

SERUM AMINO ACIDS AND GENESIS OF PROTEIN ENERGY MALNUTRITION

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ABSTRACT

Twenty four patients of classical marasmus and kwashiorkor alongwith equal number of healthy controls were selected for the study. Their serum amino acid -patterns analysis revealed a mean ratio of glutamate to alanine in fasting samples of normal individuals to be 0.33, while it was 9.3 in kwashiorkor and 1.6 in marasmus. This differences in controls, kwashiorkor and marasmus was statistically significant.

This observation may explain evolution of marasmus and kwashiorkor in children with similar diets. On the basis of the present observation it is postulated that in kwashiorkor, the conversion of pyruvate to alanine in presence of glutamate, an aminogroup donor does not proceed normally, resulting in accumulation of glutamate and low alanine. Thus the development of marasmus and kwashiorkor may not be related to dietary inadequacy alone but also to the transaminase function. This could be genetic in origin.

Key words: *Marasmus, Kwashiorkor, Protein energy malnutrition, Amino-acidogram.*

Infant malnutrition is an old but ever present problem with many aspects ranging from the purely biochemical and clinical to the economic and sociopolitical. For many developing countries like India, malnutrition is the primary problem of public health.

Right from the time of Williams(1) with the first report of kwashiorkor appearing in Lancet, the causative factor for the disease has been nutritional deficiency. Initially it was attributed to the maize diet by Williams in children of the Gold Coast colony. With tremendous advances in the understanding of the disease kwashiorkor and marasmus, the problem is getting more complex. The widely prevalent concept that predominant protein deficiency results in kwashiorkor and calorie deficiency results in marasmus, has been challenged. Many workers have now postulated that protein gap is a myth and the syndrome of kwashiorkor can occur if there be inadequacy of calories(2-5). It was thought that marasmus indicated adaptation failure(3).

In one of our unpublished observations, it was also found that there was no significant difference between protein intake and calorie intake of children who developed kwashiorkor or marasmus. This has putforth the view that the genesis of marasmus and

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kwashiorkor may not be related to diet solely but possibly occur as a consequence of a metabolic alteration.

We studied the amino acid patterns in cases of marasmus and kwashiorkor to find out if there was any difference in the two conditions and analysed them in light of the available data.

Material and Methods

This prospective study included 36 children attending the pediatric outdoor and indoor sections of our hospital. These comprised of 12 cases each of marasmus, kwashiorkor and healthy controls. Marasmus was defined by Wellcome criteria(6) as weight less than 60% of the expected without presence of edema whereas kwashiorkor was defined as weight between 60 to 80% with edema.

A detailed history, physical examination and anthropometric measurements was taken. Routine hemogram, urine and stool examination, serum proteins, albumin, globulin, were determined. Other causes of edema like renal, cardiac or hematological diseases were excluded on clinical and laboratory examination. Cases with renal or cardiac disease were excluded.

Three ml blood was collected from these patients before breakfast, on admission. Serum was deproteinized and aminoacidograms were prepared on Waters High performance Liquid chromatography Model U 6K using C18 Bondapack column with phosphate buffer, acetonitrile as solvent system and derivatives were prepared using ophthalaldehyde. Aminoacidograms in healthy children, marasmic children and

in kwashiorkor were compared. By calculating the area under curve on the graph, the mean percentages of all amino acids (3 chromatograms in each patient) were calculated. Thus a total of 108 aminoacidograms were made and studied. Absolute values in nM/100 ml were obtained using chromatograms prepared by using standard amino acid mixture of known concentration and composition.

Results

Figs. 1-3 and Table I show the aminoacidogram patterns on normal controls, and patients with marasmus and kwashiorkor. High levels of glutamate with low levels of alanine was characteristic in kwashiorkor. Ratio of levels of glutamate to alanine were 9.3 in kwashiorkor, 1.6 in marasmus and 0.3 in normal controls. These differences were statistically significant ($p < 0.0001$).

Discussion

The role of dietary inadequacy in the genesis of protein energy malnutrition, either due to lack of intake or improper intestinal absorption has been documented(5). However, why the same dietary inadequacy should produce variant clinical picture ranging from marasmus to kwashiorkor is still a matter of controversy. The view that predominant caloric deficiency leads to marasmus, though well accepted for many years has been contested successfully in recent years. It has been postulated by some that protein gap is really a myth and kwashiorkor can occur even in the presence of caloric inadequacy(2).

Gopalan(3) showed that in the Indian children where the diets are similar,

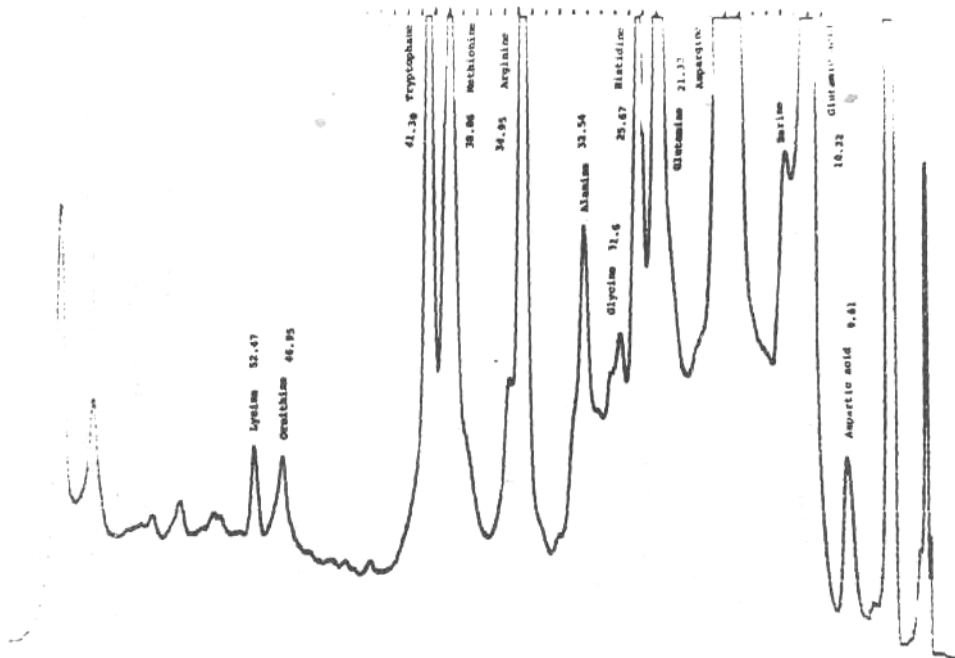


Fig. 1. Aminoacidogram in controls.

Amino acids	Standard value	Control (n=12)	Marasmus (n=12)	Kwashiorkor (n=12)
Aspartic acid	0.0016	0.002	0.020	0.012
Glutamic acid	0.0058	0.011	0.022	0.027
Serine	0.011	0.024	0.025	0.010
Asparagine	0.0037	0.004	0.005	0.0044
Histidine	0.0015	0.011	0.010	0.009
Glycine	0.023	0.052	0.015	0.010
Alanine	0.034	0.041	0.015	0.0008
Arginine	0.017	0.009	0.010	0.0068
Methionine	0.0021	0.004	0.0025	0.002
Tryptophane	0.0047	0.007	0.0025	0.002
Ornithine	0.0069	0.015	0.005	0.004
Lysine	0.017	0.027	0.015	0.014

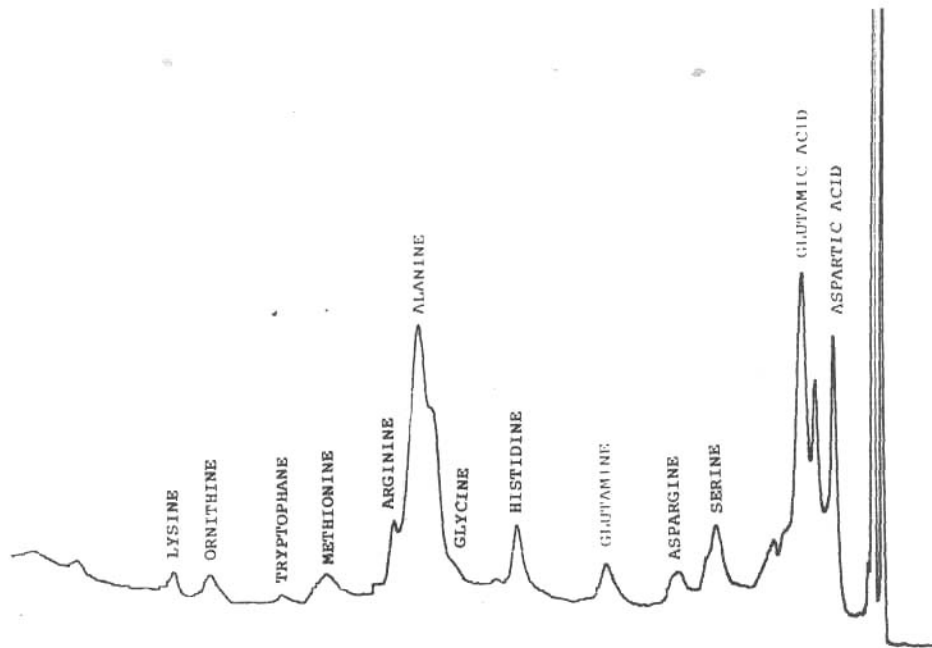


Fig. 2. Aminoacidogram in marasmus.

some children developed marasmus and some kwashiorkor even when there is no evidence of energy rich foods being consumed. Thus he put forth the theory of dysadaptation, *i.e.*, adaptation failure resulting in kwashiorkor and good adaptation resulting in marasmus under the stress of malnutrition.

Our observation suggested that the serum aminoacidogram may show distinct differences in case of marasmus and kwashiorkor. Very high levels of glutamate with low or undetectable levels of alanine were the hallmark of kwashiorkor. The clinical and biochemical implications of these observations are difficult to interpret. Low alanine levels have, however, been reported earlier in kwashiorkor(7).

One possible explanation for this can be low level transaminases.

Carbohydrates, fats and proteins enter one metabolic pool in the body through the tricarboxylic, citric acid cycle. Through this cycle transamination reactions produce aminoacids and neoglucogenesis produces glucose. These processes regulate synthesis of amino acids and blood glucose. It is possible that patients of kwashiorkor have low levels of transaminases hence show low levels of alanine in the presence of high levels of glutamate. Levels of glutamate also increase and are more in kwashiorkor compared to normals and marasmic children (*Table I*).

Low transaminase levels in the liver biopsy specimens in case of

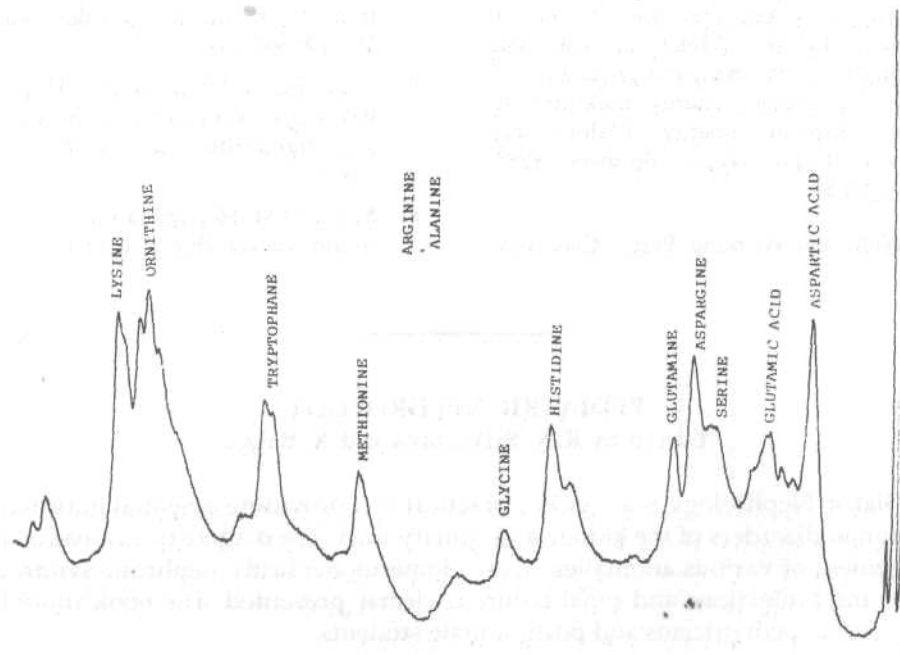


Fig. 3. Aminoacidogram in kwashiorkor.

kwashiorkor have been reported earlier(8). In fact it has also been shown that they remain low even during recovery(4,8). It is possible that this deficiency is present right from birth and is genetically transmitted and is made clinically overt when the child is exposed to stress of dietary inadequacy and may be responsible for development of kwashiorkor. Those children who have normal transaminase function develop marasmus under the same dietary insult.

Thus it is possible to explain the evolution of spectrum of protein energy malnutrition under the same dietary pattern. The presence or absence of normal transaminase function may influence the occurrence of marasmus or

kwashiorkor under similar dietary circumstances.

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