SUMMARY AND CONCLUSIONS
Thirty children with severe PEM (marasmus) in the age group of 1 year to 4 years and the ten age-matched normal control children were investigated.

The routine haematological profile including haemoglobin, red cell count, packed cell volume, absolute red cell indices (MCV, MCH, MCHC) as well as peripheral blood smear, reticulocyte count, bone marrow morphology and iron grading in marasmic and control children were investigated. Total plasma proteins, plasma iron, TIBC, UIBC and transferrin saturation (%) were evaluated in the normal controls and the marasmic children on admission. The above mentioned parameters were investigated so as to assess the degree and type of anaemia in children with PEM syndrome. The erythrocytes of normal controls and marasmic children were also evaluated for all the components of glutathione cascade (GSH, GSG-Px, GSSG-R and G6-PD).

After initial studies, thirty marasmic children were divided into two groups of fifteen
children each. They were put on two different dietary regimen for a period of two weeks. The two groups received the same diet but in the group-1, the child's body iron deficit was compensated whereas in group-2 it was not. All the above mentioned parameters, concerning the basic haematological characteristics and iron metabolism and erythrocyte glutathione metabolism were re-evaluated after the stipulated dietary period was over.

Haemoglobin, HbC count, PCV, red cell indices, reticulocyte count, total plasma proteins, plasma iron, TIBC, UIBC and percent transferrin saturation were found to be significantly low in marasmic children as compared to the normal controls. There was a significant improvement in all above mentioned parameters following dietary realimentation of the first group. However, the rehabilitation of the second group led to the development of frank iron-deficiency anaemia as indicated by low plasma iron, increased TIBC, decreased percent transferrin saturation and diminished MCV and MCH values.
The peripheral blood smear in majority of PEM children showed dimorphic anaemia with megaloblastic erythropoiesis. The bone marrow smear morphology revealed normoblastic erythropoiesis and inadequate haemoglobinization with reduced amount of reticular iron in the bone marrow. However, a few children did show iron-deficient erythropoiesis with zero iron grade in the bone marrow and peripheral blood film indicating microcytic hypochromic anaemia. After dietary therapy majority of the children of first group showed normoblastic erythropoiesis with adequate haemoglobinization. The peripheral blood film morphology revealed normocytic normochromic picture. The rehabilitation of the second group led to the development of iron-deficiency anaemia as mentioned earlier. The majority of the children of this group showed iron-deficient erythropoiesis with reticular iron either absent or it was in traces. The peripheral blood film morphology showed microcytic hypochromic anaemia.

On the basis of the above noted observations,
it was concluded that;

a) the anaemia is a common manifestation of PEM; the type, degree and severity of anaemia could vary from patient to patient depending upon relative deficiencies of haemopoietic factors;

b) the complete realimentation of marasmic children results in overall improvement in basic haematological characteristics and iron status of these children;

c) the anaemia of PEM is quite different from the anaemia of chronic disorders and iron-deficiency anaemia; and

d) the incomplete realimentation of PEM children could lead to the expression of otherwise latent deficiencies.

The concentration of reduced glutathione (GSH) and the activities of all the three enzymes of glutathione cascade, i.e., GSH-Px, GSSG-R and G-6-PD were found to be significantly reduced in erythrocytes of children
suffering from PEM as compared to the controls. There was a significant increase in all the components of glutathione cascade including GSH in the first group after dietary rehabilitation. However, the response of these components to dietary realimentation of the second group was variable. There was a compensatory increase in GSxG-R activity (IU/gHb) in this group as compared to the first. This was because of better regeneration of this enzyme as compared to haemoglobin in the second group where iron deficit was not replenished and iron being critical in haemoglobin regeneration. As these children developed frank iron-deficiency anaemia, the raised levels of this enzyme may be because of the compensatory increase seen in this enzyme of glutathione cascade. The activity of GSH-Px was still low in the second group as compared to the first group after dietary realimentation.

On the basis of the observations regarding the components of glutathione system, it can be concluded that:

a) the deficiencies of the enzymes of glutathione cascade could be referred to as acquired enzyme-
pathies since they are moderate in nature and the aetiology of PEM is nutritional in origin;

b) the erythrocytes of PEM are inefficient in handling peroxidative stress since they are deficient in cellular antioxidant defense system and it is known that nutrients are essential for all fundamental cellular processes and play an important role in modulating the cellular damage and cellular antioxidant defense system;

c) the occurrence of several moderate deficiencies of the enzymes of cellular antioxidant defense system in the same cell would advance the process of red cell damage because of their cumulative effect. This is in contrast to congenital red cell enzymopathies which are known to bring about sudden haemolysis and slow but progressive physiological red cell ageing. Thus the situation in PEM could be referred to as in between the two extremes; and

d) the diminished efficiency of glutathione cascade
along with low levels of GSH during PEM syndrome could also contribute for the shortened red cell life span and thus suggesting the haemolytic element in the pathogenesis of anaemia in PEM.