of the patients were of birth order more than two. There was no statistical significance in birth-related characteristics among the cases.

**Table 1: Distribution of Age group between groups**

Age (in months)	MAM		SAM		Total
	Female	Male	Female	Male	
6-11	0	4	2	1	7
12-23	4	3	4	3	14
24-35	2	4	3	1	10
36-47	2	2	1	2	7
48-60	2	4	4	2	12
Total	10	17	14	9	50

**Table 2: Distribution of birth parameters between groups**

Parameters	MAM	SAM	TOTAL
BIRTH WEIGHT	<2kgs	1	6
	2-2.5kgs	9	20
	2.5-3kgs	10	14
	3-3.5kgs	6	9
	>3.5kgs	1	1
BIRTH ORDER	1	7	14
	2	12	22
	3	7	11
	4	1	3

**Table 3: Comparison of Lab parameters between groups**

Parameters	MAM				P value	SAM				P value
	Before		After			Before		After		
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
SERUM PROTEIN	6.23	0.49	6.43	0.38	0.099	5.87	0.60	6.34	0.38	0.002
SERUM ALBUMIN	3.80	0.36	3.99	0.29	0.037	3.28	0.51	3.80	0.45	<0.0001
FREE T3	3.13	0.72	3.12	0.57	0.955	3.02	0.85	3.74	0.96	0.010
FREE T4	1.12	0.20	1.15	0.18	0.564	1.16	0.22	1.26	0.26	0.166
TSH	2.18	0.93	2.29	0.86	0.656	3.28	2.31	2.98	1.39	0.596

The mean value of serum protein in MAM children, before and after the nutritional intervention was 6.23±0.49 gm/dl and 6.43±0.37 gm/dl respectively, while it was 5.87±0.59 gm/dl and 6.34±0.37 gm/dl respectively in SAM children.

Serum albumin mean values before and after the nutritional intervention was 3.80±0.35 gm/dl and 3.99±0.28 gm/dl in the MAM group and 3.28±0.51 gm/dl and 3.80±0.45 gm/dl in the SAM group, respectively.

Serum-free T3 (FT3) mean values before and after nutritional intervention were 3.13±0.71 pg/ml and 3.12±0.56 pg/ml, respectively, in MAM children. However, statistically, significant mean values of serum FT3 were noted in SAM children (3.01±0.84 pg/ml before and 3.73±0.96 pg/ml after nutritional intervention).

The mean values of serum-free T4 (FT4) in MAM children before and after the nutritional intervention was 1.11±0.199 ng/dl and 1.15±0.182 ng/dl. In SAM children, the mean values of serum FT4 before and after the nutritional intervention was 1.16±0.21 ng/dl and 1.25±0.25 ng/dl, respectively.

The mean values of serum TSH in MAM children were 2.18±0.93 IU/ml and 2.28±0.86 IU/ml, and in SAM cohorts were 3.23±2.30 IU/ml and 2.98±1.38 IU/ml before and after the nutritional intervention, respectively.

## DISCUSSION

Malnutrition is responsible for claiming the lives of approximately 2.1 million children worldwide every year. In cases of protein-energy malnutrition (PEM), the body's limited supply of protein and energy leads to lowered basal caloric expenditure in an attempt to optimize utilization. PEM has been associated with various endocrine abnormalities, including fluctuations in levels of growth hormone, glucocorticoids, insulin, and thyroid hormones. There are significant changes in thyroid hormone secretion and metabolism and the structure of the

thyroid gland in PEM. As the body tries to adapt to low-calorie intake, the activity of the gland decreases. Also, PEM is linked to a decrease in plasma protein synthesis. Nutrition-sensitive and nutrition-specific interventions have been proposed to address the burden of malnutrition.<sup>[5,8-10]</sup> Therefore, the aim of this research was to investigate the levels of thyroid hormones and plasma proteins in children with PEM before and after nutritional rehabilitation.

During the study period, fifty malnourished children were enrolled and followed up. Of these, 54% belonged to the moderate acute malnutrition (MAM) category, and 46% belonged to the severe acute malnutrition (SAM) category. The highest number of cases was observed in the 12-23 month age group, with a mean age of 30 months. Of the enrolled children, 52% were males, and 48% were females. A higher incidence of SAM (61%) was noted among female children. Following nutritional rehabilitation, both the MAM and SAM groups showed a statistically significant improvement in serum protein and serum albumin levels. However, serum FT3 and FT4 values did not show a significant improvement in MAM children, whereas a significant improvement was observed in SAM children. In PEM children, low levels of T3 are likely caused by low binding proteins, impaired thyroxine monodeiodination in the liver, reduced peripheral T4 to T3 conversion, and high levels of corticosteroids, which are frequently observed in malnourished children. The reduced levels of T4 in children with PEM can be caused by a decrease in thyroid secretion rate, reserve depletion, and failure of the adaptation mechanism. Acute malnutrition causes a decrease in total T4 and T3 levels due to decreased plasma proteins, resulting in euthyroidism, whereas chronic malnutrition causes hypothyroidism since the adaptive system fails. Reduced protein intake and decreased biosynthesis could also explain changes in serum total protein and albumin and PEM.<sup>[8,11]</sup> In the present study,

TSH values did not show any statistically significant improvement in either of the groups. The intracellular monodeiodination of T4 to form T3 at the pituitary level is most likely the cause of normal TSH levels. This results in a negative feedback mechanism that inhibits TSH secretion, accompanied by central insensitivity to low T3 levels, which is attributable to low intracellular receptor capacity.

A case-control study was conducted in India, which included 50 children aged 1-5 years with MAM and SAM, who were receiving treatment at a tertiary care hospital. The study aimed to assess the impact of PEM on thyroid hormone and plasma protein levels and evaluate their interrelationship. The study found that the levels of serum protein, albumin, FT3, FT4, and TSH were significantly lower in the case group. Moreover, the levels of these variables decreased with the increasing severity of malnutrition, and the difference between the groups was statistically significant. The study concluded that PEM is associated with decreased levels of thyroid hormones, total serum protein, and albumin.<sup>[12]</sup> Similar associations with serum proteins and thyroid hormones were noted in the present study, where the mean values of the parameters studied were lower in the SAM group.

Our results agree with another cross-sectional hospital-based case-control study conducted in India. It evaluated 125 children with PEM in the age group of 1-5 years to study the effect and correlation of PEM on thyroid hormone plasma protein levels. Serum total protein and albumin levels, triiodothyronine and T4 levels were statistically low in PEM children. However, TSH levels tallied in both groups.<sup>[8]</sup>

In India, a prospective observational study aimed to evaluate the inter-connection of free thyroid hormone levels and serum proteins in MAM and SAM malnourished children. Similar to the present study, T3 values, serum proteins, albumin and globulin showed significant relation with malnutrition. There was also no link between TSH and the type of malnutrition.<sup>[12]</sup>

Our findings are consistent with Shaheen et al., who measured serum thyroid hormones and serum proteins in 30 children with protein-energy malnutrition.<sup>[13]</sup>

Similar TSH findings were noted by Turkay S et al. and Abrol et al. in their research, which documented no significant variance in TSH level in children with PEM.<sup>[10,14]</sup>

Kumar et al. discovered that as the severity degree of malnutrition increased, the serum concentrations of T3 and T4 reduced while TSH increased.<sup>[15]</sup>

Valinjkar et al. evaluated thyroid status along with serum protein levels in 100 SAM and MAM children. Analogous to the present study, serum proteins were low in both SAM and MAM, and a highly significant interrelationship was noted between the severity of hypoproteinemia and severity of PEM. Also, serum TSH values were

within limits in both groups, and there was no association between the TSH and the malnutrition.<sup>[16]</sup>

In contrast to the present study, Tamzil et al. reported normal thyroxine (T4) and TSH levels in severely malnourished children under the age of five<sup>17</sup>

Another cross-sectional study of 50 children of age group 1- 5 years, which evaluated and compared serum total protein and albumin, and thyroid hormones in PEM children with healthy controls, showed similar results. Serum TT3 and TT4 levels are statistically lower in malnourished than healthy controls.<sup>[18]</sup>

Another parameter evaluated in this study was birth characteristics and malnutrition. According to NFHS-4 data, low birth weight (LBW) is one of the major determinants of chronic childhood malnutrition. In our study, the mean birth weight among SAM and MAM cases were 2.33 kg and 2.65 kg, respectively. LBW is a critical health indicator for babies born weighing less than 2500 grammes. Nearly 52% of children were born with low birth weight.<sup>[19]</sup> Malnutrition has been linked to an increased risk of disease morbidity and mortality, according to a number of studies.<sup>[20]</sup> Ntenda studied 4047 children under the age of five years in a cross-sectional study to see a link between low birth weight and undernutrition. LBW children had significantly higher odds of being stunted, underweight and wasted than children with normal/average birth weight.<sup>[21]</sup> Abbas et al. found that LBW new-borns are at a higher risk of developing wasting and stunting.<sup>[20]</sup> These findings are synchronous with that of the present study where SAM children had low birth weight.

Although the study results are significant, there are limitations that should be considered. A larger, multicentre sample size could have improved the understanding of the relationships between the studied parameters. Additionally, further analysis could have been possible by investigating the levels of TBG and Reverse T3 (rT3).

## CONCLUSION

Malnutrition research will continue to be crucial, particularly in impoverished nations, as it claims the lives of many children under the age of five and has severe consequences such as infections and organ dysfunction. Thyroid hormones play a vital role in metabolism and are critical for normal growth and development. In children, severe protein-energy malnutrition can lead to hypothyroidism if left untreated for an extended period, resulting in delays in physical and mental growth. With this understanding, early detection and appropriate nutritional interventions are expected to aid in combating malnutrition.

## REFERENCES

1. Vassilakou T. Childhood malnutrition: time for action. *Children*. 2021 Feb;8(2):103.
2. Ghosh S. Factors responsible for childhood malnutrition: A review of the literature. *Current Research in Nutrition and Food Science Journal*. 2020 Aug 25;8(2):360-70.
3. Singh A. Childhood malnutrition in India. Perspective of Recent Advances in Acute Diarrhea. 2020 Mar 2. IntechOpen.
4. Gemechu DS, Worku Y, Alemu A, Gerema U. Determinants of severe acute malnutrition among children aged 6–59 months in the pastoral community of Liban District, Guji Zone, Oromia Regional State, Southeastern Ethiopia: a case-control study. *J Nutr Sci*. 2021 Dec 7;10:e101.
5. Campisi SC, Khan A, Zasowski C, Bhutta ZA. Malnutrition. In: *Textbook of Pediatric Gastroenterology, Hepatology and Nutrition 2022* (pp. 609-623). Springer, Cham.
6. Das P, Roy R, Das T, Roy TB. Prevalence and change detection of child growth failure phenomena among under-5 children: A comparative scrutiny from NFHS-4 and NFHS-5 in West Bengal, India. *Clin Epidemiol Glob Health*. 2021 Oct 1;12:100857.
7. Bhutta ZA, Berkley JA, Bandsma RHJ, Kerac M, Trehan I, Briend A. Severe childhood malnutrition. *Nat Rev Dis Primers*. 2017;3:17067.
8. Sandeep M, Krishnamurthy B. Thyroid hormone status in children with protein energy malnutrition. *Int J Contemp Pediatr*. 2016 Feb;3(1):193-19.
9. Brent B, Obonyo N, Akech S, et al. Assessment of Myocardial Function in Kenyan Children With Severe, Acute Malnutrition: The Cardiac Physiology in Malnutrition (CAPMAL) Study. *JAMA Netw Open*. 2019;2(3):e191054.
10. Abrol P, Verma A, Hooda HS. Thyroid hormone status in protein energy malnutrition in Indian children. *Indian J Clin Biochem*. 2001;16(2):221-223.
11. Dhanjal GS, Singh M. *Int J Contemp Pediatr*. 2017 Mar;4(2):351-355
12. Surewad GV, Ambatipudi K, Rao AVS, Rao KN. Interrelation of Free Thyroid Hormone levels and Serum proteins in Malnourished Children at Rural Tertiary Care Hospital in Andhra Pradesh. *J Adv Med Dent Sci Res* 2020;8(11):64-68.
13. Shaheen B, Haji IM, Suma MN. Serum FT3, FT4, TSH and proteins in children with protein energy malnutrition. *Int J Pharm Bio Sci*. 2013;4(3):834-9.
14. Turkay S, Kus S, Gokalp A, Baskin E, Onal A. Effects of protein energy malnutrition on circulating thyroid hormones. *Indian Pediatr*. 1995;32(2):193-7
15. Kumar S, Nadkarni J, Dwivedi R. Thyroid hormone status in malnourished children. *Indian Pediatr*. 2009;46(3):263-264.
16. Valinjkar SK, Sutay NR, Prachi, Vikas. Thyroid Status and Serum Protein Levels in Severe and Moderate Acute Malnourished Children. *J Med Sci Clin Res*. 2016; 4(1): 9059-67.
17. Tamzil SH, Fadil R, Rustama DS, Nataprawira MD. Thyroxine and thyroid stimulating hormone levels in under-five severe malnourished children. *Paediatr Indonesiana*, 2016; 43(2): 42.
18. Gamit AM, Khubchandani AS, Gamit MR, Parmar U, Adarsh A, Gaadhe P. A study of serum total protein, serum albumin and thyroid hormones in protein-energy malnutrition in children. *Intl J Med Sci and Pub Health*, 2017; 6(2):1.
19. Abbas F, Kumar R, Mahmood T, Somrongthong R. Impact of children born with low birth weight on stunting and wasting in Sindh province of Pakistan: a propensity score matching approach. *Sci Rep*. 2021;11(1):19932.
20. Rahman, M. S., Howlader, T., Masud, M. S., Rahman, M. L. Association of Low-Birth Weight with Malnutrition in Children under Five Years in Bangladesh: Do Mother's Education, Socio-Economic Status, and Birth Interval Matter?. *PLoS One*. 2016;11(6):e0157814.
21. Ntenda PAM. Association of low birth weight with undernutrition in preschool-aged children in Malawi. *Nutr J*. 2019;18(1):51.