

Can Duodenal Biopsy Be Omitted in Patient With Positive Serum tTGA Antibody in The Diagnosis of Celiac Disease?

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ABSTRACT

Background: Celiac disease (CD) is caused by a reaction to the dietary gluten in genetically predisposed individuals. Measuring of serum IgA antibodies to human tissue transglutaminase (tTGA) can be used alone for the diagnosis of celiac disease. However, it is recommended that individuals with positive tTGA antibodies should have a duodenal biopsy to confirm the diagnosis of CD.

Objectives: This study aims to clarify the extent to which the anti tTGA serological assay can replace the need for performing duodenal biopsy in the diagnosis of CD.

Patients and Methods: This study was conducted in the Basrah University Teaching Hospital laboratory, Jasim Aldiab laboratory, and Al-Moosawi private hospital in the period of 1st January 2019 to 1st October 2021. The cases included in this study are 190 individuals subjected to tTGA serological test and duodenal biopsy. Marsh I and Marsh II categories were not considered diagnostic of CD, while Marsh III category was considered diagnostic of CD. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the tTGA test were calculated.

Results: The sensitivity of the tTGA was 57.1%, the specificity was 92%, the PPV was 95.2%, and the NPV was 43.4%.

Conclusions: The study concludes that the duodenal biopsy can be omitted in patients with negative serum tTGA antibody because of high specificity but cannot be used as a sole tool for the diagnosis of CD because of low sensitivity. Thus, depending on the serological test could lead to missed diagnosis of some CD cases.

Keywords: Celiac Disease, Duodenal biopsy, serum tTGA antibody, Dietary gluten, Modified Marsh-Oberhuber classification

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INTRODUCTION

Celiac disease (CD) is caused by a reaction to the dietary gluten in genetically predisposed individuals. The disease is triggered by an immune-mediated inflammation in the small intestine. Measuring of the serum IgA antibodies to human tissue transglutaminase (tTGA) is recommended for the diagnosis of CD in most patients. The test is highly specific and sensitive.^{1,2} However, it is recommended that individuals with positive tTGA antibodies should have a duodenal biopsy to confirm the diagnosis of CD. The disease may be patchy in distribution and multiple biopsies should be taken from the distal duodenum and duodenal bulb.³ The diagnostic accuracy of the duodenal biopsy is affected by the quality of the biopsy and the subjective interpretation.⁴⁻⁶ Modified Marsh-Oberhuber classification is commonly used to classify the histologic appearance of the duodenal mucosa. Marsh I: refers to the presence of intraepithelial T lymphocytes; more than 30/100 enterocytes.

Marsh II: refers to an increase in intraepithelial T lymphocytes; more than 30/100 enterocytes with crypt hyperplasia but without villous atrophy.

Both Marsh I and Marsh II morphology are not diagnostic of CD.

Marsh III: refers to when villous atrophy can be seen along with increase in intraepithelial lymphocytes and crypt hyperplasia. This is considered diagnostic of CD.⁶ and is further subdivided into three subtypes.

Marsh IIIa: mild atrophy; “partial villous atrophy”

Marsh IIIb: moderate atrophy; “subtotal villous atrophy”

Marsh IIIc: complete atrophy; “total villous atrophy”^{7,8}

It has been previously suggested that diagnosis of CD can be based on the serological test alone with the ability of the test to diagnose the disease accurately.^{9,10} Depending on the high positive predict values (PPVs) of the serological tests, it has been proposed that duodenal biopsy is no longer required for the diagnosis of CD in some patients.

The present study aims to clarify the extent to which the anti tTGA serological assay can replace the need for performing duodenal biopsy in the diagnosis of CD.

PATIENTS AND METHODS

The current study was conducted in Basrah University Teaching Hospital laboratory, Jasim Aldiab laboratory, and Al-Moosawi private hospital from 1st January 2019 to 1st October 2021. The study includes 190 individuals with suspected CD and showing symptoms such as chronic diarrhea, chronic abdominal pain, failure to gain weight, short stature, anemia, and abdominal distention.

All the patients included in the study were subjected to tTGA serological test and duodenal biopsy. A tTGA titer of 18 IU/mL or more was considered as positive. The duodenal biopsies were taken from the second part of the duodenum by esophagogastroduodenoscopy (EGD). The

pathologists were not informed of the tTGA serological results. The pathological findings of the duodenal biopsy were classified according to the Marsh-Oberhuber categorization.^{9,10} Marsh I and Marsh II categories were not considered diagnostic of CD, while Marsh III category was considered diagnostic of CD.

The sensitivity, specificity, PPV, and NPV of the tTGA test were calculated. The duodenal biopsy was used as the gold standard. In order to reduce the overdiagnosis and underdiagnosis of CD, cases with poor quality duodenal biopsies which made the histological assessment by the pathologist uncertain were excluded from the study.

This study was analyzed using Microsoft Office Excel ,version 2016, and SPSS, version 19.

RESULTS

A total of 190 cases were included in this study; 58 were males and 132 were females. The youngest patient was 2 years old and the oldest patient was 61 years old. The mean age incidence was 30 years for the total 190 cases; 140 (73.7%) had positive histopathological results for CD, and 50 (26.3 %) had negative histopathological results. The male to female ratio was 1:2.3 (Table 1).

Table 1: Gender distribution of duodenal biopsy.

Celiac disease	Male	Female	Total
Marsh III (Positive biopsy)	40	100	140
Negative biopsy	18	32	50
	58	132	190

Table 2: Correlation between tTGA and histopathological changes.

		Duodenal biopsy outcome		
		Positive for Celiac disease	Negative for Celiac disease	
tTGA test outcome	positive	True positive (TP) = 80	False positive (FP) = 4	<u>Positive predictive value</u> = TP / (TP + FP) = 80 / (84) = 95.2 %
	negative	False negative (FN) = 60	True negative (TN) = 46	<u>Negative predictive value</u> = TN / (FN + TN) = 46 / (106) = 43.4%
		<u>Sensitivity</u> = TP / (TP + FN) = 80 / (140) = 57.1 %	<u>Specificity</u> = TN / (FP + TN) = 46 / (50) = 92 %	

The lowest tTGA serum titer was 0.15 mL/IU and the highest titer was 404.2 mL/IU.

In patients with positive pathological results (140), 80 cases (57.1%) had positive tTGA, with the mean serological level of tTGA as

69.8 U/mL, while in patients with negative pathological results (50) cases, tTGA was negative for 46 cases (92%). The mean serological level of tTGA was 4.1 U/mL.

DISCUSSION

There is an increase in the frequency and geographical distribution of CD all over the world. This has led to an increase in the methods of the CD diagnosis so that the correlation between tTGA antibody serum level and duodenal biopsy has been described.^{11,12}

Studies conducted in Iran as well as the West recommend avoiding duodenal biopsy in patients with high tTGA antibody titers, considering the high level of serum tTGA antibody, about five to ten folds than normal levels, which is enough for CD diagnosis without duodenal biopsy.^{13,14 15,16}

In North America, it is recommended that children and adolescents with high level of serum tTGA antibody get intestinal biopsy for CD diagnosis.^{17,18}

In the present study, the sensitivity of serum tTGA antibody was 57.1% and the specificity was 92%. The positive predictive value was 95.2%, while the negative predictive value was 43.4%, which is similar to another study conducted in two Danish fertility clinics wherein the sensitivity was 42.9% and the

specificity was 86.8%.¹⁹ This result is also similar to a study conducted in Pakistan which shows the sensitivity and specificity of anti-tTGA as 78.6% and 98.1%, respectively. The positive predictive value and negative predictive value were 84.6% and 97.2%, respectively.²⁰

This sensitivity makes the test unsuitable for screening for CD since the test will miss many truly diseased patients. However, the high specificity can help identify true-negative people or those without the disease.¹⁹⁻²¹

CONCLUSIONS

Our study concluded that the duodenal biopsy can be omitted in patients with negative serum tTGA antibody because of high specificity but cannot be used as a sole tool for the diagnosis of CD because of low sensitivity. Depending on the serological test will lead to missed diagnosis of some CD cases.

Duodenal biopsy cannot be avoided from the diagnostic process of CD.

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