Coeliac disease among children in Kuwait: difficulties in diagnosis and management

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SUMMARY Twenty children with coeliac disease were diagnosed over a five year period in an area with 10 000–12 000 births per year. The average annual incidence was 1:3000 births. All children presented with severe symptoms and rickets was not uncommon (25%). Mean age at onset of symptoms was 38 months (range 6–120) and 72 months at the time of diagnosis (range 13–192), with a mean delay of 34 months. No cases were diagnosed during infancy. The difficulties in the differentiation of coeliac disease from the more common causes of chronic diarrhoea, and problems with diagnosis and management are discussed.

The fact that coeliac disease (CD) is not confined to Caucasians is now well established.^{1–6} Its prevalence in developing countries may be underestimated, however, because of the lack of diagnostic resources and the overwhelming number of children with the postgastroenteritis syndromes.^{5,8} Differentiation of CD from these syndromes is difficult because of similar clinical presentation and, occasionally, similar histological findings.^{9,10}

The occurrence of CD in Kuwait has been the subject of one report.⁶ We now report our experience with the disease over a five year period, and aim at highlighting the difficulties met in the suspicion and the diagnosis of CD and the problems encountered during follow up in Kuwait, a country with a sub-tropical location that still shares with the developing countries many of their health problems.

Methods

PATIENTS

The study involves 20 children with CD diagnosed during the period between April 1980 and March 1985. The catchment area is populated by 350 000, about two thirds of whom are Arab expatriates, with about 12 000 annual births.

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On the suspicion of CD, a detailed clinical and dietary history was recorded. Blood samples were obtained for a full blood count, serum iron, immunoglobulin electrophoresis and a complete SMAC-20 profile. Sweat chloride level was estimated for all patients, and folate level, bone age and thyroid functions for some. The one hour D-xylose level was estimated after a standard dose of 1 g/kg. The stools were repeatedly examined for parasites and cultured for intestinal pathogens. Multiple intestinal biopsies were obtained from the distal part of the duodenum through peroral fibroptic endoscopy as previously described by us.¹¹ A duodenal aspirate was taken at the same time to be examined for Giardia. The histological grading was assessed according to the classification used by Lee and Tomer.¹² The biopsy specimens were also examined for Giardia.

At the start of elimination of gluten from the diet, supplements of vitamins A and D, folic acid and iron were given during the first six to 12 months. Children were seen regularly every one to three months and their growth velocity was estimated using a reference standard.¹³

A second biopsy was obtained after 12–18 months (so far accepted in 12 children). Challenge with gluten could be arranged in six children and was patient inspired in two more. The child was allowed gradually increasing amounts of wheat products until he was on non-restricted diet in two to three weeks. The third biopsy was done for only five patients.

Results

Of the 20 children studied there were seven boys and 13 girls. Two of these children were monozygotic twin girls⁶ and four were female siblings from a large family with 11 offsprings. The mean age at the time of diagnosis was 72 months (range 13–192) and at the onset of symptoms was 38 months (range 6–120), with a mean delay of 38 months.

The average annual incidence of CD in the area studied was 1:3000 births. Thirteen children were of Palestinian origin (incidence 1:2400), three were Kuwaitis (incidence 1:6500). Two were Syrians, one from Egypt and one from Yemen.

Most patients presented with severe symptoms (Table 1) and 16 of them were repeatedly admitted to other hospitals with the clinical diagnosis of milk intolerance. All children had chronic diarrhoea and growth retardation, and 80% had wasting and abdominal distension. Rickets were particularly common (25%) and a number of children (25%) were admitted with exacerbation by severe watery diarrhoea, dehydration and hypokalaemia (coeliac

Table 1 Clinical manifestations in 20 children with coeliac disease

Manifestation	n	%
Chronic diarrhoea	20	(100%)
Slow growth	20	(100%)
Abdominal distension	16	(80%)
Mood changes	5	(25%)
Coeliac crises	5	(25%)
Rickets	5	(25%)

crises). Episodes of constipation were reported in six children.

The relevant biochemical and histological abnormalities are shown in Table 2 and Figure 1(a). Seven children who underwent biopsy on suspicion of CD were excluded because of finding another aetiology. Four had *Giardia* and three had milk intolerance after salmonellosis (two patients) and *Campylobacter* infection (one patient). All seven children responded dramatically to appropriate therapy.

Acceleration of growth was most impressive during

Fig. 1 Histological appearance of a series of intestinal biopsy specimens from one representative Arab child with coeliac disease. (a) On admission: subtotal villous atrophy with dense infiltrate of the lamina propria by lymphocytes. H & E.

Table 2 Histological and biochemical abnormalities in 20 children with coeliac disease

Abnormality	n. Tested	n. Positive	%
Anaemia	20	13	(65%)
Hypochromia	20	16	(80%)
Low folate	6	4	(66%)
D-xylose (<20 mg/100 ml)	19	18	(94%)
Intestinal changes	20	20	(100%)
partial villous atrophy		4	(20%)
subtotal villous atrophy		16	(80%)

the first year of gluten elimination: the weight velocity averaged 2.7 times the normal value (range 1.2–4.1) and the height velocity averaged 1.8 times normal (range 1.4–2.5). Compliance with gluten elimination was very difficult after the first year particularly in school children: our supply of gluten free flour was very patchy and we found great difficulties in supplying sweets and sandwiches for the school child.

Of the 12 children in whom a second biopsy could be obtained there was a histological remission in seven (Fig. 1(b)). The other five showed only mild to marginal improvement and all patients admitted to marked irregularity of gluten restriction.

There was a clinical and histological relapse in all of the five children who underwent a third biopsy following gluten challenge (Fig. 1(c)). There was a clinical relapse in the other three but the family refused the third biopsy.

Discussion

In view of the high prevalence of postgastroenteritis syndromes in Kuwait,^{7,8} we decided to strictly adhere to the widely accepted criteria for the diagnosis of CD.^{14,15} With the relative ease and safety of our biopsy procedure,¹¹ we should be able to confirm the diagnosis in most patients with suspected CD.

The incidence of CD in Kuwait may be compared with that in the West of Ireland during the late 50s.¹⁶ The late 70s, however, witnessed a sharp fall in the

Fig. 1(b) Twelve months after gluten elimination: improvement of villous height and regression of the lymphocytic infiltrate. H & E.

Fig. 1(c) Four months after gluten challenge: villous shortening and broadening with hypercellularity of the lamina propria. H & E.

incidence of CD in Western countries^{17,18} and this was attributed to the delay in the introduction of cereals and to the increased practice of breast feeding. The impact of increased wheat consumption on the expression of CD has been discussed in reports from developing areas.^{14,5} It is noteworthy that CD in this study was three times more common in Palestinians with large wheat consumption than in Kuwaitis with a high consumption of rice. The figure of 1:3000 may also be an underestimate in view of the fact that most of our patients had severe symptoms (Table 1). The marked delay in the diagnosis (mean 34 months) compares poorly with a 90% rate of diagnosis during infancy.¹⁸ The repeated previous admissions is another disturbing feature suggesting that CD is being missed or, at best, the diagnosis delayed until adult life. Extending the indications for biopsy to include children with more subtle manifestations has improved the rate of detection of CD.¹⁹

The contribution of CD to the number of children with chronic diarrhoea is minimal in Kuwait^{7,8,20} and

in other developing countries.⁵ We admit about a 1000 children with diarrhoea annually, of whom over 100 have chronic diarrhoea and other manifestations indistinguishable from CD. Subjecting all these children to absorption tests and intestinal biopsies overwhelms the limited diagnostic resources. This is certainly true for less prosperous countries with similar health problems. In a study of 519 children who had intestinal biopsy on the suspicion of CD in Cuba,⁵ only 50 (8.8%) showed findings compatible with the diagnosis. The relative paucity of CD among other causes of diarrhoea in developing countries should call for a high index of suspicion of CD, and, at the same time, for proper utilisation of the limited diagnostic resources.

The dramatic offset of diarrhoea after elimination of the offending milk is characteristic of the post-gastroenteritis syndromes.^{1,7,8} This issue is complicated, however, by the fact that most special formulae used for this purpose are gluten free,¹⁰ and that many children with CD have milk intolerance.⁹ Further-

more, the flat mucosa characteristic of CD can also be seen in the postgastroenteritis syndromes.¹⁰ These difficulties are particularly relevant to paediatricians in developing countries. We think, however, that careful longterm follow up is a reasonable safeguard against missing CD or over referrals to the expensive work up. The situation can certainly be reviewed at a later date.¹⁵

The great difficulties we met with compliance to gluten restriction were anticipated. It was initially difficult to convince parents that wheat bread (called 'the survival' in the local language) is the cause of the child's severe symptoms. It was possible, however, to achieve compliance in all cases after improvement was shown, when the child becomes lively and playful after prolonged misery. In a community poorly informed about CD, extra patience and efforts are needed to ensure optimum care for the family and the child.

Coeliac disease is probably more common in Kuwait than in many developed countries.^{17,18} It is, however, still far outnumbered by other causes of diarrhoea. Paediatricians working in developing countries have to balance between a high index of suspicion and over utilisation of resources. Careful clinical follow up of all patients with chronic diarrhoea is probably a reasonable attitude towards both under-diagnosis and over referrals.

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