Coeliac disease in Sudanese children

G. I. SULIMAN¹

From the Department of Paediatrics and Child Health, Khartoum Civil Hospital, Khartoum, Sudan

SUMMARY Coeliac disease has not hitherto been documented in Sudanese children. This report describes seven Sudanese children with coeliac disease of whom two are siblings. They all had evidence of impaired intestinal absorption, severe histological changes of their jejunal mucosa with clinical and histological improvement on gluten free/sorgham free diet. Subsequently one patient had a clinical relapse when gluten was reintroduced; four had positive gluten challenge using serial one hour blood xylose estimation. They all belonged to the upper socioeconomic group of the society in the north of the Sudan.

Coeliac disease was thought originally to be confined to Europeans, but so far cases have been described in indigenous Indians (Walia *et al.*, 1966) and in the immigrant population from the Indian subcontinent in the United Kingdom (Nelson *et al.*, 1973); and recently cases have been described in Iraqi children (Al-Hassany, 1975). However, no cases have yet been described in Africans or Chinese.

Until now coeliac disease has not been recognised in the Sudan. Weaning and feeding habits are certainly different from those in Europe and this may partly explain the low incidence of this syndrome but genetic, constitutional, and environmental factors may be involved.

Kisra, a local bread made from dura or *Sorgham vulgaris* constitutes a staple diet in many Sudanese homes, while wheat is also used but to a lesser extent. Preliminary studies of dura have suggested that it may be as toxic as wheat to coeliac patients (unpublished data).

The purpose of this report is to document for the first time the diagnosis of coeliac disease in Sudanese children observed during the last three years.

Methods

The children were all studied in the Paediatric Department of Khartoum Civil Hospital during the period of November 1974 to February 1977. Clinical assessment and routine haematological and bio-

chemical investigations, including a full blood count, serum calcium, phosphate, plasma proteins, and alkaline phosphatase, were done on admission. Other investigations included the one hour blood xylose absorption test (Rolles *et al.*, 1975) using a standard dose of 5 g, by the method of Roe and Rice (1948). The five hour urinary excretion test was done simultaneously when the patient's weight exceeded 30 kg.

Stools were examined microscopically for giardia, other parasites, and for fats. A three day collection of stools was sent for quantitative estimations for fats. Barium meal and follow-through was done using non-flocculating barium (Astley and French, 1951). A bone marrow study was performed in all patients and B₁₂ assay in the older children.

Small intestinal biopsy specimens were obtained by peroral paediatric Crosby and Kugler capsule (Crosby and Kugler, 1957), from the first loop of the jejunum. The position of the capsule was confirmed by radiography. The specimens were examined immediately under the dissecting microscope and the jejunal fluid examined for presence of giardia parasites. The biopsy specimens were then fixed in formalin and stained with haematoxylin and eosin and periodic acid-Schiff (PAS) for histological examination. Histological grading was assessed according to the following classification used by Harrison *et al.* (1976): N: normal; $\pm$: minimal or doubtful lesions; +: short wide villi, elongated crypts with slight increase of cells in the lamina propria (partial villous atrophy); ++: thickened ridges, increased number of lymphocytes and elongated crypts (moderate villous atrophy); and +++: flat mucosa, pseudostratification of lining

¹Address for correspondence: G. I. Suliman, P.O. Box 412, Khartoum, Sudan.

epithelium, excess cells in the lamina propria, and elongated crypts (subtotal villous atrophy).

When sufficient evidence was obtained for the diagnosis of coeliac disease, the patients were started on a conventional gluten free diet—that is, a diet free from wheat, rye, barley, and oats; sorgham was also excluded. Patients were kept in hospital for periods of one to three weeks until their general condition improved and then followed up for clinical assessment and also to ensure that they were adhering to their diet.

A one-hour xylose test was repeated until it rose to normal levels. Shortly after, a gluten challenge was performed by giving 20 g gluten daily for two to three days. One hour blood xylose test was done initially and then repeated after the gluten load and one week later.

Results

PATIENT'S AGE, SEX, AND ETHNIC GROUP

All patients were Sudanese of mixed African and Arab blood and belonged to socioeconomic classes I and II. The parents were first cousins in three patients, second cousins in one, and unrelated in three patients including the two siblings. Family history was non-contributory for all patients.

Table 1 shows the age and sex distribution of patients; four were aged 18 months or less, while three were aged 7 years or more at the time of diagnosis. Four patients were females and three males. The number of patients was too small to draw any conclusions regarding age or sex incidence.

FEEDING PATTERN

Breast feeding was given for varying periods: three patients were breast fed for less than six weeks, two for three and seven months, and three for a year or more. Cereals were introduced at the age of 4 to 7 months with a mean of 5.7 months, which seems to correlate well with the trend in the general population. Sorgham was introduced at about the same time in all patients (Table 1).

CLINICAL FEATURES

Diarrhoea was a prominent presenting symptom starting one to five months after introduction of cereals with a frequency of two to 10 times per day. The stools generally were described as bulky and offensive. Patient 6, a male child of 11 years, had encopresis and patient 5 had intermittent diarrhoea; however, her stools were said to float even during her normal days. Patients 1 and 3 had vomiting as a significant feature.

The onset of diarrhoea was associated with deterioration in general health, failure of growth, and, particularly in the younger age group, a marked deterioration in physical abilities; severe abdominal distension was noted and their buttocks hung in folds (Fig. 1).

All patients had poor appetites and were miserable. Weight loss was remarkable and all were below the third centile for weight and height according to

Fig. 1 Patient 2. Before and after treatment

Table 1 Age, sex distribution, feeding pattern, and clinical state of patients studied

No.	Patients	Sex	Age when seen	Breast feeding	Cereals introduced	Diarrhoea		Appetite	Abdominal distension	Weight loss	Mood	Follow-up
			(m)	(m)	(m)	Duration (m)	Frequency (/day)					(m)
1	F.B.	F	18	6/52	5	9	4-5	↓	++	++	↓	29
2	A.A.	M	18	12	6	10	4-10	↓	++	++	↓	24
3	K.G.	F	17	3	4	12	2-5	↓	++	++	↓	16
4	A.H.	M	14	7	4	9	3-4	↓	++	++	↓	15
5	H.A.	F	7 yr	3/52	7	6 yr	2-7	↓	+	++	↓	12
6	O.E.	M	11 yr	14	7	10 yr	4-6	↓	++ Early	+++	↓	9
7	H.E.	F	12 yr	12	7	11 yr	4-5	↓	+ Early	+++	↓	9

European standards at the time of presentation. Patient 7, a 12 year old girl, showed no signs of secondary sex characteristics.

INVESTIGATIONS

Table 2 shows the results of investigations. All patients had anaemia with a mean haemoglobin of 9.5 g/dl (range 7.7-10.5) however, the degree of anaemia did not correlate with the age of the patients nor with the duration of their symptoms. Six had iron deficiency anaemia and three were folate deficient. B₁₂ assay, carried out in patients 5, 6, and 7, was normal.

Table 2 Results of investigations

Investigation	Range	Mean
Hb (g/dl)	7.7- 10.5	9.5
Blood urea (mg/100 ml)	12 - 22	16
Na (mmol/l)	134 -138	137
K (mmol/l)	3.6- 4.8	4.05
Ca (mg/100 ml)	9.2- 10.7	9.82
P (mg/100 ml)	3.1- 3.8	3.45
Alkaline phosphatase (KAU)	4 - 18	10.86
Plasma proteins (g%)	6.3- 9.2	7.3
1-hour blood xylose (mg %)	2.7- 18	11.5

*Conversion factors to SI units: blood urea to mmol/l, $\times 0.166$; Ca to mmol/l, $\times 0.250$; phosphorus to mmol/l, $\times 0.323$; plasma proteins to g/l, $\times 10.0$; blood xylose to mmol/l, $\times 0.0666$.

Blood urea, serum electrolytes, calcium, phosphorus, and alkaline phosphatase were within normal limits and none of the patients showed evidence of rickets. Plasma proteins were within normal limits. One hour blood xylose was significantly low with a range of 2.7-18 mg/100 ml (0.18-1.19 mmol/l) and a mean figure of 11.5 (0.76 mmol/l) (Fig. 2). Urinary xylose secretion at five hours, done in the older children 5, 6, 7, was low with values of 0.96, 0.55, and 1 mg (0.06, 0.04, and 0.07 mmol/l) after a loading dose of 5 g. A flat glucose tolerance curve was obtained in all patients.

Stool tests for giardia and other parasites repeated on at least three occasions and cultures for pathogenic organisms were negative. Twenty-four hour faecal fat excretion was increased with a range of 6.5-12.8 g (mean 9.7 g). Barium studies showed typical features of malabsorption with loss of feathery appearance, dilatation of the small bowel, and flocculation of barium (Astley and French, 1951).

Dissecting microscopic appearances were essentially flat with mosaic pattern. However, on two occasions convolutions were noted. Histologically all had subtotal villous atrophy (+++), (Fig. 3), with absence of villi, elongation of crypts, pseudostratification of lining epithelium, cellular infiltration of lamina propria, and moderate increase of intra-epithelial lymphocytes. (Table 3).

Fig. 2 Patient 1. Photomicrograph of jejunal biopsy at original diagnosis showing subtotal villous atrophy

Fig. 3 Xylose challenge test done in patients 4, 5, 6, and 7, showing a positive gluten challenge. ($\times 0.0666$ for SI units)

Table 3 Dissecting microscopic and histological appearances of jejunal biopsy specimens before and after treatment

No.	Before treatment		After gluten free diet		
	Dissecting micro.	Histology	Histology		
			Early months		Late months
1	Flat	+++	++/+++	2 $\pm$	12
2	Flat	+++	+ / ++	3 $\pm$	8
3	Flat	+++	++	3 N	6
4	Flat	+++	—	(steroids) N	12
5	Flat	+++	—	Not done	
6	Flat	+++	—	+ / ++	6
7	Flat	+++	—	+ / ++	5

RESPONSE TO TREATMENT

Following treatment with a gluten/sorgham free diet, there was a dramatic response as far as the patients' general well-being and mood were concerned. Their diarrhoea stopped and appetite returned to normal. Weight gain was remarkable especially in the younger age group, who gradually regained their physical abilities and muscle power. Weight gain was steady but less dramatic in the older age group. All patients achieved a noticeable increase in height.

One-hour blood xylose returned to normal levels in all patients in three to seven weeks with a mean period of five weeks. Subsequently, gluten challenge using serial one hour blood xylose test was performed

in four patients, nos. 4, 5, 6, and 7. The blood xylose level dropped to below 20 mg/100 ml (1.33 mmol/l) after gluten ingestion and a week later rose again to a normal level in the patients challenged (Fig. 3).

Table 3 shows results of repeat jejunal biopsies done in all but one patient who refused the procedure; however, this patient had improved tremendously on a gluten free diet and had a positive xylose challenge. Histological improvement was demonstrated in six patients, of whom two had completely normal mucosa and two others had minimal mucosal changes. Although patient 3 had a (++) mucosal abnormality after three months on a gluten/sorgham free diet, she had an unequivocally normal biopsy after treatment with steroids for two months (Wall *et al.*, 1970; Lloyd-Still *et al.*, 1972). This was prescribed in a neighbouring country where the diagnosis of ulcerative colitis was entertained. However, this diagnosis had not been substantiated and therefore steroids were tapered off and finally stopped and a gluten free diet was introduced simultaneously. She remains extremely well.

Patient 1, after attaining histological normality, was advised while abroad to go back on a gluten containing diet, as the disease was not known to occur in these countries. Three months later her symptoms reappeared. She immediately responded to a gluten/sorgham free diet and has remained well since.

Discussion

The patients discussed here represent the first documented cases of coeliac disease in Sudanese children. The fact that this disease had not been described before in the Sudan could be ascribed to the ease of missing the diagnosis in a community where the great majority of patients failing to thrive were actually suffering from protein-calorie malnutrition. All patients seen here had been previously treated for malnutrition and one child was prescribed antituberculous chemotherapy for three months.

All patients had evidence of impaired intestinal absorption and severe histological changes of their jejunal mucosa. They improved clinically on exclusion of gluten and sorgham from the diet, and in six patients there was clear evidence of histological improvement towards normality (Anderson, 1960). The stricter criteria suggested by the European Society for Gastroenterology of clinical and histological relapse after reintroduction of gluten in the diet have not been met, except in one child who had a clinical relapse three months after the reintroduction of gluten containing diets.

Recently a one hour blood xylose test, although not universally accepted as being abnormal in the initial diagnosis of coeliac disease, has been shown to be of value in providing good evidence of relapse in children challenged with gluten and who were previously on a gluten free diet (Rolles *et al.*, 1975). All patients had low xylose levels initially, which rose to normal values on a gluten free diet; in four patients in whom a xylose challenge was done it was positive.

The response to treatment was dramatic, particularly with regard to weight gain and increase in physical power in the younger children compared with the older group. This is in agreement with the findings of Young and Pringle (1971) and Challacombe *et al.*, 1972. All patients were breast fed and it did not seem to affect the course of their illness.

Sorghum vulgaris or dura was excluded from the diet, as preliminary studies had suggested that this was as toxic to coeliac patients as wheat (unpublished data). Further studies are in progress to clarify this point.

Finally, all cases presented here are from the northern Sudan, which has a heterogeneous population of mixed Africans and Arabs. The fact that these patients belonged to the more affluent part of society is important, as these parents are usually westernised in their habits of eating and the bringing up of their children.

However, the community's nutritional situation is not static and, with a change in eating habits, it is possible that the incidence of coeliac disease may increase. This is particularly so with the recent noticeable increase in gluten intake and the early introduction of cereals to babies.

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