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# Assessing Protein Energy Malnutrition in Children: Biochemical Markers Serum Total Protein, Serum Albumin and Serum Protein Electrophoresis

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## ABSTRACT

**Introduction:** Protein Energy Malnutrition (PEM) is a global problem among children. Worldwide 27% under five children are malnourished. PEM is more prevalent in India where almost half (47%) the children are underweight. Assessment of PEM has traditionally been clinical which is time consuming and skill dependent, with considerable inter-observer variability. Hence, biochemical markers like serum protein and albumin measurements may be used for the assessment of nutritional status. At the same time, there is a controversy, whether edema can be considered as a reliable clinical marker of hypoalbuminemia. Readily available and reliable tests and can often detect nutritional deficiencies before they have an adverse effect on biological functions and certainly before deficiencies can be detected by physical examination.

**Aims and Objectives:** The study was designed to assess PEM in children using biochemical markers like serum protein, albumin and protein electrophoresis and establishing a correlation between edema and hypoalbuminemia.

**Materials and Methods:** This analytical case control study was done in the Narayana Medical College and Hospital from September 2007 to September 2009. The material for the study consisted of 50 cases of PEM and 20 normal healthy children.

**Result:** In PEM cases, total protein and serum albumin were found to be significantly lower in comparison to normal healthy controls. Thus total protein and serum albumin may become useful indicators of the nutritional status of the malnourished children and good markers of PEM. Albumin and beta fractions of Serum Protein Electrophoresis were significantly lower while alpha1, alpha 2 and gamma globulin fractions were significantly higher in malnourished children in comparison to controls.

**Key Words:** PEM, biochemical markers, serum protein, hypoalbuminemia, Electrophoresis, Edema

**Running Title:** Assessing PEM in Children by Biochemical Markers

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## INTRODUCTION

Protein Energy Malnutrition (PEM) is a range of pathological conditions arising from concurrent lack in varying proportions of proteins and calories, occurring most frequently in infants and young children and commonly associated with infection<sup>1</sup>. Malnutrition is a global problem, with adverse effects on the survival, health performance and development of population groups. Globally among children under 5 years of age, 27% are underweight.

Malnutrition is more common in India (47%) than in Sub-Saharan Africa (29%). One of every three malnourished children in the world lives in India. The National Family Health Survey (NHFS) shows that PEM is most commonly seen in preschool children between the age of 6 months to 2 years, and around 50- 60% of children are malnourished by the age of 2<sup>2</sup>. PEM has been recognized as a major health and nutrition problem in India, and some 6,600 children under the age of 5 die every day from malnutrition. PEM accounts for death in 7% cases and is the underlying cause of death in 46% deaths of children under 5. A major cause of death is the potentiation of the infectious diseases due to malnutrition. In India 46 % of all children under the age of three are too small for their age, 47 % are under weight and 16% are wasted. Prevalence of severe malnutrition varies across the states with Madhya Pradesh recording the highest rate (55%) and Kerala the lowest (27%). In Andhra Pradesh it is 37%<sup>3</sup>.

Only 2-5% of pre-school age children suffer from severe PEM while the majority of cases (60-70%) are mild to moderate where features of florid PEM are not easily recognisable. The clinical parameters are subjective and time consuming, hence some biochemical markers would help to easily and objectively identify mild to moderate cases. Protein energy malnutrition is marked by low plasma protein concentration. The use of serum protein measurement is widespread for the assessment of nutritional status. The circulating concentration of transport protein, traditionally albumin, has been used to define protein deficiency<sup>4</sup>.

At the same time there is controversy whether edema can be considered as a reliable clinical marker of hypoalbuminemia. Albumin is the single most important substance that contributes to

plasma colloidal osmotic pressure<sup>5</sup>. It was proposed that serum albumin concentrations are functionally important in the development of kwashiorkor, by the recognition that the contribution of albumin to the total colloid osmotic pressure of plasma (>50 %) is greater than that of other plasma proteins, but other abnormalities occur and their importance has to be considered. Hypoproteinemia predisposes to edema, and Montgomery<sup>5</sup> demonstrated a significant correlation of hypoproteinemia with the degree of edema. Hay and Whitehead had proposed that in malnourished children only the total protein and serum albumin concentrations were the determinants of edema, and there was a well defined mathematical relation between these factors and chance of survival<sup>6-8</sup>. However, Coward proposed that a significant correlation does not exist between serum albumin concentration and edema until serum albumin concentration is very low. An increase in serum globulin resulting from infection probably explained why serum colloidal osmotic pressure was maintained despite an initial fall in plasma albumin concentration<sup>9</sup>.

Interest in biochemical parameters as a mode of nutritional assessment stems from the belief that biochemistry could provide the earliest possible indication of the change in nutritional status. It is true as the order of nutritional pathogenesis is biochemical change, then cell or organ damage and finally overt clinical malnutrition.

Readily available and reliable nutrition tests and measurements can often detect nutritional deficiencies before they have an adverse effect on biological functions and certainly before deficiencies can be detected by physical examination.

This study was designed to assess protein energy malnutrition in children using biochemical markers like serum total protein, Serum Albumin and serum Protein Electrophoresis, and establishing a correlation between edema and hypoalbuminemia.

## MATERIALS AND METHODS

**Study Design:** Analytic epidemiology case control Study. The study extended for a period of 2 years from September 2007 to September 2009.

The study was done on 50 children suffering from PEM (cases) and 20 normal healthy children (controls).

All children, who either came to outpatient department or were admitted in the Pediatric Ward of Narayana Medical College and Hospital and satisfied the case definition criteria of PEM as per Indian Academy of Pediatrics (IAP classification)<sup>10</sup> were included in the study.

Informed consent was obtained from the parents of the children.

Parameters	Method
Weight	Weighing machine
Serum Total Protein	Biuret Method
Serum Albumin	Bromo Cresol Green Method
Serum Protein Electrophoresis	Serum Protein Electrophoresis kit

#### Inclusion Criteria.

**Cases:** All children below 5 yrs who either came to the outpatient department or were admitted in the pediatrics ward of Narayana Medical College and Hospital and satisfied the case definition criteria of PEM (as per IAP Classification) were included in the study.

**Controls:** Age and sex matched normal healthy children who visited the Immunization Clinic of Narayana Medical College and Hospital, Nellore.

#### Exclusion Criteria

Children with lesion like lymphoma, tuberculosis, leukemia, dehydration, clinical evidence of infections or septicemia, nephrosis, liver cirrhosis, cardiac failure and severe anemia or any other systemic disease leading to weight loss were excluded from the study.

#### METHODS

A detailed history and thorough clinical examination including auxiologic (Height, Weight, Mid-arm circumference) measurements and relevant laboratory investigations were done as per proforma.

**Serum sample:** About 5 ml of blood sample was collected from selected children under aseptic conditions from a vein. Then the sample was transferred to plain tubes to get serum. The

samples were centrifuged and the serum thus obtained was either analysed or stored at 2-8°C.

Data analysis was done using SPSS version 12.0. Study variables were expressed in terms of Mean  $\pm$  Standard Deviation (S.D.).

The "p value"  $<0.05$  was considered significant and  $<0.001$  was considered highly significant.

Within a study group relation between 2 variables was assessed using Pearson's correlation test with "p value" less than 0.05 as significant limit.

The mean and Standard deviation of all the parameters were calculated.

#### RESULTS

Table 1 shows the comparison of weight for age between cases (children with PEM) and controls. The weight for age in cases is significantly lower than that for controls as "p value" is 0.000.

Table 2 shows the comparison of total protein and serum albumin between cases and controls. Both the total protein and serum albumin were significantly lower in cases than in controls. "p value" for both the parameters is 0.000.

Table 3 shows the comparison of different fractions of serum protein electrophoresis between cases and controls.

**TABLE 1: Age and Weight Distribution**

Parameter	Cases	Controls	t value	p value
Age (years)	3.34 $\pm$ 2.66	3.4 $\pm$ 2.4	0.128	0.898
Weight (kg)	8.16 $\pm$ 3.79	15.1 $\pm$ 5.5	6.110	0.000

**TABLE 2: Total Protein and Serum Albumin.**

Parameters	Cases	Controls	t value	p value
Total protein(g/dl)	4.42 $\pm$ 0.52	7.0 $\pm$ 0.9	14.673	0.000
Serum albumin (g/dl)	2.0551 $\pm$ 0.38	4.1 $\pm$ 0.6	17.013	0.000

The mean value of albumin and beta fractions of serum protein electrophoresis for malnourished children were 46.3  $\pm$  5.2% and 6.58  $\pm$  1.64% respectively, whereas in controls they were 59.2  $\pm$

3.1% and  $9.7 \pm 0.9\%$  respectively. So albumin and beta globulin fractions were significantly lowered in malnourished children in comparison to controls, "p value" being 0.000

The mean value of alpha 1, alpha 2 and gamma fractions of serum protein electrophoresis for malnourished children were  $7.12 \pm 2.44\%$ ,  $12.8 \pm 3.89\%$  and  $27.8 \pm 53.1\%$  respectively, whereas in controls they were  $3.3 \pm 1.0\%$ ,  $9.9 \pm 2.9\%$  and  $17.9 \pm 3.9\%$  respectively. So both alpha 1, alpha 2 and gamma fractions were significantly raised in malnourished children in comparison to controls, "p value" being  $< 0.05$ .

Table 4 shows the correlation of edema with hypoalbuminemia in cases.

Among 28 children having edema, 22 children (79%) had hypoalbuminemia, whereas 6 children (21%) did not have hypoalbuminemia. So no significant difference was found in the number of edematous children with hypoalbuminemia and those without hypoalbuminemia.

Among 41 children having hypoalbuminemia, 19(46%) children did not have edema.

Similarly no significant difference was found in the presence<sup>6</sup> or absence of edema<sup>3</sup> in children without hypoalbuminemia.

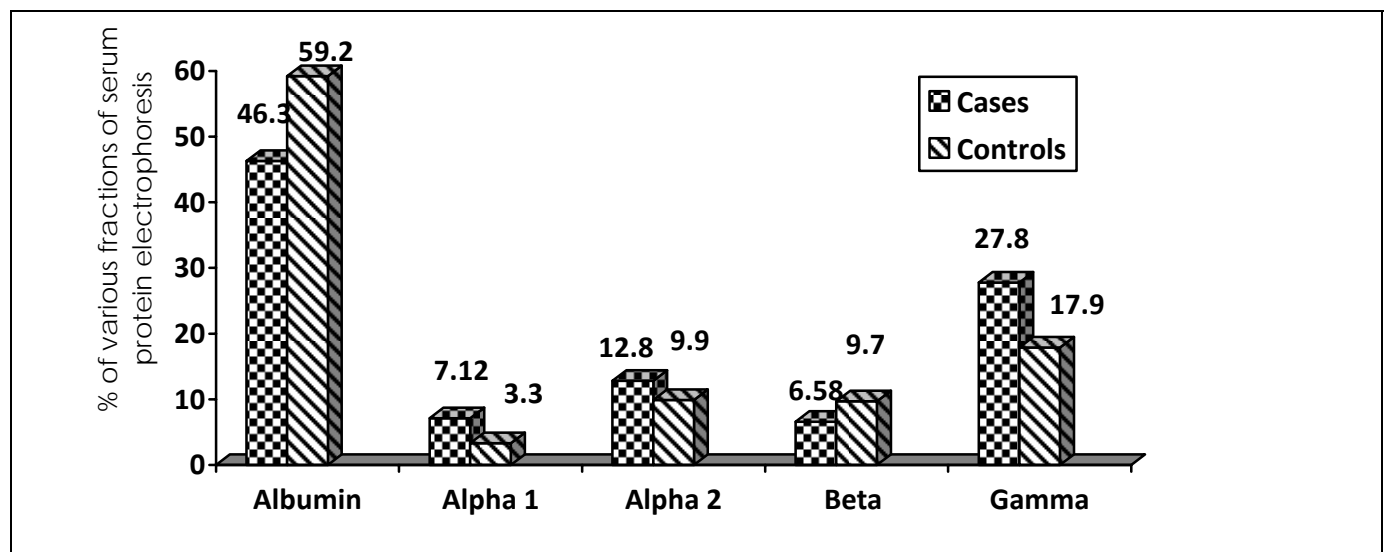
**TABLE 3: Serum Protein Electrophoresis**

Different Fractions Of Serum protein electrophoresis (%)	Cases	Controls	t value	P value
Albumin	$46.3 \pm 5.2$	$59.2 \pm 3.1$	10.071	0.000
alpha 1 globulin	$7.12 \pm 2.44$	$3.3 \pm 1.0$	6.795	0.000
alpha 2 globulin	$12.8 \pm 3.89$	$9.9 \pm 2.9$	3.025	0.004
beta globulin	$6.58 \pm 1.64$	$9.7 \pm 0.9$	7.983	0.000
Gamma globulin	$27.8 \pm 5.31$	$17.9 \pm 3.9$	7.531	0.000

**TABLE 4: Edema in relation with Hypoalbuminemia in PEM cases**

Parameter	Hypoalbuminemia Present	Hypoalbuminemia Absent	Total Number of cases
Edema			
Present	22	6	28
Absent	19	3	22

P value = 0.477.



**Fig 1: Comparison of various fractions of Serum Protein electrophoresis**

## DISCUSSION

**Total protein and Serum albumin:** A comparison of total protein and serum albumin between cases and controls has shown significantly lower values for cases than controls.

The mean value of Total protein for cases is  $4.42 \pm 0.52$  g/dl, while that for controls is  $7.0 \pm 0.9$  g/dl. (Table 2). So there is highly significant difference "p value" being 0.000.

The mean value of serum albumin for cases is  $2.0551 \pm 0.38$  g/dl and for controls  $4.1 \pm 0.6$  g/dl. So the difference is highly significant, "p value" being 0.000.

So in this study it has been observed that total protein and serum albumin are significantly lower in malnourished children when compared to normal healthy children.

Ibrahim, Elton and others had observed that the total plasma proteins and albumin were significantly lower in the malnourished cases when compared to controls<sup>11-12</sup>.

A low serum albumin concentration is a common finding in PEM; as a result it is commonly employed as a measure of the child's nutritional status<sup>13</sup>.

The practical significance of serum albumin analyses in the assessment of nutritional status has been reappraised in area where malnutrition is the major problem. The most consistently confirmed biochemical parameter in children with severe protein energy malnutrition has been a low serum albumin concentration. It is now established that changes in serum albumin concentrations are sensitive to early malnutrition.

It is often found convenient to classify children according to their albumin concentration and to relate other biochemical changes to this value<sup>6</sup>.

This study is in line with the observations seen in other studies which proposed that total protein and serum albumin are low in severely malnourished children<sup>4, 14-16</sup>.

This study is in contrast with the observation of study, which proposed that total protein and serum albumin are not sensitive markers of protein energy malnutrition<sup>17</sup>. This view point is based on the logic that since serum albumin has a long half life of 20 days and a large storage

pool and also as 60% of total body albumin is extravascular, the response to protein deficiency is slow, thereby limiting its utility as a marker of PEM<sup>17</sup>.

**Hypoalbuminemia and Various Serum Protein Fractions:** The findings of this study suggest that albumin and beta fraction of serum protein electrophoresis are significantly lowered in malnourished children in comparison to normal healthy children, while alpha 1, alpha 2 and gamma globulin fractions are significantly higher in malnourished children in comparison to normal healthy children.

The findings of this study are in accordance with those of other studies which suggest that protein energy malnutrition may account for low albumin and beta globulin and high alpha globulin with respect to rest of serum proteins and either normal or increased gamma globulin fraction<sup>18</sup>.

**Edema and Its correlation with Hypoalbuminemia:** An attempt was made to study the correlation of edema with hypoalbuminemia in the cases.

In this study 28 children among the cases had edema and 22 did not have edema. It was found that 22 children (79%) with edema had hypoalbuminemia, while 6(21%) had edema without hypoalbuminemia.

It was also found that 19 children (46%) with hypoalbuminemia had no edema, while 3 children (33%) without hypoalbuminemia also did not have edema.

79% of children with edema had hypoalbuminemia, but even then the correlation of edema with hypoalbuminemia was not significant as 21% cases had edema even in the absence of hypoalbuminemia and also as 46% cases despite having hypoalbuminemia, did not have edema. So in this correlation it has been found that though hypoalbuminemia is one of the most important determinant of edema, (79% of children with edema had hypoalbuminemia), it is not the only the important factor for development of edema as 21% of edematous children did not have hypoalbuminemia and also as 46% of hypoalbuminemic cases did not have edema.

So it can be said that while hypoalbuminemia is a major contributory factor for pathogenesis of edema, abnormalities in the mechanism

associated with sodium and water retention are undoubtedly important in the development of edema.

The findings of this study are in line with the observations seen in other studies, which state that apart from hypoalbuminemia other factors also lead to onset of edema in malnourished children<sup>9,19</sup>.

The findings of this study are in contrast with other studies which propose that hypoalbuminemia should be regarded as a marker of the susceptibility of a malnourished child to edema<sup>8</sup>.

Regarding cost of these biochemical tests, the material cost of kit for serum protein electrophoresis (Paragon, manufactured by Beckman Coulter India Pvt Ltd costs INR 20 per case and Serum Total Protein and Albumin reagent (manufactured by Siemens India Ltd) costs about INR Rs. 8 per case; hence total material cost was INR Rs. 28, As the material cost of biochemical tests usually contribute about 15-20% of the total cost (Other factors include labour, maintenance, electricity, depreciation and administrative), it is safe to assume that total cost is around INR Rs. 150 per case, which is quite cheap considering it's objectivity, ability to detect PEM early and value of clinician's time.

## SUMMARY AND CONCLUSION

The study was done in the Biochemistry Department and Pediatric Ward of Narayana Medical College and Hospital from September 2007- September 2009.

The materials for the study consisted of 50 children admitted to the Pediatric Ward and diagnosed as cases of PEM and 20 normal healthy children.

The inclusion criteria consisted of all children up to 5 years, with weight less than 80% of that expected for age.

In PEM total protein and serum albumin were found to be significantly lower in malnourished children in comparison to normal controls. So total protein and serum albumin can be considered as useful indicators of the nutritional status of the malnourished children and are so proposed as good markers of protein energy malnutrition.

In PEM different fractions of serum protein electrophoresis were also found to be useful for assessing malnutrition due to significant changes observed in their value. Albumin and beta fraction were significantly reduced, while alpha 1, alpha 2 and gamma globulin fractions were significantly raised in malnourished children in comparison to controls. So the study of different fractions of serum protein electrophoresis is also a good marker of protein energy malnutrition. In this study on PEM, edema in malnourished children was not significantly related to hypoalbuminemia. It was observed that though hypoalbuminemia is one of the most important factors responsible for pathogenesis of edema, it is not the sole factor responsible for development of edema. Other factors may also contribute to edema as edema was found even in the absence of hypoalbuminemia and more over all the malnourished children with hypoalbuminemia did not necessarily have edema. So in this study on PEM it has been observed that the correlation of edema with hypoalbuminemia is not very significant as other factors may also play a role in the pathogenesis of edema.

It's worth mentioning here that the cost for these biochemical markers (Serum Total Protein, Serum Albumin and Serum Protein Electrophoresis) was INR Rs 150 per case. Thus it is cost effective too.

All these findings justify use of biochemical markers as sensitive and objective makers of Protein Energy Malnutrition in children.

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