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Neurological manifestation of Coeliac disease in Iraqi patients

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Abstract:

Background: Celiac disease (CD/ Non tropical sprue, gluten-sensitive enteropathy) is a malabsorptive conditioning which an allergic reaction to the cereal grain-protein gluten (present in wheat, rye and barley) causes small intestine mucosal injury.

Aims: The purpose of the present study was to evaluate neurological manifestation in association with celiac disease. The specific objectives were: To study neurological manifestation of celiac disease.

Methods: Seventy-five unselected consecutive patients (32 men, 43women, mean age 25.51±8.473 years) with histologically proven CD, were enrolled and prospectively investigated. The 75patients were seen in Department of Gastroenterological out patient, medical and neurological wards of Baghdad hospital. All patients were on gluten-free diet at recruitment and median duration of disease2.56±1.670).

Results: The onset is in the first four decades of life, with a female to male ratio of 2:1. It may be associated with a wide spectrum of neurological manifestations including cerebellar ataxia, epileptic seizures, dementia, neuropathy, myopathies and multifocal leuco encephalopathy. We report three teen patients with neurological manifestations related with CD: two with cerebellar ataxia, two with epilepsy, two with carpel tunnel syndrome, two with myopathies, two with peripheral neuropathy and one with cognitive impairment. The diagnosis of CD was confirmed by serologic tests (antiendomysial,antitransglutaminase antibodies and antigliadin antibodies) and biopsy of the small intestine. In two patients the neurological symptoms preceded the gastrointestinal abnormalities and in all of them gluten restriction failed to improve the neurological disability.

Conclusion: CD should be ruled out in the differential diagnosis of neurological dysfunction of unknown cause, including ataxia, epilepsy and dementia. A gluten free diet, the mainstay of treatment, failed to improve the neurological disability.

Key words: neurological disability, neurological dysfunction.

Introduction:

Celiac disease (also called gluten-sensitive enteropathy and nontropical sprue) was first described by Samuel Gee in 1888 in a report entitled "On the coeliac Affection", although a

similar description of a chronic, malabsorptive disorder by Aretaeus from Cappadochia (now Turkey) reaches as far back as the second century AD [1] .

The cause of celiac disease was unexplained until the Dutch pediatrician Willem K Dicke recognized an association between the consumption of bread and cereals and relapsing diarrhea. This observation was corroborated when, during periods of food shortage in the Second World War, the symptoms of his patients improved once bread was replaced by unconventional, noncereal containing foods; this finding confirmed the usefulness of earlier, empirical diets that used pure fruit, potatoes, banana, milk, or meat [1-3] .

Since symptoms reoccurred when bread was reintroduced after the war, Dicke and van de Kamer initiated controlled experiments exposing children with celiac disease to defined diets and then determined fecal weight and fecal fat as a measure of malabsorption. Wheat, barley, rye, and (to a minor degree) oats triggered malabsorption, which could be reversed after exclusion of these "toxic" cereals from the diet [4] . Shortly after, the toxic agents were found to be present in gluten, the alcohol-soluble fraction of wheat protein [5] .

The celiac lesion in the proximal small intestine was first described in 1954. The primary findings were mucosal inflammation, crypt hyperplasia, and villous atrophy [6] . With the development of peroral biopsy, it became apparent that celiac disease and adult nontropical sprue shared the same features and pathogenesis [7] . When unrecognized and untreated, celiac disease is associated with a high mortality that reached 12 percent in one retrospective study of 544 children prior to the introduction of a strictly gluten-free diet [8] .

Patients and methods

Seventy-five unselected consecutive patients (32 men, 43women, mean age 25.51±8.473 years) with histologically proven CD, were enrolled and prospectively investigated.

The 75patients were seen in Department of Gastroenterological out patient, medical and neurological wards of Baghdad hospital. All patients were on gluten-free diet at recruitment and median duration of disease2.56±1.670).

Patients with associated conditions that could cause neuropathy (diabetes mellitus ; thyroid disease, alcohol abuse, vitamin B12 deficiency, exposure to neurotoxic drugs) or ataxia (alcohol abuse, genetic disorders ,syphilis, or B12 deficiency) were excluded, in order to minimize the possible confounding effect on neurological symptoms.

All patients received a questionnaire with a checklist on which they were asked to report on neurologic symptoms or conditions that required medical attention or treatment. Patients with suspected neurologic signs or symptoms underwent a full neurologic evaluation and laboratory examinations, including brain imaging and electroencephalogram if required . All investigations were performed after obtaining informed consent from patients.

Statistical Analysis:

SPSS v.20 (Statistical Package for Social Sciences) used for data input and analysis. Continuous variables were expressed as mean and standard deviation, while discrete variable were expressed as number and percent. Chi square test for

goodness of fit used to test the observed distribution of some discrete variables. Chi square test for independence used to verify the association between discrete variables. Findings with P values less than 0.05 were considered significant.

Results:

Our study consisted of 75 subjects; CD who answered the questionnaires and agreed to take part in this study The mean ages of the patients with CD were 25.1 ± 8.4 years.32male (42.7%) ,43(57.3% female).see table and figure one.

Duration of celiac disease (year)2.56±1.6.see figure 1

Table 1: Distribution of participants according to their age, duration of celiac disease, and gender.

Age (year); Mean (SD)			25.51(8.473)
Duration of Celiac disease (year); Mean (SD)			2.56(1.670)
Gender; N(%)			
	Male		32(42.7)
	Female		43(57.3)

Figure 1: Distribution of study sample according to sex. The distribution of study sample according to age

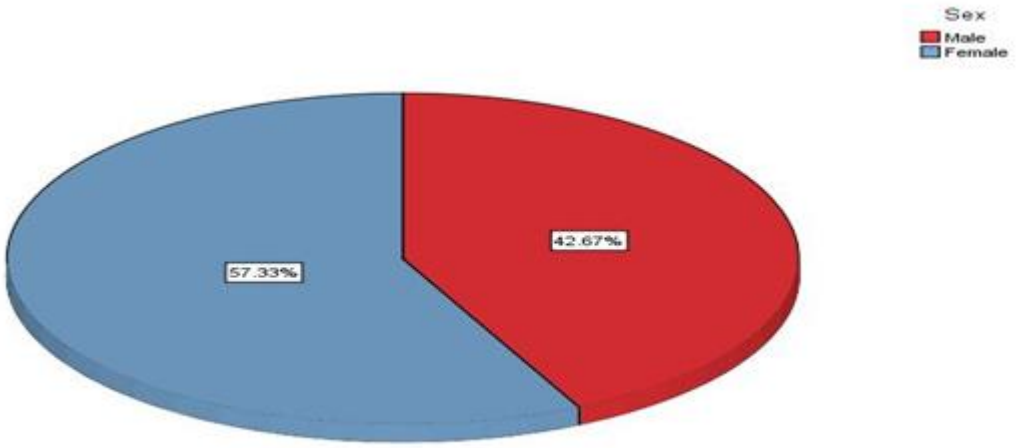

Figure 2: Distribution of study sample according to age.

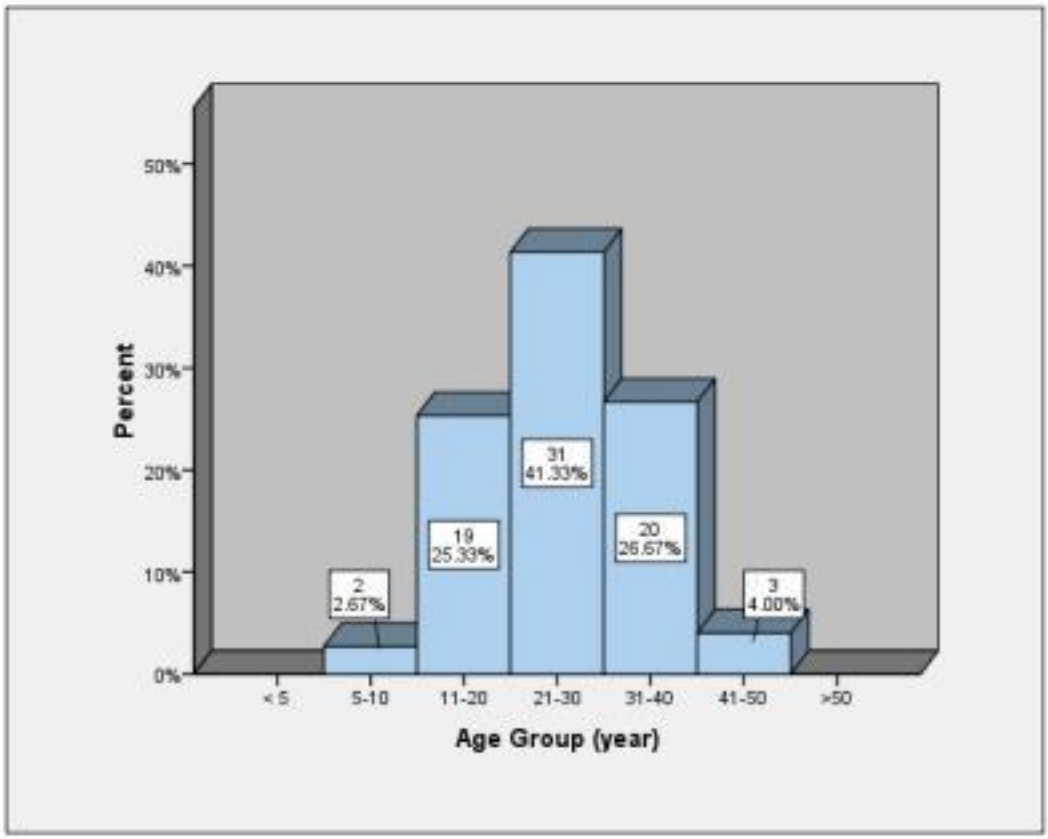

Figure 3: Distribution of study sample according to the duration of Celiac disease.

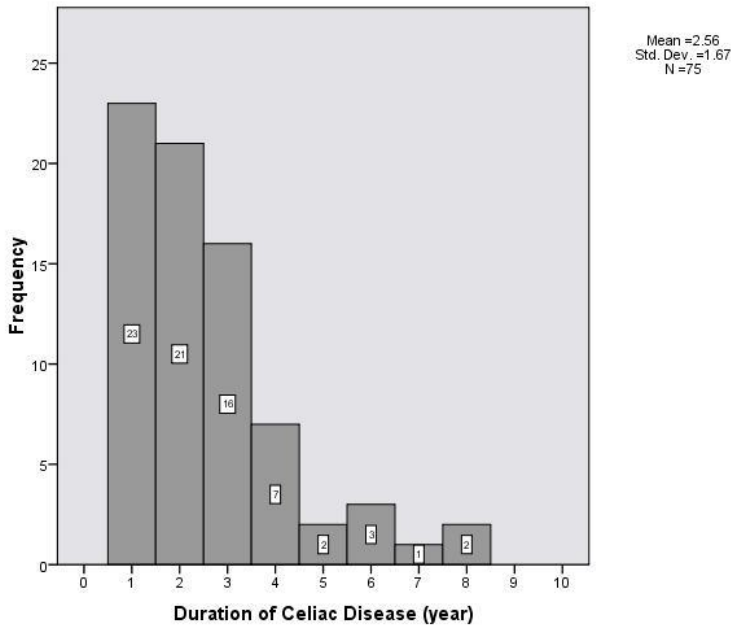

Table 2: Distribution of participants according to their clinical manifestations.

1-Intestinal manifestations:

The presence of intestinal manifestations of malabsorption such as steatorrhea, weight loss or other signs of nutrient or vitamin deficiency; and resolution of the mucosal lesions and symptoms upon withdrawal of gluten-containing foods, usually within a few weeks to months,found in 69(92%) patient.

2- Extra-intestinal Manifestations

A) NeurologicManifestations

Prevalence of neurological manifestation or findings were 17.3 % (95%CI 12.9-21.7%) . We report three teen(17.3%) patients with neurological manifestations related with CD: two(2.7%) with cerebellar ataxia, two(2.7%) with epilepsy, two(2.7%) with carpel tunnel syndrome, two (2.7%)with myopathies, two(2.7) with migraine, two(2.7%) with peripheral neuropathy and one(1.3) with cognitive impairment. see figure4.

Figure 4: Distribution of participants according to the neurological manifestations.

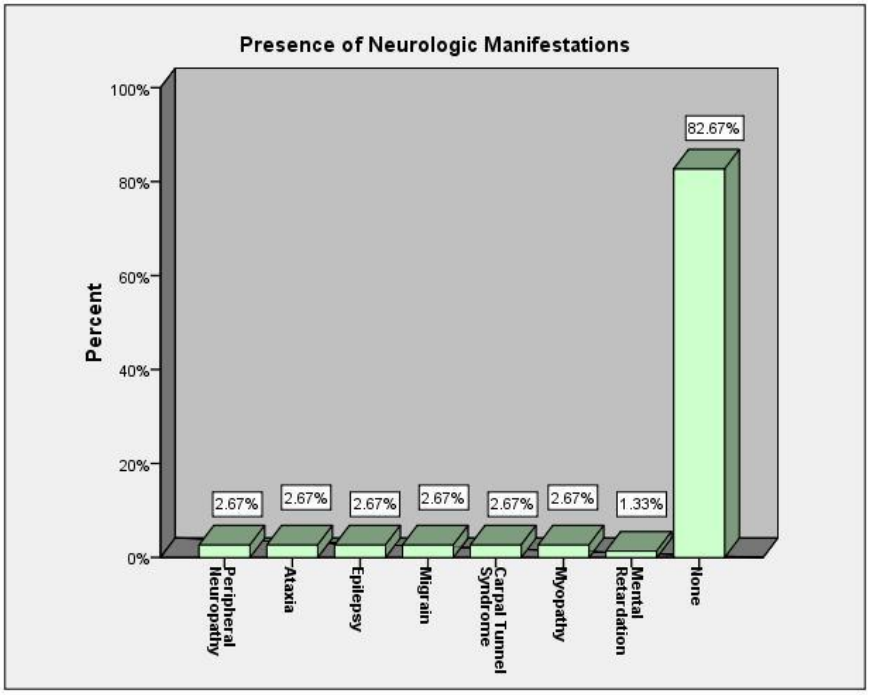

Table 2: Distribution of study sample according to the results of clinical examinations:

Manifestations	N(%)		
Total	**75(100.0)**	**X^2**	**P**
Presence of Intestinal Manifestations			
Yes	69(92.0)	52.920	**0.000**
No	6(8.0)		
Presence of Extra-Intestinal Manifestations			
Yes	21 (28.0)	14.520	**0.000**
No	54(72.0)		
A) Presence of Neurologic Manifestations	**13(17.3)**		
Peripheral Neuropathy	2(2.7)		
Ataxia	2(2.7)		
Epilepsy	2(2.7)	32.013	**0.000**
Migraine	2(2.7)		
Carpal Tunnel Syndrome	2(2.7)		
Myopathy	2(2.7)		
Mental Retardation	1(1.3)		
None	62(82.7)		
B) Presence of Non-Neurologic Manifestations			
Yes	10(13.3)	40.333	**0.000**
No	65(86.7)		

Discussion:

in the pathogenesis of both ataxia and peripheral neuropathy. Antibodies to gliadin that cross react with Purkinje\cells have been inconsistently reported in sera of celiac patients with ataxia, (15,17) and IgG antibodies to gangliosides have been found in adult CD patients with neuropathy and other neurological manifestations (18-21).

In Our study that consisted of 75 subjects; CD which answered the questionnaires and agreed to take part in this study The mean ages of the patients with CD were 25.1 ± 8.4 years.32male (42.7%) ,43(57.3% female)and the duration of celiac disease was (year) 2.56±1.6. The presence of intestinal manifestations of malabsorption such as steatorrhea, weight loss or other signs of nutrient or vitamin deficiency; and resolution of the mucosal lesions and symptoms upon withdrawal of gluten-containing foods, usually within a few weeks to months, found in 69(92%) patients.

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