

## STUDY OF ANEMIA AMONG PROTEIN ENERGY MALNOURISHED CHILDREN IN MYSORE

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**ABSTRACT: INTRODUCTION AND OBJECTIVES:** Anemia in Protein energy malnutrition (PEM) is common and its pathogenesis is multifactorial. Since the clinico-pathological patterns are reflected by their underlying etiopathogenic factors, it is important to study the associated morbidity and mortality and to establish their causes for an effective management. The purpose of the present study is to determine the prevalence, patterns, clinico-pathological and morphological types of anemia in protein energy malnutrition children. The objectives of the study are: (1) To study the clinico-pathological and morphological patterns of anemia in PEM children of age group 6 month – 5 years. (2) To assess the resultant morbidity and mortality. (3) To determine the ideal parameter for iron deficiency anemia. **METHODS:** This study was conducted on 75 clinically diagnosed Protein energy malnutrition patients of age group 6 months to 5 years. Detailed clinical history elicitation and thorough clinical examination was performed. Peripheral smears of these patients were examined. The complete hemogram including reticulocyte count was done. The special investigations like bone marrow study, Hb electrophoresis, iron studies and stool examination were done whenever required. **RESULTS:** In our study, anemia in PEM affected female population more than the males of age 36-47 months. Most of children had Grade III PEM and Microcytic hypochromic anemia was most prevalent. Most of the children had Iron deficiency anemia. This study also indicated that Serum iron assay and TIBC are the better indicators of iron deficiency anemia in patients with PEM and it is the investigation of choice when compared to serum ferritin as it gets falsely elevated in these patients with infections confirmed by elevated CRP level. **INTERPRETATION AND CONCLUSION:** Malnutrition, Infection and Anemia show a synergistic relationship. So it necessitates prompt screening and early diagnosis through proper investigation, by utilization of available advanced technical modalities in order to initiate timely treatment and appropriate management.

**KEYWORDS:** Children, Protein energy malnutrition, Complete haemogram, Iron deficiency anemia.

**INTRODUCTION:** Protein energy malnutrition is a problem of staggering magnitude. It has been estimated that prevalence of malnutrition in children is 33% in Asia. Prevalence of malnutrition is around 80% in children of age 1-5 years.<sup>1,2</sup> One out of three of the world's malnourished children live here in India. The prevalence of malnutrition varies across the states, with Madhya Pradesh recording the highest rate (55%) and Kerala among the lowest (27%). According to recent data the prevalence of malnutrition in Karnataka is around 41.1%.<sup>3</sup>

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Prevalence of anemia among children with malnutrition is around 40%. Iron deficiency anemia is the most important cause while folate, vitamin B12 and protein deficiency also plays a significant role in its etiology.<sup>2</sup> According to WHO the Protein Energy Malnutrition (PEM) is "the cellular imbalance between the supply of nutrients and energy, and the body's demand for them to ensure growth, maintenance, and specific metabolic functions".<sup>4</sup>

Malnutrition in children is not affected by food intake alone; it is also influenced by access to health services, quality of care for the child and pregnant mother as well as good hygiene practices.<sup>3</sup> Nutritional Anemia is a state where in normal levels of hemoglobin cannot be maintained by erythropoiesis due to deficiency of one or more nutrients.<sup>2</sup> The various factors that influence anemia in PEM are: (a) Metabolic changes in the red cell, (b) Protein deficiency and adaptation anemia, (c) Iron deficiency, (d) Deficiency of vitamins (folic acid, B12, etc.) or trace elements (copper, zinc), (e) Erythropoietin deficiency, (f) Infection and chronic diseases.<sup>5</sup>

Anemia in children causes reduced exercise capacity, slower growth, impaired wound healing. These children are also at greater risk of dying due to complications of malnutrition and infection.<sup>6</sup> since the clinico-pathological pattern of anemia in children is reflected by their underlying etiopathogenic factors, it is important to study their effect on morbidity and mortality, to establish their causes and to guide effective management. Because of these factors, study of etiopathogenesis of anemia in infancy and childhood has attracted wide attention in recent years especially in India.

Most children with anemia are asymptomatic and have abnormal hemoglobin or hematocrit level on routine screening. Infrequently, a child with anemia may have pallor, fatigue, and jaundice but may or may not be critically ill. Thorough elicitation of history and findings on physical examination can reveal the underlying cause of anemia.<sup>7</sup>

The clinico-pathological patterns of anemia in children with PEM are often reflected by their underlying etiopathogenic factors and the investigation of anemia is mainly hematological. The present study was undertaken to evaluate blood picture and biochemical parameters to aid in understanding the clinico-pathological patterns of anemia in children with PEM. Aim of the study was to determine the prevalence, patterns and various morphological types of anemia in children with PEM.

## OBJECTIVES:

1. To study the clinico-pathological patterns of anemia in children with PEM of age group 6 months to 5 years.
2. To detect the morphological types of anemia prevalent among children with PEM in the age group of 6 months to 5 years.
3. To study the effect of clinico-pathologic patterns of anemia on mortality and morbidity of children with PEM in the age group 6 months to 5 years.

**METHODOLOGY:** With the prevalence of malnutrition in Karnataka 41.1%,<sup>3</sup> effect size 15% and level of significance 5% using estimation technique the sample was calculated to be 43. The cross sectional study was planned on 75 clinically diagnosed PEM registered patients of age group of 6 months to 5 years in a government teaching hospital Pediatric wing, Mysore. A purposive

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sampling method was adopted for the selection of the subjects. Children with other primary hematological disorders involving diseases of WBCs, platelets and with intra uterine growth retardation were excluded from the study. Ethical committee clearance was taken along with the consent form from the patients. A detailed history was elicited, clinical examination was carried out and the data were recorded in the proforma. Anthropometric measurement such as Height for age, Weight for age, Weight for height, Body Mass Index (BMI), Head and mid arm Circumferences was recorded. The grading of PEM was done according to the IAP Classification<sup>8</sup> with

- I degree malnutrition - 71-80% of reference weight (mild)
- II degree malnutrition - 61-70% of reference weight (moderate)
- III degree malnutrition - 51-60% of reference weight (severe)
- IV degree malnutrition - < 50% of reference weight (very severe)

After obtaining consent from parents, the required quantity of venous blood was collected in EDTA tubes and plain vials. The collected blood was analyzed using Sysmex KX-21 autoanalyser, having three part differentials, from which the parameters viz Hb%, PCV, RBC count, RBC indices including MCV, MCH, MCHC, RDW, Platelet count, Total WBC count including the differential count were obtained.

Peripheral smears were prepared on glass slides and stained with Leishman's stain. Reticulocyte count was done by the supra-vital staining technique using brilliant cresyl blue. Among the microcytic hypochromic anemia, iron deficiency anemia was diagnosed by serum iron studies and also by iron storage assessment of bone marrow examination using Perl's stain. Among the macrocytic anemia, suspected cases of megaloblastic anemia were confirmed by bone marrow examination, serum B12 and folate estimations. The hemolytic anemia cases which were suspected on clinical and peripheral blood examination were taken up for a complete hematological work up including Hb electrophoresis, osmotic fragility and Coomb's test depending on the specific requirement.

Biochemical parameters like Serum Iron and TIBC (Total Iron Binding Capacity) were estimated by colorimetric method. Serum ferritin estimation was done when IDA (Iron deficiency anemia) was suspected. The test was done by chemiluminescence immuno assay (CLIA method).

Other ancillary tests including stool examination, urine examination, liver function tests, renal function tests, Mantoux test, radiological investigations like X-ray, ultrasonography and CT scan were done whenever required.

**RESULTS:** The present study was carried out on 75 PEM pediatric patients in the age group of 6 months to 5 years. These 75 patients were categorized in to four groups based on their severity of malnutrition as Grade 1 to Grade 4 PEM (Table -1).

57% (43 cases) of PEM cases were of grade 3, followed by 27% (20 cases) grade 2, 09% (07 cases) were of grade 1 and 07% (05 cases) were of grade 4 PEM.

Out of 75 cases 60 (80%) cases were of Marasmus type and 15 (20%) cases were of kwashiorkor type of PEM.(Figure -1) Marasmus type exceeds of kwashiorkor type of PEM with a significance difference (Chi-square = 27, df = 1, p-value < 0.0005).

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Severe degree of anemia was prevalent in pre-school children (36-47 months) with majority having grade 3 PEM. This was found statistically significant in the cross tables with approximate significance of  $< 0.03$  for  $<1$  year and  $< 0.001$  for 1-5 years of age. Among 75 cases majority of the cases affected were females in all grades of PEM with maximum of 32 cases belonging to grade 3 PEM being with a significance difference in favour of females (Chi-square = 20.280, d. f = 1, p-value  $< 0.0005$ ). (Table -2).

In the present study, among the patients with grade 1 PEM (7 cases) all patients had hemoglobin  $> 10$  gm/dl. In grade 2 PEM patients (20 cases), 16 cases (80%) had hemoglobin  $< 7$  gm/dl. Remaining 4 cases (20%) had hemoglobin 7-10 gm/dl.

In grade 3 PEM patients (44 cases), 22 (51%) cases had hemoglobin  $< 7$  gm/dl. Eleven (25%) cases had hemoglobin 7-10 gm/dl and 10 (23%) cases had hemoglobin  $> 10$  gm/dl.

In grade 4 PEM patients (5 cases), 4 (80%) cases had hemoglobin  $< 7$  gm/dl.

In all grades of PEM, females were most affected where the cross table showed the approximate significance of 0.215. (table 3,4).

Among 75 cases, 12 cases were non-anemic and remaining 63 cases had anemia. Among 63 cases, 41 (55%) cases had microcytic hypochromic anemia, 10 (13%) cases had normocytic normochromic anemia, 7 (9.3%) cases had macrocytic anemia and 5 (6.7%) cases had dimorphic anemia. Among the patients with PEM, majority of the patients had microcytic hypochromic anemia and this was found statistically significant with the Yates Chi-square value of 54,  $df=4$  and p value  $< 0.001$ . (Table 5).

Among 75 cases, 7 cases were of grade 1 PEM which showed normal peripheral blood picture. In 20 cases of grade 2 PEM showed 12 (60%) cases showed microcytic hypochromic anemia, 3 (15%) cases showed macrocytic blood picture, 4 (20%) cases showed dimorphic blood picture and 1 (5%) case showed normocytic normochromic anemia picture. In grade 3 PEM, among 43 cases 25 (58%) cases showed microcytic hypochromic blood picture, 9 (21%) cases showed normocytic normochromic blood picture, 3 (7%) cases showed macrocytic blood picture and 1 (2%) case showed dimorphic blood picture. In patients with grade 4 PEM, among 5 cases 4 (80%) cases had microcytic hypochromic blood picture and 1 (20%) case had macrocytic blood picture. (Table-5).

This study showed that majority of patients with grade 1 PEM had normal blood picture and among other grades of PEM, microcytic hypochromic anemia was most common which on the cross-table showed approximate significance of  $< 0.001$ .

In the present study 12 (29%) cases out of total 41 microcytic hypochromic anemia cases had serum ferritin  $< 12$  microgm/l which stated the presence of true iron deficiency anemia and remaining 29 (71%) cases had serum ferritin  $> 12$  microgm/l in which few had normal and few had above normal values. Reduced serum ferritin confirmed the presence of iron deficiency anemia while normal or increased serum ferritin may be seen in multiple causes like anemia of chronic disease, thalassemia and iron deficiency anemia with acute infections which gives falsely elevated values. (Table-6).

Table also depicts, 21 (81%) cases out of 26 patients with reduced serum iron had elevated TIBC levels and 5 (19%) cases had reduced TIBC levels. Elevated TIBC levels were seen in iron deficiency anemia with acute infections and reduced TIBC levels were seen in anemia of

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chronic disease. In the present study, 21(81%) cases out of 26 patients with reduced serum iron had elevated serum CRP levels and 5(19%) cases had normal serum CRP levels. Elevated serum CRP levels were seen in iron deficiency anemia with acute infections and normal serum CRP levels were seen in anemia of chronic disease. 26(90%) cases out of 29 cases with elevated serum ferritin showed reduced serum iron and remaining 3(10%) cases had normal serum iron levels. Reduced serum iron implicated that patient can have anemia of chronic disease or iron deficiency anemia with acute infections and normal serum iron implicated that patient can have thalassemia which was confirmed by hemoglobin electrophoresis.

It was observed that, among 16 pure iron deficiency anemia cases, 12 cases had microcytic hypochromic anemia and 4 cases had varied morphology (3 had normocytic normochromic anemia and 1 had dimorphic anaemia). Twenty-one cases had iron deficiency anemia with acute infections where all of them presented with microcytic hypochromic anemia. Among 5 cases of anemia of chronic disease all of them presented with microcytic hypochromic anemia. 11 cases had megaloblastic anemia (7 cases had macrocytic anemia and 4 cases had dimorphic anaemia). Three cases of thalassemia presented with microcytic hypochromic anemia. 7 cases were grouped under anemia of unknown etiology which presented with normocytic normochromic anemia. (Table 7).

It was observed that gastrointestinal symptom was the chief complaints among the patients followed by fever with 28 cases (Figure 2). The most common signs found were pallor with 72 cases and koilonychias with 60 cases. The other common signs included signs of dehydration, dry skin; signs of malnutrition, fever, frontal bossing, Flag sign, edema, tachycardia, muscle wasting, microcephaly and cervical lymphadenopathy were seen in some cases (Figure 3). The most common associated symptoms were gastrointestinal with 31 cases that include vomiting, diarrhea and pain abdomen followed by fever. Second major associated symptoms were respiratory diseases with 22 cases and followed by nutritional diseases, cardiac and CNS disorders. (Figure 4).

**DISCUSSION:** Iron deficiency anemia is the commonest form of nutritional deficiency in the world responsible for the staggering amount of ill health, cost productivity, increased morbidity and mortality.

The clinicopathological pattern, the morphological and the etiological types of anemia as analyzed in the present study of 75 protein energy malnutrition cases were compared with other similar studies.

## Tables and figures:

Grade of PEM	No. of cases
Grade I	07
Grade II	20
Grade III	43
Grade IV	05

Table 1: Distribution of grades of PEM in pediatric patients

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Grades	Age group					Gender	
	6 -11 mon	12-23 mon	24-35 mon	36-47 mon	48-60 mon	Male	Female
Grade I	0	0	3	2	2	2	5
Grade II	4	3	5	4	3	4	16
Grade III	4	10	9	13	8	11	32
Grade IV	0	0	1	3	1	1	4

Table 2: Distribution table for Age, Gender and PEM grades

Hemoglobin	No. of cases	Percent
11 gm/dl- normal	12	16.1%
10-11 gm/dl-mild	05	6.6%
7-9.9 gm/dl-moderate	16	21.3%
< 7 gm/dl- severe	42	56%

Table 3: Hemoglobin distribution

Yates Chi-square= 17; df=2; p<0.001.

Grades	<1 Year			1-5 Years			Male			Female		
	<7	7-10	>10	<7	7-10	>10	<7	7-10	>10	<7	7-10	>10
Grade I	00	00	00	00	00	07	00	00	02	00	00	05
Grade II	04	01	00	12	03	00	04	00	00	12	04	00
Grade III	03	01	02	19	10	08	04	05	02	18	06	08
Grade IV	00	00	00	04	01	00	01	00	00	03	01	00

Table 4: Age, gender wise and PEM grade-wise gradation of anemia

PEM Grade	Peripheral Smear				
	MHA	NNA	DA	Mac A	Normal
Grade I	00	00	00	00	07
Grade II	12	01	04	03	00
Grade III	25	09	01	03	05
Grade IV	04	00	00	01	00
No. of cases based on MCV	41	07	05	10	12

Table 5: Morphological pattern of Anemia

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Parameters	Levels	Frequency (%)
Serum Ferritin	<12	12 (29)
	≥ 12	29 (71)
Serum Iron (for increased Serum Ferritin patients)	< 50	26 (90)
	≥ 50	3 (10)
TIBC	> 400	21 (81)
	< 250	5 (19)
Serum CRP for patient with reduced Serum Iron (mg/l)	> 10	21 (81)
	< 10	5 (19)

Table 6: Biochemical parameters in Microcytic hypochromic anemia

Etiological type	Morphological type				
	MHA	NNA	Macro cytic	DA	Total
Iron Deficiency Anemia (IDA)	12	3	0	1	16
IDA with injection	21	0	0	0	21
ACD	5	0	0	0	5
Megaloblastic anemia	0	0	7	4	11
Aneamia of unkinwn origin	0	7	0	0	7
Thalasemia	3	0	0	0	3

Table 7: table showing comparative prevalence of morphological and etiological types of anemia

Studies	M:F
Present study	1:3
Odebode <sup>9</sup>	1:1.7
Bobby <sup>10</sup>	1:1.4
Kaneta <sup>11</sup>	1:0.9

Table 8: Comparative study of gender distribution of nutritional anemia

In the present study, more females were found to have nutritional anemia as compared to males. A similar gender distribution was noted in the study by Odebode<sup>9</sup> et al, Bobby<sup>10</sup> et al. But in a study conducted by Kaneta<sup>11</sup> et al. males were found to be more affected than females.



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<b>Studies</b>	<b>Age group</b>	<b>Percentage</b>
Present study	36-47 mon	29.3%
Chakraborty <sup>12</sup>	1-5 years	67%
Susan <sup>13</sup>	9 mon-1 year	64%
Bobby <sup>10</sup>	24- 35 mon	77.8%
Kaneta <sup>11</sup>	<12 mon	21.7%

**Table 9: Comparative study of maximally affected age groups**

In the present study, children of age 36-47 months were maximally affected but in the study by Chakraborty<sup>12</sup> et al. 1-5 years were taken in general and were maximally affected. In a study by Susan<sup>13</sup> et al. infants were maximally affected, whereas in study by Bobby<sup>10</sup> et al. children of age 24-36 months were maximally affected. In a study by Kaneta<sup>11</sup> et al. children of age less than 12 months were maximally affected.

<b>Grades</b>	<b>Present study</b>	<b>S. Jain<sup>7</sup></b>	<b>V.G Rao<sup>14</sup></b>	<b>NFHS<sup>15</sup></b>
Normal	16.1%	—	13.3%	29%
Mild	6.6%	26.8%	15.6%	29%
Moderate	21.3%	49.8%	63.8%	39%
Severe	56%	24.3%	7.3%	03%

**Table 10: Comparative study of grades of anemia**

In the present study, severe degree of anemia was found in maximum number of cases, whereas in a study by S. Jain<sup>7</sup> et al. V.G Rao<sup>14</sup> et al. and NFHS<sup>15</sup> survey showed moderate degree of anemia was most prevalent type.

<b>Morphological variants</b>	<b>Present study</b>	<b>Kapur et al.<sup>16</sup></b>
Microcytic hypochromic anemia	54.7%	44.3%
Normocytic normochromic anemia	13.3%	42%
Macrocytic anemia	9.3%	2.7%
Dimorphic anemia	6.7%	10%
Normal (no anemia)	16%	Nil

**Table 11: Comparative study of morphological variations of nutritional anemia**

This study reveals that, microcytic hypochromic anemia (54%) was the most common type followed by normocytic normochromic anemia (13.3%), macrocytic anemia (9.3%) and dimorphic anemia (6.7%). This finding was in concurrence with the study by Kapur<sup>16</sup> et al., wherein microcytic hypochromic anemia (44.3%) was found to be the most common followed by normocytic normochromic anemia (42%), dimorphic anemia (10%) and macrocytic anemia (2.7%).



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Grade	Present study	Joshi HS et al. <sup>17</sup>	Gomber et al. <sup>18</sup>
Normal	-	-	50.5%
Grade 1	9%	45.4%	35.87%
Grade 2	27%	38.6%	12.6%
Grade 3	57%	14%	1.2%
Grade 4	6%	2%	-

Table 12: Distribution of grades of PEM in pediatric patients

In our study, Grade 3 PEM (43 cases, 57%) was seen in the maximum number of cases followed by grade 2 PEM (20 cases, 27%), grade 1 PEM (07 cases, 09%) and grade 4 PEM (05 cases, 06%), whereas in the study by HS Joshi<sup>17</sup> et al. Grade 1 PEM cases were maximum cases (45.4%) followed by grade 2 (38%), grade 3 (14%) and grade 4 (2%) cases. In a study by Gomber<sup>18</sup> et al. among PEM cases Grade 1 were maximum number of cases.

**CONCLUSION:** One of the most important areas for scope is in the improvement of primary health care prevention of nutritional deficiency because, it has been associated with delay in the psychomotor development and increased morbidity and mortality in children with PEM.

Steps need to be undertaken to educate the masses and improve their living standards, so that, the initial symptoms of illness are ignored and the children are brought to the hospital at the earliest for timely diagnosis and effective management.

Children are the most vulnerable group, require early screening for anemia and associated illnesses. Initial screening and subsequent diagnostic tests enable early diagnosis and appropriate management. Utilization of technological advances is beneficial in arriving at a definitive diagnosis. The basal blood parameters are mandatory before initiating treatment in nutritional anemia cases and it's important to differentiate mainly iron deficiency anemia with acute infections and anemia in chronic disease as treatment varies in both.

Nutritional anemia imposes financial, emotional and psychological stress on the patients and their families besides draining valuable resources of the country. Hence, early screening for it is mandatory. Early detection would ensure tremendous benefits and alleviation of suffering.

In the present study, the preschool children were found to be the most affected. Hence, it is recommended that, this age group must be compulsorily screened for anemia.

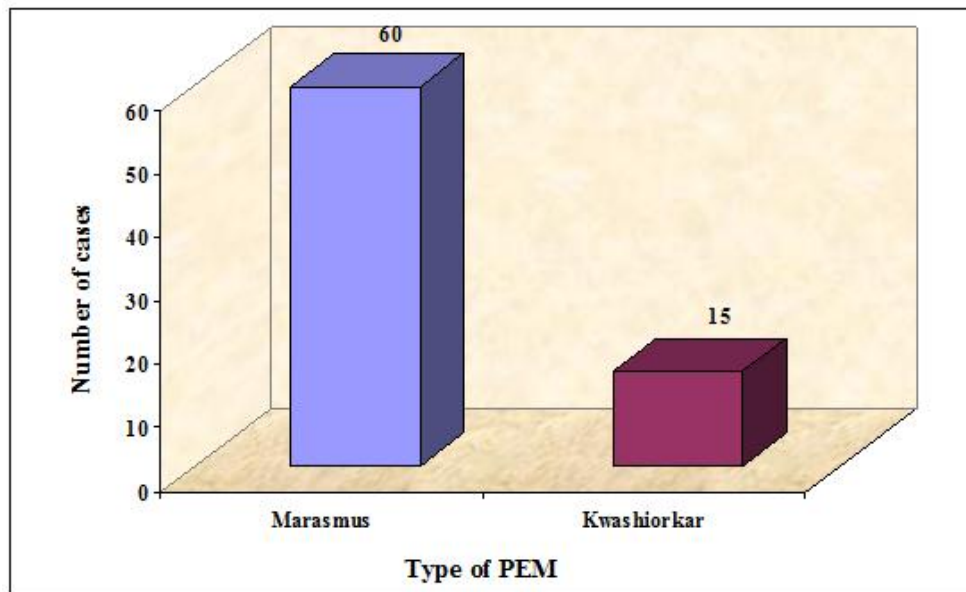
A uniform definition of screening criteria and an effective system to respond to abnormalities is the need of the hour. The present study was undertaken, keeping this need in view.

**SUMMARY:** The present study was undertaken from November 2011 to May 2013, in the Department of Pathology, Mysore Medical College and Research Institute, Mysore. Pediatric patients whom were clinically diagnosed as protein energy malnutrition children of age 6 months to 5 years of Cheluvamba hospital, Mysore were included in the study.

- Seventy-five pediatric patients clinically diagnosed as PEM were studied.
- Majority of them had grade 3 PEM as per IAP criteria of malnutrition assessment.

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- Among the type of PEM, marasmus was most prevalent type.
- Among 75 patients, 63 had anemia as per the WHO criteria.
- Preschool children of age group 36-47 months were found to be the most affected.
- Anemia was more common in female patients than male.
- Most of the children presented with GI symptoms.
- Among the preschool children, severe degree of anemia (Hb<7 gm/dl) was more prevalent in female children.
- Microcytic hypochromic anemia was the most common morphological type of anemia and dimorphic anemia was least common.
- Iron deficiency anemia was the most common etiologic type of anemia.
- As in patients with PEM, serum ferritin gives false positive values due to infections; confirmation of iron deficiency anemia is always done with CRP level estimation, serum iron and TIBC level.
- Among 63 patients with anemia, 3 patients had thalassemia confirmed by hemoglobin electrophoresis.
- The lowest hemoglobin observed was at 1.6 gm/dl and the highest was at 13.6 gm/dl with mean being 7 gm/dl.
- Among total 75 cases of PEM, maximum number (21cases) had Iron deficiency anemia with acute infections for which serum ferritin was falsely high and CRP was raised with decreased TIBC.



**Figure 1: Distribution of type of PEM**

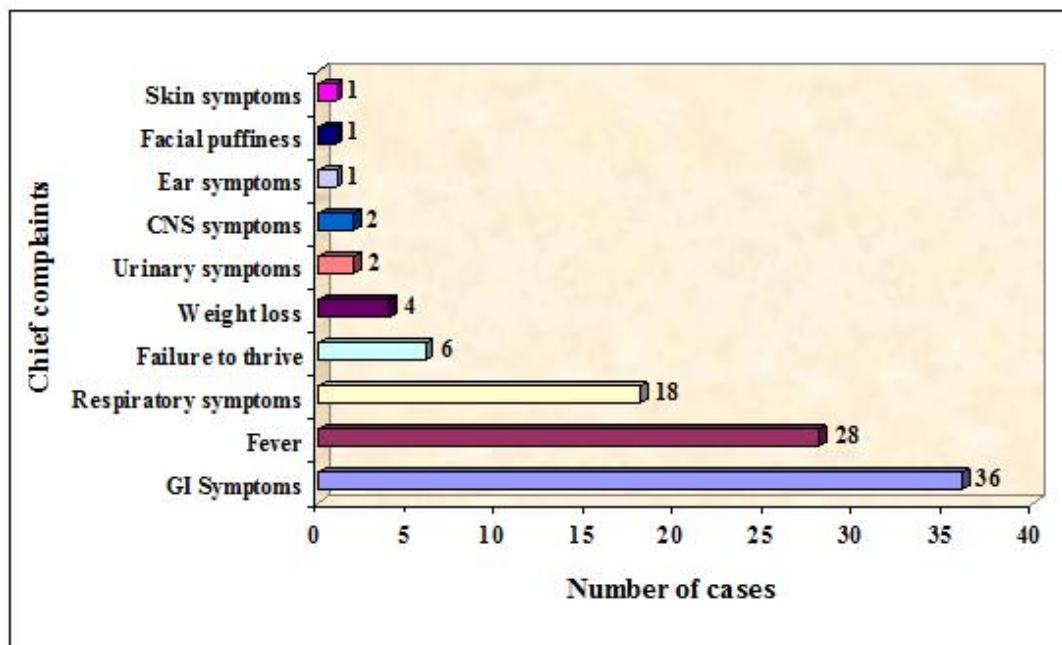


Figure 2: Chief complaints

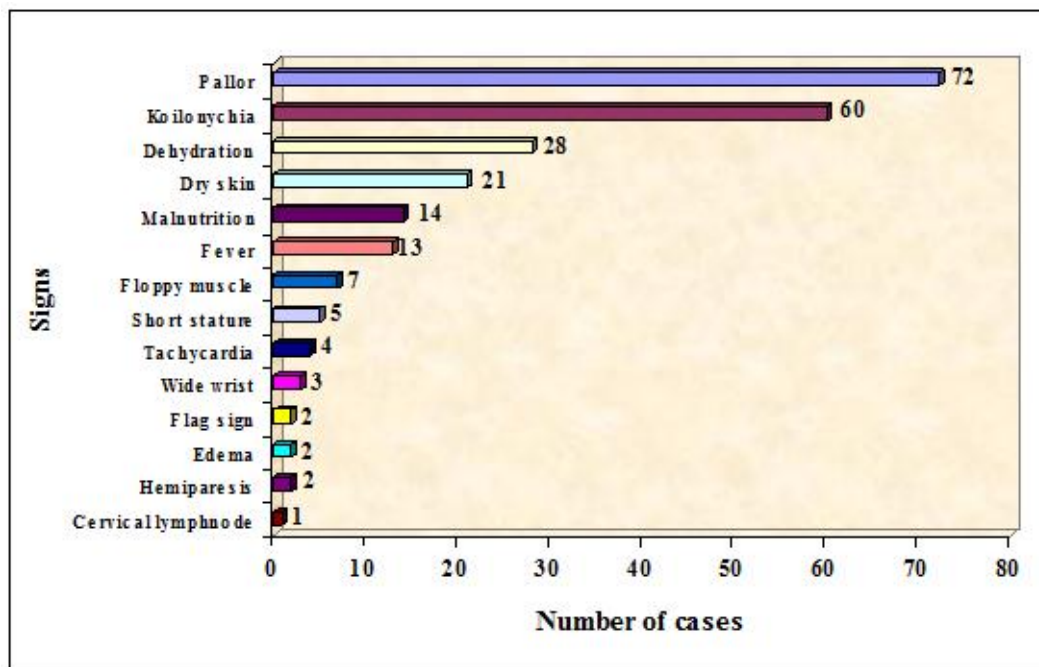
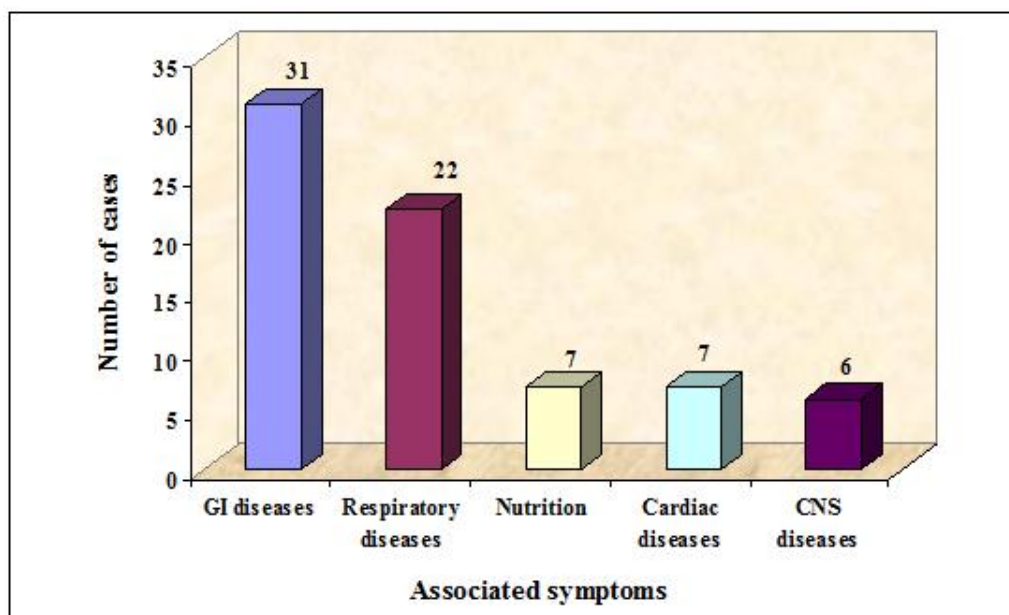


Figure 3: Common presenting signs



**Figure 4: Associated symptoms**

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