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To Study Serum Triiodothyronine (T3), Thyroxine (T4), Thyroid Stimulating Hormone (TSH) Levels in Children with Grade III and Grade IV Protein Energy Malnutrition (Cases) And in Children with Grade I and Grade II Protein Energy Malnutrition (Controls)

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Original Research Article

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Abstract: The main objective of the study was estimation of serum T3, T4 and TSH levels in severely malnourished children admitted in nutrition rehabilitation centre of Teritary level care hospital, and find out any co-relation with serum protein and serum albumin levels. In NRC, during study period, 164 children were admitted. A total of 40 severely malnourished children and 20 children with grade I and II PEM were included. Serum levels of T3, T4 and TSH, and total protein and albumin were estimated in both groups. The mean serum T3 levels were significantly lower in severely malnourished children, whereas T4 and TSH levels were in normal range. As the severity of PEM increased, there was progressive decrease in mean T3 levels; the levels of T3 were significantly low only in grade IV PEM. In spite of low T3, none of children were clinically hypothyroid. The low T3 in malnutrition is attributed to impaired thyroid secretion rate, low thyro-binding protein, and impaired T4 mono-deiodination in liver due to reduced activity of 5'deiodinase system. Cortico-steroid which is elevated in acute PEM, also inhibits T3 generation from T4 by inhibiting 5'deiodinase system.
Keywords: Serum Triiodothyronine, Thyroxine, Thyroid Stimulating Hormone & Protein Energy Malnutrition.

INTRODUCTION

Majority of the children in India who live below the poverty line in an environment of multi-deprivation and starvation have physical and developmental retardation. It has been estimated that in India 65% that is nearly 80million children under 5 years of age suffer from varying degree of malnutrition [1,3].

Manifestations of PEM include retarded growth rate and limited weight gain with delayed skeletal maturation. These effects may be mediated by alterations in hormonal and metabolic balance such as changes in thyroid hormone metabolism. Normally, 100% of circulating thyroxine (T4) and 20% of circulating triiodothyronine (T3) originate from the thyroid gland; majority of T3 is produced by 5'-deiodination of thyroxine, primarily by the liver and kidney. In energy and protein restriction, several aspects of thyroid hormone and iodine metabolism are affected. Serum proteins including thyroxine-binding globulin (TBG), thyroxine-binding pre-albumin (TBPA) and albumin are all reduced due to decreased protein intake and reduced hepatic biosynthesis. In acute PEM there is reduction in total T3, T4 secondary to reduced plasma proteins with maintained euthyroid state, in prolonged PEM there is overriding of adaptive mechanism leading to hypothyroidism. These changes play an important role in adaptive process of energy and protein metabolism in PEM, help in energy conservation when energy producing substrate is scarce, protects the child from early death due to low calorie reserve [2, 4, 5,6].

MATERIALS & METHODS

This was a hospital based case control study, conducted in the Nutrition Rehabilitation Center of tertiary level care Hospital, Indore from October 2011 to September 2012.

SELECTION OF CASES

Inclusion criteria

Cases were children between 6 months to 5 years of age with grade III and IV malnutrition admitted in NRC.

Criteria for NRC admission

Children between 6 months to 60 months of age (37)

Weight \height or Weight\length <-3 Z score
OR
Mid upper arm circumference <115 mm
OR
Presence of bilateral odema

Exclusion criteria

- Children suffering from endocrine disorders.
- Children suffering from malabsorption syndrome, protein losing nephropathy.
- Children with congenital anomalies.
- Children with severe systemic illness.

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SELECTION OF CONTROL

Children with PEM grade I and II without any other pathological problem. The children admitted in the NRC, department of paediatrics, during the study period fulfilled the NRC criteria for admissions were included in the study. They were divided into two groups. The first group was study group with 40 children admitted in NRC. Second was the control group with 20 children with grade I and II PEM. Consent was taken appropriately from parents.

Anthropometry

Weight, height\length, head circumference and MUAC were measured using standard technique. All of them were then classified according to IAP classification of malnutrition (44).

A. General Examination - thorough examination was done, emphasis was given to detect any signs of vitamins deficiency and hypothyroidism.
B. Systemic Examination - All systems were examined.

And at the end, clinical diagnosis was made i.e. children were nutritionally deprived. Then routine blood investigations were done of all children at the time of admission including haemoglobin, total WBC count, differential count, platelet count, random blood sugar, serum electrolytes, chest x-ray, mantoux test , stool and urine routine and microscopic examination. On this basis final diagnosis was made.

On the first day of admission, 2 venous blood specimens (3ml and 2ml) were collected from all children of case and control group. Following investigations were done-

- SERUM T3, T4, TSH
- SERUM PROTEIN
- SERUM ALBUMIN

SERUM T3 ESTIMATION

Serum T3, T4 & TSH was estimated by CLIA method by using commercial kits (Seimens Ltd, ADVIA Centaur by Thyrocare)

STATISTICAL ANALYSIS

The data was then analyzed, p-value for serum T3 was 0.013 and was statistically significant.

OBSERVATION & RESULTS

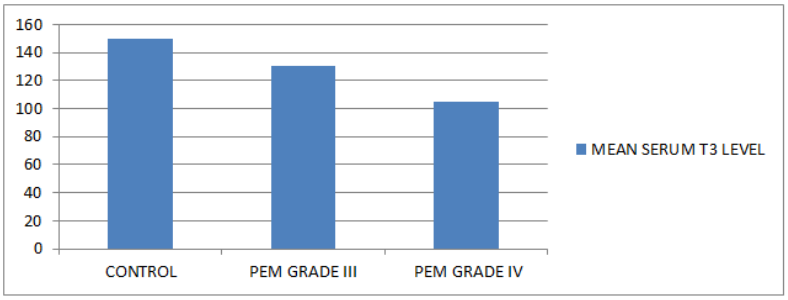

Fig-01: Mean serum t3 level

This graph shows as the severity of malnutrition increases there is progressively fall in serum T3 levels.

Table-01: Mean serum t3 level

	Range	Mean	S.D.
Control	112-206	149.5	23.50
PEM grade III	71-192	130.7	42.18
PEM grade IV	69-199	105.3	45.20

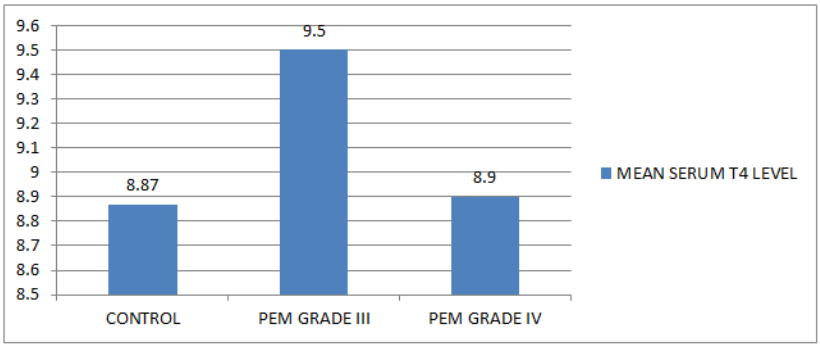

Fig-02: Mean serum t4 level

This graph shows that there was no major difference in serum T4 levels in both study and control group.

Table-02: Mean serum t4 level

	Range	Mean	S.D.
Control	6.4-11.2	8.87	1.25
PEM grade III	4.7-13.4	9.50	2.39
PEM grade IV	4.9-12.8	8.90	2.20

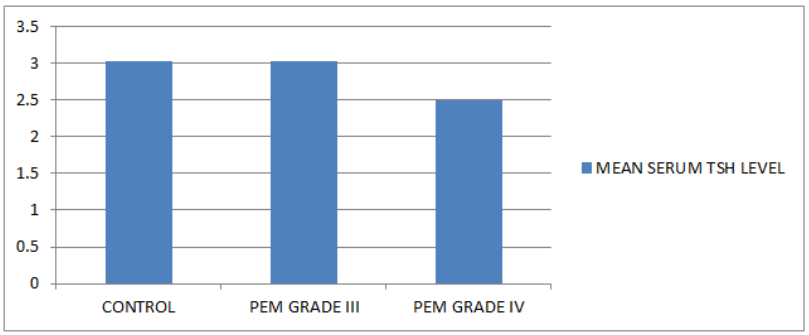

Fig-03: Mean serum tsh level

This graph shows that there was no major difference in serum TSH levels in the study and control group.

Table-03: Mean serum tsh level

	Range	Mean	S.D.
Control	1.30-5.30	3.02	1.02
PEM grade III	0.85-5.27	3.03	1.56
PEM grade IV	0.99-5.80	2.50	1.80

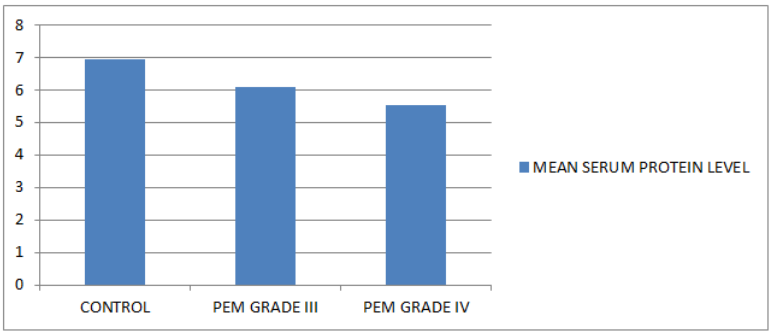

Fig-04: Mean serum protein level

Table-04

	Range	Mean	S.D.
Control	6.09-8.29	6.95	0.47
PEM grade III	3.09-7.99	6.10	1.22
PEM grade IV	4.50-7.49	5.52	0.81

This graph shows that majority of children in study group had lower level of serum protein levels as compared with control group, and there is progressive fall in its level as the severity of malnutrition increases.

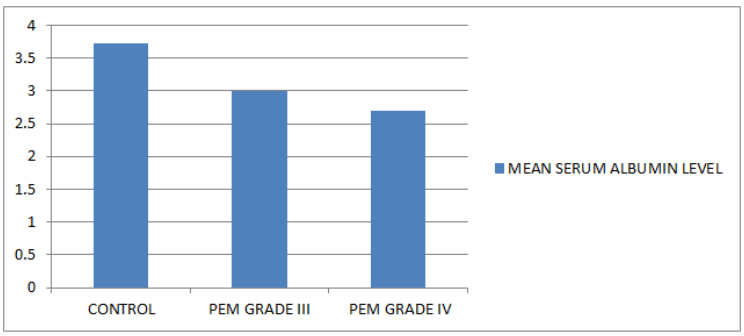

Fig-05: Mean serum albumin level

Table-05

	Range	Mean	S.D.
Control	3.09-4.09	3.72	0.29
PEM grade III	1.29-3.69	3.00	0.63
PEM grade IV	2.00-3.89	2.69	0.58

This graph shows that majority of children in study group had lower level of serum albumin levels as compared with control group, and there is progressive fall in its level as the severity of malnutrition increases.

STATISTICAL ANALYSIS

	ALL CASES Vs CONTROL	PEM III Vs CONTROL	PEM IV Vs CONTROL	PEM III Vs PEM IV
T3	0.013	0.076	0.001	0.113
T4	0.506	0.285	0.962	0.488
TSH	0.580	0.980	0.318	0.376
S.PROTEIN	0.001	0.005	<0.001	0.170
S.ALBUMIN	<0.001	<0.001	<0.001	0.178

METHOD OF STATISTICAL ANALYSIS

One way Analysis Of Variance (ANOVA) test was used to analyze the statistical significance of results as data are quantitative and more than 2 groups are compared.

DISCUSSION

This Hospital based case control study has shown low level of serum T3 levels, more significant in children with SAM in case group, while we found that there was no significant difference in value of serum T4 and serum TSH levels between case and control groups. We found that low serum T3 levels in SAM children may be due to low conversion of T4 to T3, as low serum protein levels. Serum protein and albumin levels were also measured in all cases and control, the serum levels of protein and albumin were found to be decreased in PEM children. Mean value of serum albumin in control group was 3.72, while it was 3.00 in children with grade III malnutrition, and 2.69 in children with grade IV malnutrition. So there was progressive decrease in serum protein and serum albumin levels as the severity of malnutrition increased.

In present study, T3 levels showed a strongly positive correlation with the acute malnutrition is attributed to an adaptation process. T4 levels depend upon an unsteady mass equilibrium between carrier proteins and available body thyroxine.[7] In acute PEM, there is gradual drop in thyro-binding protein allowing rise of T4 in opposite direction. However, low T4 observed in severe grade of PEM suggests failure of the adaptive mechanism in severe and long term malnutrition.

Das *et al*. [12] also studied 76 malnourished infants and children also found low mean serum T3 levels, where as TSH and T4 levels were within normal limits. Normal TSH levels was due to intracellular monodeiodination of T4 toT3 at pituitary level and normal T4 levels was due to adaptive process.

Sanjeev Kumar *et al*. [8] in their study on 60 children with malnutrition (cases) made an observation that there was significant correlation between severity of malnutrition and anthropometry, mean serum total protein and albumin levels were significantly lower in grade II and III cases. With progressive increase of

severity of malnutrition the T3 level decreased significantly, mean serum T4 level also showed a significant fall in grade III PEM, serum TSH level progressively increased with increasing severity of malnutrition. Low plasma T3 levels was due to decreased peripheral conversion of T4 to T3 and attributed to impaired thyroid binding proteins like TBG, TBPA and Albumin [5].

Rahman M Z *et al*. [9] in their study on 30 children suffering from protein energy malnutrition of different grade made an observation that Serum total protein and albumin levels in grade-I grade-II and grade-III PEM were significantly lowers than controls. Serum albumin/globulin ratio (A/G) of grade-1 & grade-II PEM were high than that of control, but not significantly, but in grade-III PEM this values were significantly higher than that of control[11].

Pankaj abrol *et al*. [10] also compared thyroid hormones status between different grades of PEM with age matched healthy controls found T3 and T4 were significantly lower in PEM cases whereas TSH levels were similar with the controls groups.

Normal TSH in spite of low T3 is explained on the basis that T4 undergoes intracellular de-iodination to T3 at pituitary level, it might be compensating for decreased availability of T3. The circulating T4 fraction perhaps reflects the actual thyroid status; whereas intracellular T3 resulting from T4 conversion is principal metabolically active hormone. In most conditions with low T3, TSH hypersecretion is recorded only when T4 levels drop to hypothyroid range. Another reason for normal TSH level is central unresponsiveness to low T3 due to low intracellular T3 receptor capacity.

CONCLUSION

This study concluded the mean level of Serum T3 were significantly decreased severely malnourished children, whereas T4 and TSH levels were in normal range. As the severity of PEM increased, there was progressive decrease in mean T3 levels; the levels of T3 were significantly low only in grade IV PEM. In spite of low T3, none of children were clinically hypothyroid. The low T3 in malnutrition is attributed to impaired thyroid secretion rate, low thyro-binding protein, and impaired T4 mono-deiodination in liver due to reduced activity of 5'deiodinase system. Altered thyroid profile in PEM is perhaps a defense mechanism against excessive metabolic stimulation and energy consumption. The resultant hypometabolism protect the malnourished child with low calories reserve from an early death.

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