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Research Article



Some immunological characteristics in Iraqi women with celiac disease

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Abstract

Celiac disease is a chronic small intestinal inflammatory disease characterized by a lifelong reaction to dietary gluten in individuals with genetic predisposed. Many studies were suggests the presence of celiac disease predominance in women than man patients. This study was conducted in Thi-Qar province – south of Iraq. The blood samples were collected from healthy and celiac patients whose diagnosed by serology tests using Enzyme Linkage Immuno Sorbent Assay. The current study was designed to demonstrate women's serologic parameters and their characters in Thi-Qar province. This case-control study demonstrates that women are predominantly incidence with celiac disease. Using the two-step testing is a quite precise strategy for diagnosing suspicious persons and can be a potent marker for monitoring celiac disease activity.

Keywords: Celiac disease, Anti-tTG, Anti-GA, Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value, Positive Likelihood Ratio and Negative Likelihood Ratio

Introduction

Celiac Disease (CD) is also named Celiac sprue, Gluten-sensitive enteropathy, and Non-Tropical sprue (Al-Toma et al., 2019). CD is a chronic small intestinal inflammatory disease characterized by a lifelong reaction to dietary gluten in individuals with genetic predisposed. When celiac patients ingest gluten and related proteins of grains, the body mounts an immune system that attacks the small intestine cells causing inflammation and destruction of villous architecture concomitant with quite strong signs and symptoms of CD, which normalize on obviating gluten intake (Tye-Din et al., 2018).

CD became a common dietary health problem issue as the disease is spreading worldwide over the public, with considerable variation in prevalence around the world (Fasano and Catassi, 2001). Until a few decades ago, CD was thought to be a rare disease that only affect a small portion of the population, and the variation in CD prevalence between regions of the world is because of variations in their healthcare

systems and a number of diagnostic tests (Fasano and Catassi, 2012 ; Mohta et al., 2021).

CD has an extensive epidemiological distribution, affecting all countries and ethnicities, and represented one of the most prevalent types of food intolerance in the world, with an estimated prevalence as high as (0.5 - 2.0) % in the general population with slight variations between geographical regions (Mohta et al., 2021). It can arise at any time during the patient's life course, from weaning up to adulthood of both sexes with a great variety of signs and symptoms (Caio et al., 2019).

Reports of CD in Iraq first appeared in 1975 through Al-Hassany study relying on a proper small intestinal biopsy, and it was found that CD was a prevalent problem in Iraqi patients and share with other countries in the diagnostic problems of this disease (Arif et al., 2009), and other studies about enumerating a number of celiac patients were done and found it ranges between (10-11.2) % in patients with T1DM (Mansour and Najeeb, 2011). In addition, the study conducted at Al-Yarmouk teaching hospital involving 140 patients with

irritable bowel syndrome illustrated that CD records (12.1) % of patients (Ibrahim, 2020).

Women are diagnosed with CD more than men, and these women predominant is clear in the extant literature on individuals-based studies in numerous countries of Europe, notably Finland, the United Kingdom, Denmark, and the Netherlands. These studies feature large sample sizes and many were conducted on a nationwide scale, and describing CD populations in Sweden and Italy has seemed, in the range, a 2:1 woman-to-man ratio. Studies in North America have shown a similar if not more pronounced woman majority. This sex skew is applicable to both children and adults. Celiac literature from Asia also has indicated that in CD, women outnumber then men (Jansson-Knodell et al., 2019). Therefore, this study aimed to study the presence of CD predominance in women and their serologic parameters, and the characteristics of CD tests.

Methods

During the period between December 2020 and June 2021, celiac women have admitted to hospitals in Thi-Qar province –south of Iraq. Celiac patients were diagnosed based on European Society for Pediatrics Gastroenterology, Hepatology and Nutrition guidelines (Husby et al., 2020), and the patients had to fulfill two criteria: firstly clinical history of CD manifestation and secondly serology evidence of autoantibodies for CD diagnostic tests. The control group included healthy women who were free from signs and symptoms of CD and matched in age and gender with patients who had no history of any chronic disease.

The blood sample (3mL) was collected from celiac and healthy individuals and left at room temperature, then centrifuged at 3000 cycles for 10 minutes to get serum and divided into several Eppendorf tubes then preserved at (-20)°C until use. Exclusion criteria included patients with other diseases such as cancer or other autoimmune diseases as well as those who were denied to be included in this study. The results are expressed as mean ± standard error mean (SEM), student t-test and ANOVA, and Pearson correlation used to analyze results by using SPSS version 24. P-value ≤ 0.05 was considered significant.

The appropriate diagnostic parameters are determined using the following equations:

- Sensitivity (se %) $tp \times 100 / (tp + fn)$.
- Specificity (sp %) $tn \times 100 / (tn + fp)$.
- Diagnostic efficiency (de %) $(tp + tn) 100 / (tp + fp + tn + fn)$.
- Positive predictive value (PPV%)= $tp \times 100 / (tp + fp)$.
- Negative predictive value (NPV%)= $tn \times 100 / (fn + tn)$.
- Positive Likelihood Ratio=Sensitivity/(1-Specificity).
- Negative Likelihood Ratio=(1- Sensitivity)/Specificity (Shreffler, 2022).

tp: true positive (sick people correctly diagnosed as sick); fp: false positive (healthy people wrongly diagnosed as sick); fn: false negative (sick people wrongly diagnosed as healthy); tn: true negative (healthy people correctly diagnosed as healthy).

Ethical approvals were obtained from all individuals or their guardians (for minors) prior to the study. Women patients underwent four serologic tests that have been used in local hospitals for CD diagnosis by ELISA technique using kits of Aeskulisa company (AESKU DIAGOSTICS GmbH and Co. Wendelsheim, Germany). The results were analyzed based on the manufacturer's instructions of principle, procedure, and result interpretation.

Result

One hundred celiac patients are involved in this study which includes (66) women and (34) men (1.94:1 woman: man), in addition, sixty-six healthy women, were involved in this study as a healthy control group. Cases with questionable, unconfirmed diagnoses of CD were excluded. The age range of study individuals at diagnosis was (1-60 years) and the mean age of them was (21.52 ± 6.61) years. All individuals in this study underwent to four CD tests including Anti-tTG IgA, Anti-tTG IgG, Anti-GA IgA, and Anti-GA IgG by ELISA technique.

The present study finds out that a higher prevalence of CD in the woman age group (7-12 years) reaches (33.33) % and is lower in the woman age group (13-18) than in other age groups as seen in Table 1.

Table 1. Distribution of celiac women according to the age

Patients with CD	Age groups (years)					Total
	1 – 6	7 – 12	13 – 18	19 – 24	> 25	
Woman	18	22	8	9	9	66
%	27.27%	33.33%	12.12%	13.64%	13.64%	100%

Immunological study of CD serology tests

The results of the current study show that sixty-six celiac women sera tests: (47 of 66) samples are positive for Anti-tTG IgA, whereas for Anti-tTG IgG there are (60 of 66) samples were positive and this test is the more delineated test

compared to other study serology tests, whilst the Anti-GA IgA test is the lower accuracy that reaches to (39 of 66) sample positive only, as for Anti-GA IgG test there are (49 of 66) samples are positive and significant differences between celiac and healthy women as in [Tables 2 and 3](#).

Table 2. Results of Anti-tTG-IgA and Anti-tTG-IgG in study women

Serology test results	Anti-tTG IgA		Anti-tTG IgG	
	Celiac women	Healthy women	Celiac patients	Healthy women
Seropositive	47 71.21%	3 3.00%	60 90.91%	2 2.00%
Seronegative	19 28.79%	63 63.00%	6 9.09%	64 64.00%
P value	P< 0.05 ^S		P< 0.05 ^S	
S: Significant, NS: Non-Significant				

Table 3. Results of Anti-GA-IgA and Anti-GA-IgG in study individuals

Serology test results	Anti-GA IgA		Anti-GA IgG	
	Celiac women	Healthy women	Celiac patients	Healthy women
Seropositive	39 59.09%	5 5.00%	49 74.24%	4 4.00%
Seronegative	27 40.91%	61 61.00%	17 25.76%	62 62.00%
P value	P< 0.05 ^S		P< 0.05 ^S	
S: Significant, NS: Non-Significant				

Characters of study serological tests

No, any serologic tests are definitely specific for CD, and the detection of autoantibodies often supports the diagnosis in

spite of the dramatic difference in the diagnostic accuracy of these tests.

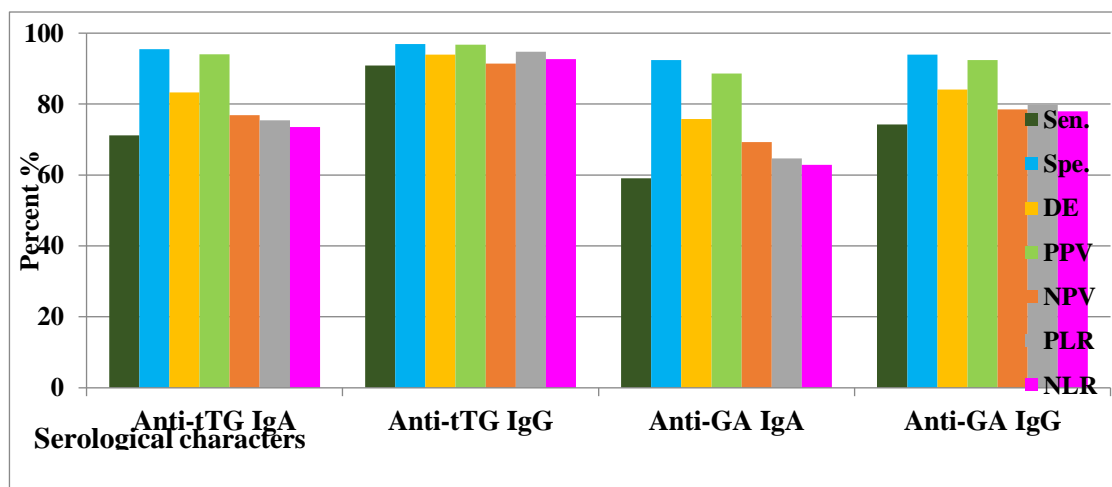


Fig. 1 Characters of serological tests for celiac patients. Damage the percentage with numbers. Damage serological characters with the abbreviation

The current study includes calculating characters of study serology tests such as Sensitivity (Sen), Specificity (Spe), Diagnostic Efficiency (DE), Positive Predictive Value (PPV), Negative Predictive Value (NPV), Positive Likelihood Rate

(PLR), and Negative Likelihood Rate (NLR). The results unveil that Anti-tTG IgG is the highest values and the Anti-GA IgA is the lowest values in all serological characters than in other tests as shown in Table 4 and Fig 1.

Table 4. Serology characters for celiac patients

Serological characters	Serological tests for celiac patients			
	Anti-tTG IgA	Anti-tTG IgG	Anti-GA IgA	Anti-GA IgG
Celiac women	66	66	66	66
Seropositive	47	60	39	49
Seronegative	19	6	27	17
Healthy women	66	66	66	66
Seropositive	3	2	5	4
Seronegative	63	64	61	62
Sensitivity	71.21%	90.91%	59.09%	74.24%
Specificity	95.46%	96.97%	92.42%	93.94%
Diagnostic efficiency	83.33%	93.94%	75.76%	84.09%
Positive Predictive Value	94.00%	96.77%	88.64%	92.45%
Negative Predictive Value	76.83%	91.43%	69.32%	78.48%
Positive Likelihood Ratio	75.39%	94.73%	64.64%	79.88%
Negative Likelihood Ratio	73.55%	92.72%	62.85%	77.97%

Discussion

Despite the utilization of the random sample procedure during patient recruitment, predominantly woman patients are detected in the study population. Generally, the woman is much higher than a man to incidence with CD and some studies show that women were at increased risk for CD incidence, with an average ratio of women to men (2:1) (Kuja-Halkola et al., 2016; Ludvigsson et al., 2016; Al-Toma et al., 2019) and with Mohta’s study that found the woman is (1.3-2.1) more than a man to affliction with CD (Mohta et al., 2021) and this is in line with the published results that is corresponding with as study involved 1,682 patients diagnosed with CD divulge (68.00) % are found to be women and (32.00) % are man, results which are usually observed as there is a prevalent rate of autoimmune disease among women (Dixit et al., 2014).

Other studies have also reported similar predominance with CD, for example, more than fifty percent of women in 249 celiac patients (Rubio-Tapia et al., 2013), and as a consequence, the findings of this study are comparable to the conclusion of a study of (Green and Cellier, 2007; Singh et al., 2018) which enumerated CD was 2 to 3 times more frequent in woman than in men patients.

Reasons suggested for woman's predominance to affliction with CD have not been well defined, but it proposed that women were at greater risk to develop immune-mediated diseases maybe the man Y-chromosome has a protective role against autoimmune diseases (Quintero, 2012). However,

delay in presentation of clinical symptoms, short span of clinical manifestation as well as less frequency of diagnosis in men especially in early adulthood (Dixit et al., 2014), or associated with hormonal differences in women than men, or role of sex hormones as estrogen and androgens in immune response regulation which might explain sex differences or its complications as well as the nature of women's lifestyle, pregnancy, parturition, and menstruation (Quintero, 2012; Jansson-Knodell et al., 2019).

In many studies, a woman is more affected by CD than a man, but this disagrees with many studies that explained that CD seems to be more frequent in man than woman patients as a study was done in Iran (Mehrdad et al., 2012), and with a study conducted in the center for gastrointestinal diseases in Baghdad province that demonstrated the men were represented 51 of 93 patients whereas the woman was represented 42 of 91 patients because of this study didn't include patients in all age and conducted on patients under 18 years (Arif et al., 2009), and also with a study that shown (62.20) % were man compared to (37.80) % of woman patients because this study conducted on under 12 years old celiac patients (Alshebani and Abdalhamza, 2018).

The results of the current study demonstrate that two steps serology testing approach represents good diagnostic tools for screening and monitoring patients with CD as these CD tests are manifested by high sensitivity, specificity, accuracy, and positive predictive values which agree with similar Iraqi studies were obtained by (Shorouq, 2020; Alaa, 2021; Majeed, 2021). Thus, based on the specificity and sensitivity of the

study CD serology tests can be ranked in the order: Anti-tTG IgG > Anti-tTG IgA > Anti-GA IgG > Anti-GA IgA. The high frequency of patients with seropositivity to Anti-tTG IgG can be attributed to its high sensitivity and specificity in the existing study; thus, supporting its diagnostic potency. The autoantibodies belong IgG class having a significantly higher specificity and sensitivity to CD, whereas the IgA class is related to a low rate of false negative results, so it is recommended to be used in patients with IgA deficiencies (Werkstetter et al., 2017).

The Anti-tTG and Anti-GA are considered the most important double diagnostic tests and the most common initial screening for CD (Brusca, 2015). It has been shown that Anti-tTG together with Anti-GA tests sensitive markers for the diagnosis of CD-suspected persons (Al-Kazraji, 2009). The findings of this study and other studies indicate the diagnostic potential of double diagnostic serology tests when conducting screening surveys for celiac patients (Aldaghi, 2016).

The current study's results revealed significant differences between celiac and healthy women groups ($P < 0.05$). The two steps serology testing approach represents a good diagnostic tool for screening and monitoring celiac patients as these CD tests show high sensitivity, specificity, accuracy, and (Al-Assaf et al., 2021) obtain positive predictive values that are compatible with similar results. The high frequency of patients with seropositivity to Anti-tTG IgG may be attributed to its high sensitivity and specificity in the existing study, thus supporting its diagnostic potency.

Conclusions

The main conclusions of this study demonstrate that women are more susceptible to incidence with CD than men, and using the two steps testing approach for serologic diagnosis of CD is a quite precise strategy for the diagnosis of suspicious persons and can be potent marker for monitoring the activity of this disease.

List of abbreviations

Anti-GA, Anti-Gliadin; Anti-tTG, Anti-tissue Transglutaminase; CD, Celiac Disease.

Ethics approval and consent to participate

Due to the samples being collected from human candidates the committee of Ethical Standards of the University of Basrah and the Ministry of Health was dependent on all samples.

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Conflict of Interest

The author hereby declares no conflict of interest.

Consent for publication

The author declares that the work has consent for publication.

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References

- Alaa, J. K. (2021). Evaluation of HLA-DQ2 and DQ8 haplotypes in patients with Celiac Disease Correlation with Circulating Anti-Tissue Transglutaminase and Anti-Gliadin Antibodies. Master dissertation Submitted to the Council of the College of Medicine, University of Kerbala.
- Al-Assaf, A. I., Ali, H. M., and Ad'hiah, A. H. (2021). Gene Expression of NLRP3 Inflammasome in Celiac Disease of Iraqi Children. *Ibn AL-Haiitham Journal For Pure and Applied Sciences*, 15(22). <https://DOI.org/10.30526/2021.IHICPAS.2645>.
- Aldaghi, M. A., Dehghani, S. M., and Haghghat, M. (2016). Evaluation of the correlation between tTG-IgA titer and duodenal biopsy findings in children with suspected celiac disease. *Iranian journal of pediatrics*, 26(1). DOI: 10.5812/ijp.3615.
- Al-Kazraji, K. (2009). Celiac disease: presentation with clinical and serological response. *Med. J. Tikrit University*, 2, 145.
- Alshebani, A. M. and Abdalhamza, Z. S. (2018). The Role of celiac disease antibodies in the follow up of Patient on Gluten free diet. *Revista Latinoamericana de Hipertension*, 13(6), 561-566.
- Al-Toma, A., Volta, U., Auricchio, R., Castillejo, G., Sanders, D. S., Cellier, C. and Lundin, K. E. (2019). European Society for the study of Coeliac Disease (ESsCD) guideline for coeliac disease and other gluten-related disorders. *United European gastroenterology journal*, 7(5), 583-613. <https://DOI.org/10.1177/2050640619844125>.
- Arif, H. S., Al-Hadithi, R. and Elah, S. A. (2009). Some Diagnostic Aspects of Celiac Disease in Iraqi children. *Iraqi Journal of Medical Sciences*, 32.
- Brusca, I. (2015). Overview of biomarkers for diagnosis and monitoring of celiac disease. In *Advances in Clinical Chemistry* (1st ed., Vol. 68). Elsevier Inc. <https://DOI.org/10.1016/bs.acc.2014.12.006>.
- Caio, G., Volta, U., Sapone, A., Leffler, D. A., De Giorgio, R., Catassi, C., and Fasano, A. (2019). Celiac disease: A comprehensive current review. *BMC Medicine*, 17(1), 1 - 20. <https://DOI.org/10.1186/s12916-019-1380-z>.
- Dixit, R., Lebwohl, B., Ludvigsson, J. F., Lewis, S. K., Rizkalla-Reilly, N. and Green, P. H. (2014). Celiac disease is diagnosed less frequently in young adult men. *Digestive diseases and sciences*, 59(7), 1509-1512. <https://DOI.org/10.1007/s10620-014-3025-6>.
- Fasano, A., and Catassi, C. (2001). Current approaches to diagnosis and treatment of celiac disease: an evolving spectrum. *Gastroenterology*, 120(3), 636-651. <https://DOI.org/10.1053/gast.2001.22123>.
- Fasano, A. and Catassi, C. (2012). Celiac disease. *New England Journal of Medicine*, 367(25), 2419-2426. DOI: 10.1056/NEJMc1113994.
- Green, P. H., and Cellier, C. (2007). Celiac disease. *New England Journal of Medicine*, 357(17), 1731-1743. DOI: 10.1056/NEJMra071600.
- Husby, S., Koletzko, S., Korponay-Szabó, I., Kurppa, K., Mearin, M. L., Ribes-Koninckx, C. and Wessels, M. (2020). European Society Paediatric Gastroenterology, Hepatology and Nutrition guidelines for diagnosing coeliac disease 2020. *Journal of pediatric gastroenterology and nutrition*, 70(1), 141-156. DOI: 10.1097/MPG.0000000000002497.
- Ibrahim, M. M. (2020). Prevalence of Celiac Disease among Cases of Irritable Bowel Syndrome in Baghdad, Iraq. *Executive editor*, 11(01), 1943. DOI: 10.37506/v11/i1/2020/ijphrd/194139.
- Jansson-Knodell, C. L., Hujoel, I. A., West, C. P., Taneja, V., Prokop, L. J., Rubio-Tapia, A. and Murray, J. A. (2019). Sex difference in celiac disease in undiagnosed populations: a systematic review and meta-analysis.

- Clinical Gastroenterology and Hepatology*, 17(10), 1954-1968. DOI:10.1016/j.cgh.2018.11.013.
- Kuja-Halkola, R., Lebowitz, B., Halfvarson, J., Wijmenga, C., Magnusson, K., and Ludvigsson, J. (2016). Heritability of non-HLA genetics in coeliac disease: a population-based study in 107 000 twins. *Gut*, 65(11), 1793-1798. [http://dx.DOI.org/10.1136/gutjnl-2016-311713](http://dx.doi.org/10.1136/gutjnl-2016-311713).
- Ludvigsson, J. F., Agreus, L., Ciacci, C., Crowe, S. E., Geller, M. G., Green, P. H. and Husby, S. (2016). Transition from childhood to adulthood in coeliac disease: the Prague consensus report. *Gut*, 65(8), 1242-1251. DOI: 10.1136/gutjnl-2017-313882.
- Majeed, M. S. (2021). Correlation of Serum Soluble Interleukin-2 Receptor and Interleukin-18 with Auto-antibody Profile In Patients With Celiac Disease In Karbala Province (Doctoral thesis, University of Kerbala).
- Mansour, A. A. and Najeeb, A. A. (2011). Coeliac disease in Iraqi type 1 diabetic patients. *Arab Journal of Gastroenterology*, 12(2), 103 - 105. <https://DOI.org/10.1016/j.ajg.2011.04.007>.
- Mehrdad, M., Mansour-Ghanaei, F., Mohammadi, F., Joukar, F., Dodangeh, S. and Mansour-Ghanaei, R. (2012). Frequency of celiac disease in patients with hypothyroidism. *Journal of thyroid research*. <https://DOI.org/10.1155/2012/201538>.
- Mohta, S. S., Rajput, M. S., Ahuja, C. V. and Makharia, G. K. (2021). Emergence of Celiac disease and Gluten-related disorders in Asia. *Journal of Neurogastroenterology and Motility*, 27(3), 337. DOI: 10.5056/jnm20140.
- Quintero, O. L., Amador-Patarroyo, M. J., Montoya-Ortiz, G., Rojas-Villarraga, A., and Anaya, J. M. (2012). Autoimmune disease and gender: plausible mechanisms for the woman predominance of autoimmunity. *Journal of autoimmunity*, 38(2-3), J109-J119. <https://DOI.org/10.1016/j.jaut.2011.10.003>.
- Rubio-Tapia, A., Hill, I. D., Kelly, C. P., Calderwood, A. H., and Murray, J. A. (2013). ACG clinical guidelines: diagnosis and management of celiac disease. *Official journal of the American College of Gastroenterology/ACG*, 108(5), 656-676. DOI: 10.1038/ajg.2013.79.
- Shorouq, N. K. (2020). Association of HLA-DQ2, DQ8 and Immunological Markers with Especial Emphasis on IL-17A, with Celiac Disease. Southern Technical University. Master dissertation.
- Shreffler, J. (2022). Diagnostic Testing Accuracy: Sensitivity, Specificity, Predictive Values and Likelihood Ratios. <https://www.statpearls.com/ArticleLibrary/viewarticle/96435#>.
- Singh, P., Arora, A., Strand, T. A., Leffler, D. A., Catassi, C., Green, P. H. and Makharia, G. K. (2018). Global prevalence of celiac disease: systematic review and meta-analysis. *Clinical gastroenterology and hepatology*, 16(6), 823 - 836. <https://DOI.org/10.1016/j.cgh.2017.06.037>.
- Tye-Din, J. A., Galipeau, H. J., and Agardh, D. F. (2018). Celiac disease: a review of current concepts in pathogenesis, prevention, and novel therapies. *Frontiers in pediatrics*, 6, 350. DOI:10.3389/fped.2018.00350.
- Werkstetter, K. J., Korponay-Szabo, I. R., Popp, A., Villanacci, V., Salemme, M., Heilig, G. and Sadat, A. T. E. (2017). Accuracy in diagnosis of celiac disease without biopsies in clinical practice. *Gastroenterology*, 153(4), 924-935. <https://doi.org/10.1053/j.gastro.2017.06.002>.

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