D-Xylose, fat load test and antigliadin antibody in children with coeliac disease

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ABSTRACT

Objective: To study the clinical pattern of coeliac disease in children living in the northwest coast of Libya, to investigate the sensitivity and specificity of D-Xylose, fat load test and antigliadin antibody and their correlation to each other and changes in jejunal biopsy.

Methods: A 4 year prospective study began in 1993. It includes all suspected coeliacs referred to our department for further evaluation. All have suction jejunal biopsy "using Crosby capsule" performed for diagnosis, screened at the same time with one hour D-Xylose, 3-5 hours urinary D-Xylose, fat load test and antigliadin antibody and followed up for 2-4 years.

Results: The mean age at presentation was 8 years. There was no significant correlation between D-Xylose, fat load test and antigliadin antibody. Antigliadin antibody has 87.5% sensitivity and 50% specificity in this study. Three hours urinary D-Xylose has 93% sensitivity where as one hour D-Xylose has 82% sensitivity and only 25% specificity, whereas fat load test has 69% sensitivity.

Conclusions: Blood and urinany D-Xylose and fat load tests are not useful for diagnosing coeliac disease. They have no correlation to each other or to jejunal histology. Antigliadin antibody is superior to the above tests.

Keywords: D-Xylose, fat load test, antigliadin antibody, coeliac disease, jejunal biopsy.

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Coeliac disease is quite common in North Africa. The estimated incidence in this area is around 1: 700.[1] We expect a total of 2000 patients with coeliac disease in Tripoli alone (1.5 million) and about 800 in the pediatric age group. Coeliac disease is induced by the introduction of gluten to the diet of susceptible children. Gluten is a large complex molecule which consists of gliadins, glutenins, albumins and globulins. A-gliadin which accounts for about 40% of the flour protein was shown to be the most toxic fraction in wheat, barley, rye and oats. There have been several screening tests advocated in suspected coeliac disease, aiming towards selecting patients for jejunal biopsy.

Abnormal jejunal biopsy and proper follow up remains the crucial points in diagnosing coeliac disease, whereas one hour blood and 3-5 hours urinary collection for D-Xylose, fat load test, and antigliadin antibodies are among those screening tests. Our aim in this part of the study is to present the pattern of coeliac disease in Libyan children living in the northwest coast of Libya. To investigate the sensitivity and specificity of D-Xylose, fat load test and antigliadin antibody (1gG) and their correlation to changes in jejunal biopsy.

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Patient selection. A prospective study over a 4 year period was carried out in Tripoli. One hundred and four suspected coeliac patients referred to our department for further evaluation (1993, 1994) were screened initially including jejunal biopsy and were followed up for a minimum of 2 years (2-4 years). (Table 1).

The results of the first 100 Libyan infants and children with confirmed coeliac disease according to modified criteria of ESPGAN (European Society of Pediatric Gastroenterology and Nutrition) 1990[2] are presented. (Table 2).

Methods. ***D-Xylose.*** After an overnight fast (6-8 hours) a sample of blood and urine were collected at fasting, followed by 5g of D-Xylose in 100 ml of water orally, for children over 30kg the oral dose of D-Xylose was 0.5g/kg (maximum of 25g) in 5% solution. A second sample of blood was collected one hour after the oral dose of D-Xylose, urine was collected for 3 hours post oral dose, only water was allowed during collection. D-Xylose was estimated as described by Silverman et al.[3]

Calculation. Calculation was carried out according to these formulas. Blood = D-Xylose (one hour - 0) times m^2 = mg% divided by 1.73. Normal value is more than 9.8 mg%. Urine = D-Xylose (3 hours X v-0), divided by 100 X urinary creatinine. Normal urinary level is more than 25% of the total oral dose, whereas 0 = zero time, M^2 = surface area, V = volume of urinary collection

Fat load test. After an overnight fast for 6-8 hours, fasting blood collected for zero plasma triglyceride, 1g/kg of fat (20% intralipid) was given orally, followed by a 2 hour blood sample for triglyceride. Triglyceride was measured using the spectro photometer method. Triglycerid (2 hrs - 0) X 100 = percentage, divided by Triglyceride (0). Abnormal plasma triglyceride is less than 40%.[4]

Antigliadin antibody. Serum collected from patients, stored at 4°C for 24-48 hours or frozen for a longer period were assayed for antigliadin antibody (1gG type) using indirect immunoflourescence assay, using kits provided by GmbH labor-diagnostik/ munchen, and carried out at the research laboratory, Department of Toxicology and Forensic Medicine, Faculty of Medicine, Tripoli. Positive results started from 1:10 dilution.

Jejunal biopsy. Jejunal biopsy was carried out in every suspected coeliac patient using Crosby suction capsule with radiological screening. The histological examination was performed by a histopathologist independently, a histological picture of absent or blunted villi, crypt hyperplasia, increased intraepithelial lymphocytes, plasma cells in the lamina propria supported the diagnosis. Abnormal jejunal histology was graded independently. Severe total villous atrophy, partial total atrophy and mild

Table 1 - Investigations in suspected coeliac.

1. Anthropometric Measurements:-

Ht, Wt, OFC.

2. Laboratory:-

FBP, serum iron, total iron binding capacity, calcium, phosphate, alkaline phosphatase, prothrombine time and immuno globulins. Total protein and electrophoresis. Stool for microscopic ex for ova, cyst, parasite, fat globules and occult blood.

3. Screening tests:-

Fat Load Test, D-Xylose, Antigliadin antibodies

4. Jejunal biopsy.

Table 2 - Clinical features of confirmed coeliac disease in Libyan children.*

Clinical features	Percentage
Failure to thrive	93
Iron deficiency anemia	79
Abdominal distension	72
Diarrhoea	71
Anorexia	45
Vomiting	44
Abdominal pain	33
Wasting	29
General weakness	23
Others	59
Delayed puberty	7
Nocturnal enuresis	6
Cow's milk intolerance	6
Hypocalcamia/Rickets	5
Stomatitis	5
Dysmorphic features (Russel silver, achondro plasia)	5
Clubbing	4
Hypoproteinemia/Oedema	4
Poor school performance	4
Developmental delay	3
Macrocytic anemia (Responded to folic acid)	1

*Updated ESPGAN criteria[2]

Table 3 - Correlation between D-Xylose and fat load.

(n)	D-Xylose "blood"	p value (two tailed)
Urinary D-Xylose (27)	r 0.2807	0.1561 (-)
Fat load test (90)	r 0.1334	0.2102 (-)
Fat load test*(56)	r 0.2432	0.0709 (-)

Spearman correlation
*D-Xylose>9.8 and fat load test>40% were excluded
(-)Not significant

villous atrophy.

Statistics. Spearman correlation was applied to estimate the coefficient correlation and p.value. Sensitivity is the probability of a positive test result in a patient with disease, calculated from this formula; True positive divided by true positive + false negative.

Specificity is the probability of a negative test result in a patient without disease, calculated from this formula; True negative divided by true negative + false positive.

Results. Mean age at presentation was 8 years (range 1-15 years). Twenty percent of the total were between 1-2 years. Forty eight percent of totals were males and 52% were females. Failure to thrive is the most common presenting feature followed by anemia (iron deficiency). Abdominal distension accounts for 72% and diarrhoea accounts for 71%. There was no significant correlation between one hour blood D-Xylose and urinary D-Xylose (r= 0.28) and fat load test (r=0.133) even after excluding all results of blood D-Xylose of more than 10mg% and fat load test of more than 40% (r = 0.24) (Table 3).

Table 4 - Sensitivity and specificity of D-Xylose, fat load test and antigliadin antibody.

(n)	Sensitivity	Specificity
Urinary D-Xylose (15)	93	0
Blood D-Xylose (38)	82	25
Fat load (46)	69	0
AGA (42)	87.5	50

No correlation with the severity of mucosal damage
*Abnormal urinary D-Xylose: If <15% of the oral dose

Three hours urinary D-Xylose has 93% sensitivity, one hour D-Xylose has 82% sensitivity and 25% specificity where as fat load test has only 69% sensitivity. (Table 4). Antigliadin antibody (1gG) used in this study has 87.5% sensitivity and 50% specificity. There was no correlation with the severity of mucosal changes. Out of 42 patients, (screened for antigliadin antibody) 4 patients with coeliac disease would be missed and in 4 children jejunal biopsy was unnecessary.

Discussion. Coeliac disease is a permanent intolerance to dietary gluten in susceptible children characterized by abnormal jejunal mucosa, leading to malabsorption and other features. It is quite common in North Africa. The problem arises since the wheat is a staple food in these countries. The onset of symptoms in Arab children appears to begin at a later age. In a prospective study of 20 coeliac children diagnosed between 1980 - 1985 in Kuwait[5] the mean age at onset of symptoms was 38 months. In a retrospective study of 19 Saudi Arabian coeliac children, the mean age of onset was 24 months.[6]

In a recent study of 34 Jordanian children with coeliac disease, the mean age at presentation was 55 months.[7] Our Libyan children were presented later than expected, prolonged latent period, atypical forms and late referral to our center are among the possible explanation. Failure to thrive was the most common presenting feature, iron deficiency anemia was the second most common presenting sign, probably because more than 75% of our Libyan coeliacs were over the age of 2 years at presentation. Diarrhoea with pale, bulky and foul smelling stools was the fourth common presenting symptom in contrast to others.[5-7] A small bowel biopsy showing characteristic abnormalities is considered the gold standard for diagnosing coeliac disease. The European Society For Pediatric Gastroenterology, hepatology, and nutrition issued the diagnostic criteria for coeliac disease in 1990 which stated that small intestinal biopsy must remain the essential step in diagnosis.[2]

Performing a small bowel biopsy is invasive and requires skilled medical personnel in specialized medical centers. A diagnostic test which is non-invasive and readily available would be ideal not only for patient convenience but also for optimizing the health care resourses.

Blood and urinary D-Xylose have been used extensively for monitoring coeliac disease. Their use for diagnosis has been criticized by others which is in keeping with our results because of poor specificity. Fat load test showed poor specificity and sensitivity in our patients with confirmed coeliac disease; low or abnormal fat load test may reflect a wide range of abnormalities i.e mucosal damage, pancreatic insufficiency abeta-or hypobeta lipoproteinemia and deficiency of bile salts. All these, explain the poor

correlation of jejunal histology with either D-Xylose or fat load test. The serum antigliadin antibody (AGA) assay is a simple screening test that measures immunoglobulin (1g) G and (1g) A classes,[8-10] sensitivity and specificity vary.

Among different centers, however, studies in children showed sensitivity of 83-98% and specificity of 52-89% for 1gG,[10-12] our results are consistent with the above reports, the only limitation for the use of serum AGA (1gG) in our country is the cost. It is quite expensive.

In this study, we found no correlation between the AGA 1gG titre and the severity of jejunal histology in contrast to others.[9,10] Recently antiendomysium antibody (EmA. 1gA) has become a more reliable test for coeliac disease since first described in 1983.[12] This test is currently under investigation in our department.

In conclusion, blood and urinary D-Xylose and fat load test are not useful for diagnosing coeliac disease. They have no correlation to each other or to jejunal histology. Antigliadin antibody (1gG) is superior to the above tests. Further studies using other antigliadin, antiendomyosium antibodies are necessary.

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