

**SERUM FT₃, FT₄, TSH AND PROTEINS IN CHILDREN WITH PROTEIN ENERGY MALNUTRITION.****SHAHEEN B^{*1}, ISMAIL M HAJI², SUMA M B³,
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Protein-energy malnutrition (PEM) is one of the important causes of under 5 morbidity and mortality in our country. The aim of this study was to assess the thyroid hormone levels and to correlate the levels with serum protein levels in the PEM patients with that of healthy controls. Serum thyroid hormones and serum proteins were measured in 30 protein energy malnourished children of different grades (I-IV). Serum levels of free tri-iodo thyronine (FT₃), Free thyroxine (FT₄) and thyroid stimulating hormone (TSH) were measured by chemiluminometric assay, serum total proteins by biuret method and serum albumin by BCG Dye method. The results were compared with 30 healthy, age and sex matched controls. There was a significant decrease in serum FT₃, FT₄ and TSH and serum total proteins in PEM patients, when compared to the control group. There was a significant positive correlation between serum thyroid hormones and serum albumin levels in PEM cases.

KEYWORDS: Protein energy malnutrition, tri-iodo thyronine , thyroxine, total proteins, albumin.**SHAHEEN B**Department of Biochemistry, Institute of Medical Sciences
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INTRODUCTION

Protein Energy Malnutrition (PEM) is widely recognised major health problem in the developing countries of the world. It is the most prevalent form of malnutrition among children. PEM is an important cause of childhood morbidity and mortality, leading to permanent impairment of physical and possibly mental growth of those who survive. The child may be marasmic or kwashiorkor^{1,2}. Prevention of PEM is becoming an important issue world wide. Determining the prevalence of PEM in any country is important for planning the care of patients affected by it. UNICEF reports that India has unfortunate distinction of having 75 million malnourished children below 5 years of age. So planning for the prevention and strategies for the treatment of PEM are becoming key issue for all countries, including India³. PEM is a range of pathological condition arising from coincident lack of protein and calories and usually associated with infections and deficiency of micronutrients⁴. PEM affects every organ system. As PEM progresses, organ dysfunction develops. Multiple system affection and several metabolic derangements are expected. Hepatic synthesis of serum proteins decreases and depressed levels of circulating proteins are observed. Thyroid hormones play an important role in the regulation of lipid and carbohydrate metabolism and necessary for normal growth and maturation. Absence of thyroid hormones

causes mental and physical slowing, mental retardation and dwarfism⁵. Studies have shown that in PEM, there are marked changes in secretion and metabolism of thyroid hormones and in the structure of thyroid gland. This results in reduction of activity of the gland and hence decrease in T₃ and T₄⁶. Though few studies have been done on status of thyroid hormones, the studies on free thyroid hormones levels (FT3/ FT4) in childrens are not many^{7,8}. With this view the aims and objectives of this study was to estimate the concentration of serum thyroid hormone levels and proteins in PEM patients and healthy controls and to find out if there is any correlation between serum thyroid hormones and serum proteins levels in PEM cases.

MATERIALS AND METHODS

This prospective study was carried out on 30 children with age range of 12-48 months. An equal number of age and sex matched healthy subjects formed the control group. The present study was conducted on diagnosed patients of PEM admitted in paediatric ward of J.S.S. Medical College and Hospital, Mysore. Diagnosis of PEM was diagnosed by anthropometric measurements and physical examination.

I A P Classification⁹.

This is based on weight for age values.

Table 1
I A P classification of malnutrition.

Grade of malnutrition	Weight for age of the standard (median) (%)
Normal	> 80
Grade I	71-80 (mild malnutrition)
Grade II	61-70 (moderate malnutrition)
Grade III	51-60 (severe malnutrition)
Grade IV	< 50 (very severe malnutrition)

Exclusion criteria: Patients with chronic infectious diseases like nephrotic syndrome, chronic glomerulonephritis and acute renal failure in which there is an excessive loss of proteins and patients with lead poisoning, thalassemia and with congenital anomalies

were excluded from the study. A semi-structured questionnaire (Performa) was used to obtain information from the subjects using interview method. Sample collection, separation and preservation: Aseptically 5ml of venous blood was collected with due consent from the

parents of patients and controls .As soon as the blood was collected from the patients, it was carried to the laboratory in an ice-container. The blood was allowed to clot and serum was separated by centrifugation at 5000 rpm for 5 minutes. It was used to estimate various parameters. Analytical procedure: Serum FT₃, FT₄ and TSH were estimated by chemiluminometric assay, using ADVIA centaur CP, Siemens. Serum total proteins by biuret method and serum albumin by BCG Dye method. All the parameters were estimated in Rx Daytona autoanalyzer using kits provided by Randox. The quality control was done for all the tests performed.

STATISTICAL ANALYSIS:

SPSS for windows Version-16 (2007) was employed for statistical analysis. The Independent- Sample's 't' test procedure was used to compare the mean for two groups of cases. The One-Way ANOVA was used for one-way analysis of variance for a quantitative dependent variable by a single factor

(independent) variable. The correlation between the parameters was worked out using Pearson's correlation. 'p' value < 0.05 was considered to be statistically significant. The study protocol was approved by the institutional ethical committee before the commencement of the study. Informed consent was obtained from the parents/caregivers of participants.

RESULT

In the present study the mean age of PEM patients was 2.86±1.02 years where as in controls, it was 2.72±0.96 years. Sixty five % of PEM cases and sixty five % in controls were males. Table 2 shows weight and height distribution in all the groups. In PEM cases, the mean weight was 9.60 ± 1.64 (kgs) and the height was 101.30 ± 2.95 (cms). In the control group, the mean weight was 13.70 ± 2.47 (kgs) and mean height was 102.86 ± 3.03 (cms). The difference was statistically insignificant.

Table 2
Showing the mean ± SD of weight and height distribution in cases and controls.

Subjects	Weight (kgs)	Height (cms)
Controls (n = 30)	13.70 ± 2.47	102.86 ± 3.03
Cases (n = 30)	9.60 ± 1.64	101.30 ± 2.95

SD = Standard Deviation

Table 3 shows mean serum concentration of FT₃, FT₄ and TSH were significantly decreased in patients when compared to control group. The mean FT₃ value in PEM cases was 1.53 ± 0.27 pg/ml and in controls was 2.25 ± 0.48 pg/ml (p<0.0001). The mean FT₄ value in PEM cases was 1.42±0.31ng/ml and in controls it was 1.66 ± 0.39 ng/ml (p<0.05). The mean TSH value in cases was 1.30±0.41 µIU/ml and in controls was 1.69 ± 0.062 µIU/ml (p<0.004). Also, there was a significant decrease in the

mean TSH values in PEM patients when compared to the control group (p<0.05). In our study, we found a significant decrease in serum total proteins and albumin levels, but A/G ratio was not decreased significantly. The mean total protein levels in cases was 6.57 ± 0.42 g/dl and in controls was 7.36 ± 0.31g/dl (p<0.001). The mean total albumin levels in cases was 3.25 ± 0.39 g/dl and in controls was 4.14±0.36 g/dl (p<0.001) (Table 3).

Table 3
Showing the mean ± SD of FT₃, FT₄, TSH, total proteins and albumin, with their significant differences between cases and healthy controls.

	Cases (n = 30)	Controls (n = 30)	t value	p value
FT ₃	1.53 ± 0.27	2.25 ± 0.48	-6.91	<0.0001(HS)
FT ₄	1.42 ± 0.31	1.66 ± 0.39	-2.54	<0.05(HS)
TSH	1.30 ± 0.41	1.69 ± 0.62	-2.76	<0.05(HS)
Total protein	6.57 ± 0.42	7.36 ± 0.31	-8.03	<0.0001 (HS)
Albumin	3.25 ± 0.39	4.14 ± 0.36	-8.86	<0.0001 (HS)
A/G ratio	1.09 ± 29.3	1.35 ± 1.17	-1.17	NS

SD = Standard Deviation

HS = Highly Significant

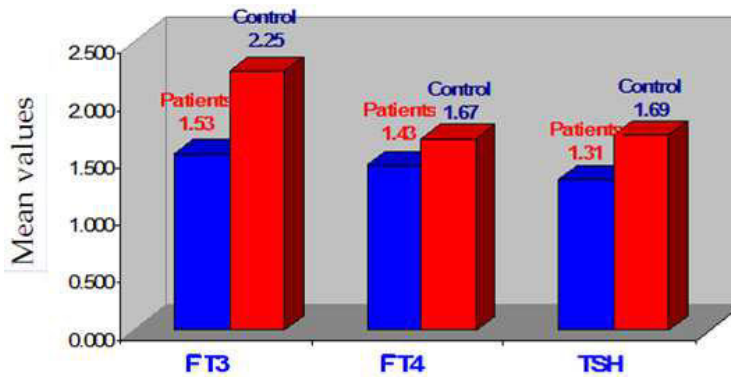
'p' value < 0.05 → Statistically significant

P value = level of significance

t value = test of significance

NS → Not significant

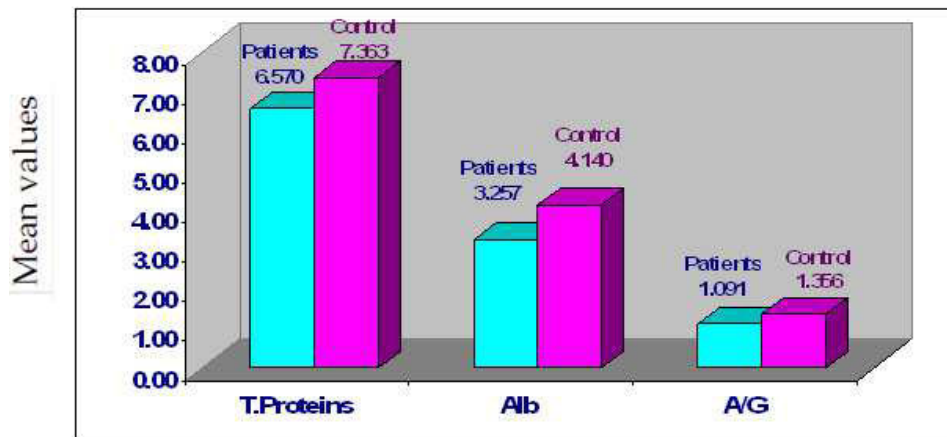
Figure 1
Bar diagram showing the mean values of FT₃, FT₄ and TSH in the study groups



Thyroid profile

This is also shown graphically in terms of mean ± SD as bar diagrams in figure 1. It shows that there is a significant decrease in the mean FT₃, FT₄, and TSH in PEM patients when compared to control group.

Figure 2
Bar diagram showing the mean values of serum total protein, albumin and A/G ratio in the study groups.



Parameters

This is also shown graphically in terms of mean ± SD as bar diagrams in figure 2. It shows that the serum total proteins and albumin are decreased in PEM patients compared to the control group which is statistically significant.

DISCUSSION

Protein energy malnutrition (PEM) continues to be a major public health problem through out the developing world. Malnutrition increases one's susceptibility to and severity of infections, and is the major component of illness and death from diseases. The risk of death is directly correlated with the degree of malnutrition¹⁰. UNICEF reports that India has unfortunate distinction of having 75 million malnourished children below 5 years of age¹. The National Child nutritional survey conducted in 2000 demonstrated that among the children of 6 to 71 months of age, almost 49% were found stunted and nearly 12% wasted and 52% were underweight¹¹. The present study has been undertaken to assess the thyroid hormone levels and to correlate the levels with serum protein levels in the study group. In the present study (table 3) it was observed that mean serum concentration of FT₃, FT₄ and TSH were significantly decreased in patients with PEM when compared to control group. The mean FT₃ value in PEM cases was 1.53 ± 0.27 pg/ml and in controls was 2.25 ± 0.48 pg/ml ($p < 0.0001$). The mean FT₄ value in PEM cases was 1.42 ± 0.31 ng/ml and in controls it was 1.66 ± 0.39 ng/ml ($p < 0.05$). The mean TSH value in cases was 1.30 ± 0.41 μ U/ml and in controls was 1.69 ± 0.062 μ U/ml ($p < 0.004$). Our findings are comparable with previous studies done by Pankaj Abrol et.al, who have found that there was significant decrease in thyroid hormone levels in PEM cases¹. Osman A et. al., have also observed decreased thyroid hormone levels in PEM patients when compared to the control group¹². Another study done by Turkay S et.al, have demonstrated a positive correlation between thyroid hormone levels and albumin levels. Our values of thyroid hormones and albumin can be compared with this study⁸. The findings of the present study and the previous studies show decreased levels of thyroid hormones. The possible changes in thyroid metabolism in PEM probably represent adaptive changes to

the diseased state of malnutrition. Another mechanism for decrease in thyroid hormone levels is due to low levels of binding proteins, altered rate of total and free fractions and decreased peripheral conversion of T₄ to T₃¹³. The reduction of T₃ in PEM patients could be explained by impaired liver function and carbohydrate deficiency, since glucose is an important factor for the liver microsomal enzyme responsible for conversion of T₄ to T₃¹⁴. Animal studies have shown that during starvation, T₄ uptake by liver¹⁵ and the activity of enzyme 5-deiodinase are decreased¹⁶. Low level of thyroid hormones binding proteins in malnutrition are thought to be due to decreased proteins intake and their reduced hepatic biosynthesis¹⁷. After thyroid hormones binding proteins decreases, free thyroxine levels also fall and that explains altered FT₃, FT₄ in PEM¹⁸. In our study, we found a significant decrease in serum total proteins and albumin levels, but A/G ratio was not decreased significantly. The mean total protein levels in cases was 6.57 ± 0.42 g/dl and in controls was 7.36 ± 0.31 g/dl ($p < 0.001$). The mean total albumin levels in cases was 3.25 ± 0.39 g/dl and in controls was 4.14 ± 0.36 g/dl ($p < 0.001$) (Table 3).

Our findings are supported by the previous study done by Rahman MZ et.al, where they observed significant decrease in serum total protein and albumin in PEM patients¹⁹. The levels of serum total protein and albumin were decreased due to decreased protein intake and reduced hepatic biosynthesis of protein in the liver²⁰.

CONCLUSION

In conclusion, the results of our study and as revealed by other studies in review of literature indicate that, the serum thyroid hormone levels were decreased and were positively correlated with serum albumin levels.

REFERENCES

1. Pankaj A, Ashok V, Hooda HS. Thyroid hormone status in protein energy malnutrition in Indian children. *Indian Journal of Clinical Biochemistry*, 16(2):221-223, (2001).
2. Ingenbleek, Y. Thyroid dysfunction in protein calorie malnutrition. *Nutr. Rev* , 44: 253-262, (1986).
3. Wartofsky L and Burman K. Alteration in thyroid function in patients with systemic illness. *Endocrine Rev*, 3:164-217, (1982).
4. Mishra SK, Bastola SP, Jha B. Biochemical nutritional indicators in children with protein energy malnutrition attending Kanti Children Hospital, Kathmandu, Nepal. *Kathmandu University Medical Journal*, 7(26):129-134, (2009).
5. Robert B, Baron MD. Nutritional Disorders. *In: Stephen JM, Maxine AP, editors. Current Medical Diagnosis and Treatment (CMDT). 48th edn: New York: McGraw Hill: 2009, pp 1107-1125.*
6. Stirling G.A. Thyroid status in malnutrition. *Arch Dis Child* ,37: 99-102,(1962).
7. Hatemi N ,Haktan M, Genca E and Cuma T .Thyroid function in protein energy malnutrition . *Turk .J Peditr* , 24 : 29-34,(1982).
8. Turkay S, Kus S, Gokalp A, Baskin E and Onal A . Effects of protein energy malnutrition on circulating thyroid hormones. *Ind. Peditr* , 32: 193-197,(1995).
9. Heird WC. Food insecurity, Hunger and undernutrition. *In: Kliegman, Behrman, Jenson, Stanton, editors. Nelson Textbook of Pediatrics. 18th edition: Elsevier:Saunders, 2008 , pp 227-232.*
10. Fernandex ID, Himes JH, De Oris M. Prevalence of nutritional wasting in populations: building explanatory models using secondary data. *Bull World Health Organ* , 80:282-91,(2002).
11. Rahman MA, Mannan MA, Rahman MH. Serum iron and total iron binding capacity in severely malnourished children. *Bangladesh Journal Pharmcol*, 2:61-65, (2007).
12. Osman A, Khalid BA, Tan TT. Serum thyroid stimulating hormone in malnutrition: Preliminary results. *Singapore Med J*, 34:225-228,(1993).
13. Ingbar SH. The thyroid gland: Nutritional influences. *In: Wilson JD, Foster DW, editors. William's text book of endocrinology. 7th edition; Philadelphia: WB Saunders, 1985, pp 708-712.*
14. Momura S, Pittman CS. Hormones in protein energy malnutrition. *J Clin Endocrinol Metab* , 36:776-779,(1973).
15. Jennings A, Ferguson D. C and Utiger R D. Regulation of the conversion of thyroxine to tri – iodothyronine in the perfused rat liver. *J. Clin . Invest*, 64: 1614- 1619,(1979).
16. Balsam A and Ingbar S H. The influence of fasting, diabetes and several pharmacological agents on the pathways of thyroxine metabolism in rat liver . *J .Clin . Invest*, 62: 415-423,(1978).
17. Kalk WJ, Hofman KJ , Smith AM , Drimmelen MY , Walt LA and Moore RE. Thyroid hormone carrier protein interrelationship in children recovering from kwashiorkor. *Amer J Clin Nutr* , 43 : 406-413,(1986).
18. Tibaldi JM and Surks MI. Effects of non – thyroidal illness on thyroid function. *Med Clin North Am*, 69: 899-911,(1985).
19. Rahman MZ, Begum BA. Serum total protein, albumin and A/G ratio in different grades of protein energy malnutrition. *Mymem Singh Med J*, 14(1):38-40,(2005).
20. Kalk, Hoffman WJ, Smit AM, Drimmelen, Watt MY, Moore. Thyroid hormone and carrier protein interrelationships in children recovering from kwashiorkor. *Amer J Clin.Nutr*, 43:406-413, (1986).