

## Some Immunological Parameters in Women With Celiac Disease

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### Abstract

Celiac disease is one of an autoimmune disease in the world and genetically linked . This disease may be cause many problems for pregnant women and their children . There are many markers specific for celiac disease like anti-tissue transglutaminase and anti-gliadin antibodies which associated with development of celiac disease. In this study, we wished to determine whether there are relationship between celiac disease and fertility , effect on newborn and to identify the possible implications of these factors to disease course. Thirty female patients with a celiac disease with ages ranged between (15- 46) years were taken from (Al-Hussein Medical City/Kerbala). Control group consisted of 20 healthy people who were free from signs and symptoms of celiac disease who matched in age and gender with patients, and had no history for any celiac disease problem. TTG , IgA & IgG ,AGA (EASIA Kit, Generic assay ) and was studied using the enzyme-linked immunosorbent assay (ELISA) method. T-test and ANOVA and Pearson correlation used to analyze results by using SPSS version 24. P-value  $\leq 0.05$  was considered significant. TTG and AGA levels were increased significantly ( $p < 0.05$ ) in patients compared with the control group . TTG and AGA levels were increased significantly ( $p < 0.05$ ) in patients compared with the control group. Also, there were significant abnormality and complication when compared with control groups. So there was significant correlation between celiac disease and infertility and there is some effect on baby of women with celiac disease.

**Keyword :** Celiac disease ,fertility ,Anti -gliadin antibodies ,Anti -Tissue transglutaminase .

### الخلاصة

تعد حساسية الحنطة من أكثر أنواع أمراض المناعة الذاتية شيوعاً في العالم . والذي قد يتسبب في مشاكل كثيرة لدى النساء الحوامل وأطفالهن . هنالك بعض العلامات الخاصة بحساسية الحنطة مثل المستضد Anti- tissue transglutaminase ، ومستضد Anti- gliadin antibodies والتي تساهم في تطور حساسية الحنطة وانتشاره . نأمل في هذه الدراسة أن نحدد فيما إذا كان هنالك علاقة ارتباط بين حساسية الحنطة والقدرة على الإنجاب وتأثيرها على حديثي الولادة وكذلك التعرف على النتائج المحتملة لهذه العوامل. نفذت هذه الدراسة على 30 حالة مرضية ( جميع المرضى كانوا من النساء ) مع أعمار تتراوح بين 15- 46 سنة و جمعت العينة من مدينة الحسين الطبية في محافظة كربلاء ، كما و شملت الدراسة على مجموعة سيطرة بعدد 20 أنثى خالين تماماً من أعراض وعلامات الإصابة بحساسية الحنطة وقد تطابقوا من حيث العمر مع المرضى، كذلك اخذ بنظر الاعتبار خلوهم تماماً من تاريخ الإصابة بالمرض . استخدمت طريقة الامتزاز المناعي المرتبط بالأنزيم لفحص المستضد Tissue transglutaminase ، ومستضد anti- gliadin والتي تساهم في تطور حاله المرضى ،حللت البيانات إحصائياً "الرمزة الإحصائية (SPSS version 24 – ANOVA – person correlation) وكذلك تم مقارنة القيم بواسطة العينة المستقلة ( T – test ) ، إذا كان مستوى المعنوية اصغر أو يساوي 0,05 مع المقارنة بمجموعة السيطرة فتعتبر عالية المعنوية. أظهرت النتائج ارتفاع مضاد الكليادين ومضاد الاندوميزيم بشكل معنوي عند المقارنة مع مجموعة السيطرة . وأظهرت النتائج إن هنالك علاقة معنوية بين حساسية الحنطة والخصوبة . وكذلك هنالك تأثير لحساسية الحنطة على حديثي الولادة .

**الكلمات المفتاحية:-** حساسية الحنطة ، الخصوبة ، مضاد الكليادين ، مضاد الاندوميزيم .

### Introduction

Celiac disease consider one of the most common autoimmune disease associated with small intestine trigger by ingestion of food containing gluten . ( Elli *et.al.*, 2014) That lead to malabsorption syndrome and different types of extra-

intestinal manifestation .these atypical symptoms shown more than classical presentation .( Foroutan , 2013) Until in the past decade ,celiac disease was considered to be a rare disease ,but known consider highly distributed in world and involved all races with mean prevalence about 2% in general population .T there are many association between coeliac and reproductive abnormalities ( Morris ,1970 ) . There are high majority of patients who have recurrent or new symptoms when the gluten-free diet are in fact ingesting gluten, either intentionally or unintentionally, that lead to serious complication of celiac disease: intestinal adenocarcinoma, enteropathyassociated T-cell lymphoma, or refractory ( sprue *et al.*, 2000 ; Rampertab *et al.*, 2014) However, since this study , the literature addressing complications of CD in women, specially rates of infertility, fertile life span, perinatal complications and adverse pregnancy outcomes, has been included (Machado *et al.*, 2013; Di Simone *et al.*, 2010; Ludvigsson *et.al.*, 2005).

## Patients and Methods

### Selection of patients

During the period 1/ November /2016 to 1/March /2017, thirty patients with celiac disease (All Patients are female ) with ages ranged between (24-46) years were taken from (Al-Hussain Medical City/Karbala. The control group consisted of 20 healthy people who were free from signs and symptoms of celiac disease who matched in age and gender with patients, and had no history of any celiac disease problem.

### Sample collection and assay procedure

Blood sample (4ml) was collected from patients and left at room temperature and then centrifuge for 10 min. at (3500 rpm). Serum was then separated and preserved at -70c until time of analysis. Estimation of TTG anti-tissue transglutaminase ( IgA & IgG ) , AGA - anti-glidian (Generic \ Germany), in serum of patients using commercially available and performed as recommended in the leaflet of the kits.

## Statistical Analysis

Results are expressed as mean  $\pm$  standard error mean (SEM), student t-test and ANOVA and Pearson correlation used to analyze results by using SPSS version 24. P-value  $\leq 0.05$  was considered significant .

## Results

A total of 30 patients with celiac disease divided into three groups according to the age (15-25) yrs 13 (43.3%) ,and age (25-35)yrs 15(50%)and (> 35)yrs 2(6.7%) .The distribution of patients according to disease duration was as followings : • 10 yrs 11 (36%) and • 10 yrs 19(63.3%) Respectively table 1.

**Table1: Information of patients with celiac disease.**

| Variable                 |       | No. | Percentage(%) |
|--------------------------|-------|-----|---------------|
| Total number of patients |       | 30  | 100 %         |
| Age groups (years )      | 15-25 | 13  | 43.3 %        |
|                          | 25-35 | 15  | 50 %          |
|                          | >35   | 2   | 6.7 %         |
| Disease duration(years)  | <10   | 11  | 36.7 %        |
|                          | >10   | 19  | 63.3 %        |

The distribution of cases and controls according to the presence of risk factors is depicted in ( Table 2 ). The cases show a higher age at marriage as compared to the controls; however, the difference was statistically significant. The mean duration of breastfeeding in cases and controls was  $9\pm5.78$  and  $15\pm3.56$  months, respectively ( $P<0.023$ ). However, the cases had a significantly higher number of abortions ( $1.3\pm1.0$ ) as compared to the controls ( $0.6\pm1.0$ ). There was a statistically significant difference in the mean mode of delivery in cases and controls, the infants weights also show highly significant between study groups.

There are many risk factors effects on patients with celiac disease, according to table 2 results the highly significant result showed on the mode of delivery specially in comparing between the vaginal delivery and lower segment caesarean section (LSCS) and the infants weights also show highly significant in compare between patients and healthy women.

**Table 2: Distribution of Risk factors for pregnant and baby in control and Patients with celiac disease .**

| Risk Factors                          | Mean $\pm$ SD (n=50) |                   | Sig   |
|---------------------------------------|----------------------|-------------------|-------|
|                                       | Celiac cases (n =30) | Controls (n =20)  |       |
| Age                                   | 27 $\pm$ 10.31       | 27 $\pm$ 10.7     | 0.67  |
| age at a marriage (per year )         | 21.48 $\pm$ 4.84     | 16.95 $\pm$ 3.18  | 0.04  |
| Mode of delivery                      |                      |                   |       |
| Vaginal                               | 9(30%)               | 16(80%)           | 0.001 |
| LSCS                                  | 21(70%)              | 4(20%)            |       |
| Breast feeding duration ( per months) | 9 $\pm$ 5.78         | 15 $\pm$ 3.56     | 0.023 |
| Number of abortion                    | 1.38 $\pm$ 1.0       | 0.6 $\pm$ 1.0     | 0.033 |
| Infants weights (g)                   | 1.93 $\pm$ 250.3     | 2.850 $\pm$ 160.7 | 0.003 |

**Table (3) :The levels of parameters under study in patients with celiac disease**

|                             | Control<br>n=20       | Patients<br>n=30       |             |
|-----------------------------|-----------------------|------------------------|-------------|
| Parameters                  | Mean $\pm$ SD         | Mean $\pm$ SD          | p-Value     |
| Anti-gliadin antibodies IgA | 14.9810 $\pm$ 5.04912 | 81.4138 $\pm$ 61.78167 | $\leq 0.05$ |
| Anti-gliadin antibodies IgG | 13.1429 $\pm$ 5.32753 | 87.9828 $\pm$ 49.06121 | $\leq 0.05$ |
| Anti-tissue TG IgA          | 12.1429 $\pm$ 4.64603 | 36.5276 $\pm$ 16.93576 | $\leq 0.05$ |
| Anti-tissue IgG             | 13.2048 $\pm$ 4.95262 | 92.7931 $\pm$ 80.26826 | $\leq 0.05$ |

**Table (4) :Correlation between age and the parameters under study in patients with celiac disease.**

| Parameters                  | Age of patients with celiac disease |         |
|-----------------------------|-------------------------------------|---------|
|                             | r                                   | p-value |
| Anti-gliadin antibodies IgA | 0.431                               | 0.019** |
| Anti-gliadin antibodies IgG | 0.632                               | 0.01*   |
| Anti-tissue TG IgA          | 0.350                               | 0.06    |
| Anti-tissue IgG             | 0.469                               | 0.01*   |

**Table (5) :Correlation between disease duration and the parameters under study in patients with celiac disease.**

|                             | Disease duration of patients with celiac disease |         |
|-----------------------------|--|---------|
| Parameters                  | r  | p-value |
| Anti-gliadin antibodies IgA | 0.535  | 0.003*  |
| Anti-gliadin antibodies IgG | 0.677  | 0.001*  |
| Anti-tissue TG IgA          | 0.403  | 0.03**  |
| Anti-tissue IgG             | 0.454  | 0.013** |

**Table (6): Correlation between No. of pregnancy and the parameters under study in patients with celiac disease.**

|                             | No. of pregnancy of patients with celiac disease |         |
|-----------------------------|--|---------|
| Parameters                  | r  | p-value |
| Anti-gliadin antibodies IgA | 0.262  | 0.171   |
| Anti-gliadin antibodies IgG | 0.491  | 0.007*  |
| Anti-tissue TG IgA          | 0.284  | 0.136   |
| Anti-tissue IgG             | 0.509  | 0.005*  |

## Discussion

The present study conducted at Al- Hussein Medical City / Kerbala, included 30 celiac disease cases and 20 control subjects. Celiac disease showed many of reproductive complications . It has been suggested maternal infertility and perinatal morbidity in untreated celiac disease may be associated with malabsorption of iron and folate , that lead to vitamin deficiency in mother ( Ferguancy *et.al.*, 1982 ) celiac disease may be associated with adverse events related to pregnancy, ( Sher *et.al.*, 1996 ) there for it important to diagnose celiac disease in a population having a poor reproductive outcome that lead to simple therapeutic invention and favorable outcome of pregnancy .

In the present study for the first time shows that the celiac disease associated with many complication of infertility.

There are many studies on celiac disease showed there was a relationship between celiac disease and female infertility such as Jackson et al described in his cohort study on females suffering from celiac disease and tested them by serology(Jackson *et.al.*, 2008 ). This researcher described a comparison between the prevalence of celiac disease in his study and in US, ,and he found their cohort study is lower than in US .

In another and resent study, which done on Swedish – population by zugna et al showed the fertility of females with celiac disease had low fertility in compare with control groups ( Zugna *et.al.*, 2012) .

The Sher et al described there was decrease in the number of children in comparison to health group . ( Sher *et.al.* , 1994)

In our study there results show there were many effect of celiac disease in females and her baby and that agreed with many studie,and these data showed there is impaired infirmity in cases of active celiac disease .

## Conclusion

Significantly correlation between celiac disease and infertility. So there was some effect on newborn of women with celiac disease.

## Reference

- Cellier C. Delabesse E. Helmer C. *et.al.*, 2000 Refractory sprue, coeliac disease, and enteropathy-associated T-cell lymphoma. *Lancet*;356:203-8.
- Di Simone N. Silano M. Castellani R. *et.al.*, 2010, Anti-tissue transglutaminase antibodies from celiac patients are responsible for trophoblast damage via apoptosis in vitro. *Am J Gastroenterol.*;105:2254–2261.[PubMed]
- Elli L, Discepolo V, Bardella MT, Guandalini S. ,2014 ,Does gluten intake influence the development of celiac disease –associated complications ? *J Clin Gastroenterol .* ; 48 :13-20.
- Fergusson R. ,Holmes K., Cooke WT , 1982 . Coeliac disease ,fertility ,and pregnancy .*Scand J Gastroenterol*; 17 :65-68 .
- Foroutan M. Nejad MR. Molanaee S. Hogg-Kollars S. Rostami K. , 2013 , Celiac disease hidden by cryptogenic hypertransaminasemia mistaken for fatty liver .*Bratislav Lek Listy*;114:547-548.
- Jackson JE ,Rosen M, MC Lean T, Moro J , Croughan M, Cedars MI . , 2008 , prevalence of celiac disease in a cohort of women with unexplained infertility .*Fertil Steril* ;89(4):1002-1004.
- Ludvigsson JF. Montgomery SM. Ekbom A. Celiac , 2005, disease and risk of adverse fetal outcome: a population-based cohort study. *Gastroenterol.*;129:454–463. [PubMed]
- Machado AP, Silva LR, Zausner B. *et.al.*, 2013, Undiagnosed celiac disease in women with infertility. *J Reprod Med.* ;58:61–66. [PubMed]
- Morris JS, Adjuikiewicz AB, Read AE. ,1970 ,Coeliac infertility :an indication of dietary gluten restriction .*Lancet*;1:213 .
- Rampertab SD, Forde KA, Green PH. , 2003 , Small bowel neoplasia in coeliac disease. *Gut*;52:1211-4.
- Sher KS ,Mayberry JF. , 1994 , Female fertility ,obstetric and gynaecological history in coeliac disease .A case control study .*Digestion* ;55 (4):243-246.
- Sher KS, Mayberry JF . , 1996 , Female fertility ,obstetric and gynecological history in celiac disease : a case control study . *Acta Paediatr Suppl*; 412 :76-7.
- Zugna D, Richiardi L. , Akre O. Sjöström O. Ludvigsson JF >A nationwide population , 2010 ,–based study to determine whether coeliac disease is associated with infertility .*Gut* ;59 (11):1471-1475.