

From Kwashiorkor to Edematous Malnutrition

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In 1967, the 31-page August issue of *Indian Pediatrics* had four original articles besides case reports and the editorial. Amongst these, we decided to review the original article on “Kwashiorkor in Kabul and Hyderabad – A comparison on certain salient features.” Nearly seventy years post-independence, malnutrition still continues to be a major scourge responsible for mortality and morbidity in Indian children. Through this communication, we present the changes in understanding of the etiopathogenesis and the management of children with edematous malnutrition over last 50 years.

THE PAST

The study published by Samadi [1] in August 1967 issue of *Indian Pediatrics* was a cross-sectional study on 45 cases of Kwashiorkor <6 years of age admitted in the Department of Paediatrics at Mirmano Rooghtoon, Kabul (Afghanistan). The objective of the study was to evaluate the role of diet, environment and socioeconomic factors on the phenotypic features of kwashiorkor, and to compare the clinical profile of their cases with that reported from Hyderabad (India) [2]. After a comprehensive history with special attention to nutrition and examination of the children, serum protein, albumin and globulin were determined. The peak incidence of kwashiorkor in the Kabul series was reported in 1-3 years (42.3%) compared to 2-4 years (55.1%) in the Hyderabad series. Nearly all cases belong to low socioeconomic strata; nutritional inadequacy and chronic diarrhea was associated in 60% of the enrolled children. The higher proportion of infants (4.4%) with kwashiorkor reported in the index study than in Hyderabad series (2.8%) were attributed to probable maternal malnutrition with suboptimal breast milk output.

The author reported behavioral (irritability, apathy and peevishness), skin and hair changes in 89%, 6.7% and 80%

of the children, respectively. The frequency of vitamin A deficiency in the Kabul series (11.2%) was much lower than in the Hyderabad series (32.6%). The authors attributed this to prolonged breastfeeding, which would have helped meet the children’s vitamin A requirements. Prevalence of vitamin B complex deficiency was also lower in the Kabul series (22.2%) as compared to the Hyderabad series (32%); a likely explanation for the higher incidence of skin lesions (55%) in the latter. In concordance with the Hyderabad series, the Kabul series found low mean serum protein (4.54 g/dL) and albumin (1.86 g/dL) levels while serum globulin (2.68 g/dL) levels were relatively high. Thus, the study highlighted the spectrum of clinical and biochemical profile in kwashiorkor and the associated regional variations, though the precise etiopathogenesis remained to be unravelled.

Historical background and past knowledge: The term kwashiorkor, introduced by Cicely D Williams in 1935, was taken from the Ga language of Ghana to indicate ‘disease of the deposed baby when the second one is born’ [3]. She described this clinical syndrome amongst children living on the Western coast of Africa, who were weaned onto low-protein and starchy diet (cooked plantain, sweet potato and cassava), after being displaced from the breast by a younger sibling. The phenotype comprised of edema in the hands and feet, darkening and thickening of the skin followed by peeling, and a reddish tinge to the hair in the worst affected cases. The disease was largely confined to the tropical and subtropical parts of Africa, Asia and America, and the poor townships of the southern European countries. Post Second World War, it was widely accepted that kwashiorkor was due to primary protein deficiency (Classical theory) [4], while marasmus was considered an outcome of combined energy and protein deficit. Infections (particularly measles and gastroenteritis) were observed to complicate and precipitate this clinical syndrome.



THE PRESENT

The latest WHO classification of children (under 5 years of age) with severe malnutrition divides them into edematous and non-edematous category based on the presence of bilateral pitting edema (of nutritional origin) regardless of other features of kwashiorkor [5]. The presence of edema is used as an independent tool to screen cases of malnutrition as it has a strong association with mortality [6]. Kwashiorkor represents the most severe phenotype of edematous malnutrition, when other striking clinical features such as the skin (flaky paint dermatosis/crazy pavement sign) and hair changes are present.

Since the publication of the reported article, there has been a lot of research on the etiology and pathogenesis of kwashiorkor. The mechanism of edema still remains elusive and several hypothesis have been put forth to explain it. The classical theory was refuted by Golden, *et al.* [7] as he failed to establish the causal relationship of serum albumin with edema. In 1968, Gopalan proposed the theory of dysadaptation to elucidate the clinical phenotype in kwashiorkor [8]. He explained the genesis of edema to be due to the impaired hormonal response to stress; mediated via insulin, cortisol and growth hormone. Srikanthia [9] postulated that malnutrition results in structural and functional changes in liver, which leads to defective inactivation of ADH. Golden, *et al.* [10] proposed the landmark hypothesis of oxidative stress to account for the pathological changes in kwashiorkor. This was later supported by other researchers who observed high blood concentration of biomarkers of inflammation while the antioxidants levels were low in children with kwashiorkor [11]. However, the free radical/anti-oxidant theory was challenged by Ciliberto, *et al.* [12], who failed to establish protective effect of antioxidant cocktail in such children. A recent research has put forth the association of the Gut Microbiota (GM) dysbiosis with edematous malnutrition. This study reported a greater diversity in the gut microbiota in children with edematous malnutrition than in cases without edema [13].

Children with edematous malnutrition are recommended to be managed in a health facility as inpatients with therapeutic diets [14]. These children are in a state of reductive adaptation and hence overzealous introduction of a diet rich in calories and proteins can precipitate refeeding syndrome [15].

To conclude, kwashiorkor represents the worst form of edematous malnutrition and its genesis is multifactorial. There is a need to strengthen the reporting of cases with edematous malnutrition, and to determine the factors that complicate its clinical course and outcome. Genome wide

linkage studies can go a long way to explore the host factors that can explain the variability in clinical phenotype.

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