



An Association Between Celiac Disease Specific Autoantibody and Infertility in Male :Across Sectional Study

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ABSTRACT:

Background:The male infertility is considered a health problem ,which attributed to many factors such as genetic ,environmental , previous infections, bad lifestyle and others.these factors have been reported in previous studies.However, this study aimed to determine the effect of anti-tissue transglutaminase antibodies (IgA-tTG)as celiac disease product on the male infertility

Objective: This study was aimed to find out the incidence of celiac disease-specific antibodies, which is known as IgAanti-tissue transglutaminase antibodies (IgA-tTG) in the group of infertile male in Al-Najaf city by across sectional study.

Methodology: Seventy six infertile men have been enrolled in this study,which was extended from Jun - August 2014At Fertility Center -AlSader Medical City in Al-Najaf governorate. Ages of patients ranged between (52 – 20) (Mean \pm SD) = 31.1 \pm 7.18). IgA-tTG studied by using ELIS kit (IBL international company, Germany).

The results:Although, the findings of present study showed that there is a high significant difference in sperm concentration between IgA-tTG antibodies positive and negative male infertility patients, but this outcome not means that, these autoantibodies have critical role in the spermatogenesis, thus this results may be due to other factors such as ,growth hormone ,obesity or bad lifestyle ,thus we can see that the correlation between the sperm concentration and the incidence of autoantibodies type IgA against tissue transglutaminase was non-significant with a p value > 0.31 , either in patients with normozoospermia or in patients with oligozoospermia. In addition to that the percentage of incidence of IgA- tTGA in the infertile men was 4%.These results have obtained by using statistical mean , standard deviation and chi-square.

Conclusion: we revealed that IgA-tTGhas no implicated with factors that responsible for infertility in males , thus celiac disease as autoimmune disease may not produce any effectiveness of male reproductive system activity.

Recommendations:Investigate other autoimmune disease products that may be contributing to thisdisease.

Key words : infertility ,celiac disease , IgA-tTG,oligozoospermia

INTRODUCTION

Infertility is unfitness of a sexually active,non contracepting couple to achieve pregnancy during the first year of marriage⁽¹⁾,thus the couple need to medical advice. Both male and female are implicated in this trouble effects and there are different factors that are responsible for infertility of each one of them such as a genetic heterogeneous disorder which affects nearly 22% of thetwosome in reproductive age group⁽²⁾Infertility also can be affected by the level of hormones, age factor,exercise, obesity , infectiousdisease; autoimmune diseases , psychological state, resultfrom surgery or obstruction, or be associated with definedabnormalities in the gametes (for example aberrantsemen parameters).



Perhaps the most common cause of infertility is simply 'unexplained' and this accounts for about 20% of couples⁽³⁾. In about 50% of these cases the underlying trouble lies in the male either merely or in combination with female factor. In males, the main reasons of infertility, including anatomical defects, gametogenesis dysfunction, endocrinopathies, ejaculatory failure and environmental toxicity, congenital or acquired urogenital abnormalities, the immunological factors are also being considered⁽⁴⁾⁽⁵⁾. About 60%–75% of male sterility cases are idiopathic⁽⁶⁾, these males present with no obvious former history of fertility problems, neither have any abnormal findings on physical examination or endocrine laboratory or any other laboratory results. The unexplained male infertility was investigated to detect the causes and conditions responsible for this obstacle. Some researchers focused on studies the abnormal germline DNA methylation in males⁽⁷⁾, while others focused on the relationship between the sterility and immune response products such as autoantibodies and cytokines. Under normal circumstances the cytokines are considered one of the diversified factors that are concur to accomplish spermatogenesis, they are including Tumor necrosis factor- alpha (TNF- α); Interleukin -1 alpha (IL-1 α) and Interleukin -1 beta (IL-1 β) which have certain physiological functions in this vital process. However, when the level of expression and secretion of these cytokines are diminished or increased more or less than normal range, they are leading to some pathological conditions such as inflammation which effects on sperm production process^{(8),(9)}. Also the pathological conditions may be produced by other immune response products for instance autoantibodies. Where, Soares *et al.*,⁽¹⁰⁾ was observed on their consequences that the gonad function is severely affected in male systemic lupus erythematosus (SLE) patients due to testicular damage and consequent hormone disturbances. Furthermore some autoimmune disease can impact the reproductive organs directly, by specific antibodies that are directed against the tests, or ovaries. Another group of autoimmune disease can cause infertility through causing blood clotting disturbances, as in case anti-phospholipid syndrome in systemic lupus erythematosus SLE. Therefore, autoimmunity as a possible cause for infertility needs to be revised and considered hardly when we look for infertility both in females and males. Thus, this study was focused on celiac disease-specific antibodies, which is known as IgA anti-tissue transglutaminase antibodies (IgA-tTG) in the group of infertile male. These autoantibodies are manufactured exclusively in the mucosa of the small intestine against tissue transglutaminase (tTG)⁽¹¹⁾, in response to the intake of food containing gluten and related proteins⁽¹²⁾. Tissue transglutaminase (tTG) belong to Transglutaminases (TGases), a family of enzymes which, have an important function in hemostasis, wound healing, assembly and remodeling of the extracellular matrix, cell signaling and apoptosis. as well as in inflammatory and autoimmune diseases in spite of many members of this class of enzymes have been discovered for long ago, their role in various physiological and pathological processes is still a subject of substantial research and argue⁽¹³⁾. However the tTG is considered as an important factor in pathomechanism of celiac disease which is deemed as one of inflammatory autoimmune disease⁽¹⁴⁾. The diagnosis of this disease is depending on the presence of (IgA-tTG) which represent highly sensitive and specific serological marker.⁽¹⁵⁾

OBJECTIVE: This study was aimed to find out the incidence of celiac disease-specific antibodies, which is known as IgA anti-tissue transglutaminase antibodies (IgA-tTG) in the group of infertile male in Al-Najaf city by a cross sectional study

METHODOLOGY:

During the period from Jun - August 2014 a total of (78) patients suffering from primary or secondary infertility attending the Fertility Center - Al-Sader Medical City in Al-Najaf, were taken. Their ages ranged between (52 – 20) (Mean \pm SD) = 31.1 \pm 7.18). After assembling the data regrade age, address, occupation drug and smoking and body mass index (BMI), five ml of blood were drawn from the antecubital vein of each patient and subsequently the



serum was separated by leaving the blood at room temperature (20-25°C) for 15-30 minutes, centrifuged at 3,000 RPM for 10 minutes to separate the serum. After that, the serum samples, then were stored at -20° C for the future studying by ELISA to detect IgA anti-tissue transglutaminase (IgA-tTG). After there, all serum samples werethawed and studied by using ELIS kit (IBL international company, Germany). This kit is new generation and it is a solid phase enzyme immunoassay for thequantitative and qualitative detection of antibodies against neo-epitopes of tissue transglutaminase (tTG) inhuman serum. The assay employing human recombinant transglutaminase crosslinked with gliadin-specific peptides displays neo-epitopes of tTg which ensures a significantly increased sensitivity andspecificity of the test.

Statistical Analysis

The following statistical approaches are used in order to analyze the data of the study under application of the statistical package Mega stat (2005): tables (Frequencies, Percentages) ; statistical figures (pie plot) ; statistical mean and standard deviation and chi-square.

RESULTS:

Table (1) : The General Characteristics of Infertile Couple

Character	Mean ± SD	Range
Age of the male (year)	31.1 ± 7.18	52 - 20
Age of the female (year)	27.4 ± 6.46	42 - 18
Duration of Infertility (year)	5.24 ± 3.03	15 - 1
BMI (for males)	28.11 ± 6.26	53.05 – 16.8

Table (1) shows the general characteristics of infertile couples which were recorded in the current study .

The mean age of the male patients who attended the fertility center was 31.1 years, the females were 27.4 years, while the mean of duration of infertility was 5.24 years , and the BMI mean was 28.11.

Table (2) : Subgroups of patients, according to sperm count, infertility type , smoking and BMI

Character		Frequency	Percentage %
Sperm count	Normozoospermia	19	24.36
	Oligozoospermia	59	75.64
Type of infertility	primary	66	84.62
	Secondary	12	15.38
smoking	Smokers	43	55.13
	Non-smokers	37	47.44
BMI	Underweight	2	2.56
	Normal	23	29.49
	Overweight	28	35.90
	Obese	24	30.77

The Infertile male group was distributed on three subgroups according to classes of sperm count, infertility type , smoking and BMI as shown in table (2) . It reveals the two subgroups of infertile patients classified according to the types of infertility , The majority of the patients have primary infertility 84.62 % while the secondary infertility represents 15.38% of the total patients . The same table also shows the percent of the smoker patients are about 55.13 % and the non-smokers are 47.44 % .Subgroups of infertile males classified according to the



BMI were constituted into: underweight (2.56%). Normal (29.49%), overweight (35.9) and obese (30.77%)

Table (3) : Relationship between sperm count and incidence of IgA-tTG

Patients subgroups	Positive IgA-tTG	Negative IgA-tTG	Total	Chi square	P value
Normozoospermia	0	19	19	1	0.31
Oligozoospermia	3	56	59		

The correlation between the sperm concentration and the incidence of autoantibodies type IgA against tissue transglutaminase was non-significant with a p value > 0.31, either in patients with normozoospermia or in patients with oligozoospermia. This was indicated in the table (3)

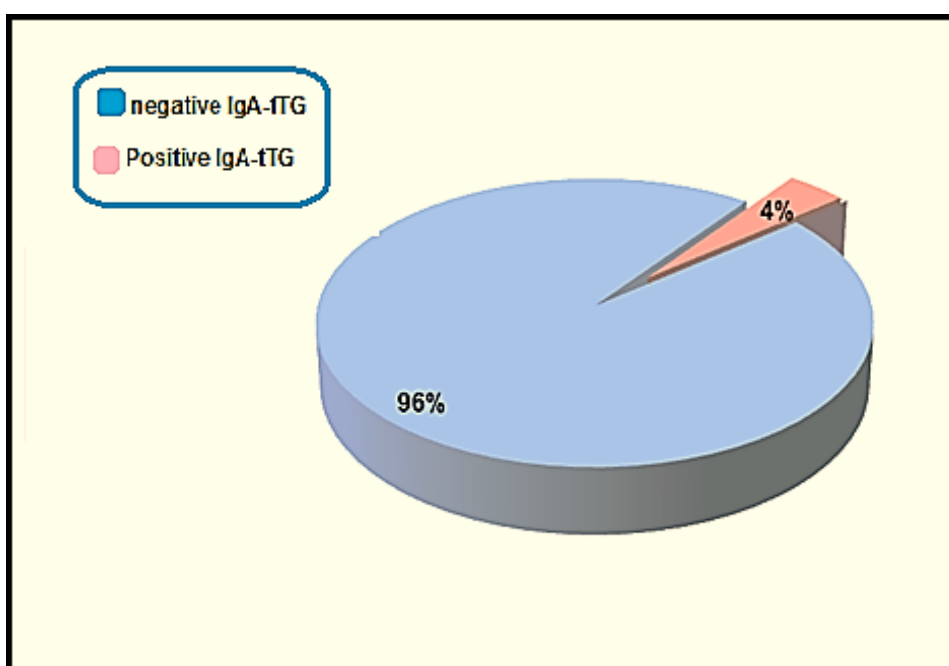


Figure (1) : Percentage of incidence of IgA- tTGA in the infertile men

Figure (1) displays that about (4%) of the patients having positive IgA- tTGA and (96%) were negative.

Table (4) : Sperm concentration between IgA- tTGA positive and negative males

Patients subgroups	Sperm concentration	P value
Positive IgA- tTGA	7 ± 3.61	0.003*
Negative IgA- tTGA	14.7 ± 14	

* highly significant at p < 0.01

Table (4) shows that there is a high significant difference in sperm concentration between tTGA positive and negative male infertility patients.

Discussion:

The infertility in male and its relation with celiac disease products still controversial point thence, the present research have been focused on the investigation of the IgA anti tTG effect on sterility in male in the other words, the impacts of this autoantibody on the certain



reproductive parameters in male with infertility, because this autoantibody considered highly sensitive and specific serologic marker (95%-99%) of celiac disease⁽¹⁵⁾. The consequence of the current study revealed that, this autoantibody have no effects on normozoospermia and oligozoospermia, although the previous study mentioned that 90% of deficiency of spermatozoa in the semen is idiopathic, but our finding not confirm any respect between IgA anti tTG and this parameter, so that oligozoospermia may be belong to other reasons such as environmental, genetic or certain medications⁽¹⁶⁾. Our results also detected that the percentage of incidence of Ig A -tTGA in the infertile men was equal to 4% that is meant the celiac disease was not implicated in the pathomechanism of infertility in the men. Furthermore this outcome was in accord with previous research which mentioned that, a two male out of 223 (or about 0.9%) tested positive for these autoantibodies⁽¹⁷⁾ (Kovács et al., 2014). As well as this finding is agreement with previous which denoted that does not find any effect for celiac disease prevalence in infertile male⁽¹⁸⁾. In addition to that, although, the findings of present study showed that there is a high significant difference in sperm concentration between IgA-tTG antibodies positive and negative male infertility patients, but this outcome not means that, these autoantibodies have critical role in the spermatogenesis, thus this results may be due to other factors such as, growth hormone which possess role in process of the production or development of mature spermatozoa, as mentioned to that Magon *et al.*,⁽¹⁹⁾ Or this result may be attributed to overweight or obesity, where 35.9% of patient were overweight, while 30.77% were obese, thereby this factor influences on the spermatogenesis as denoted to that Palmer *et al.*,⁽²⁰⁾ in their study.

Conclusion: In this study we revealed that the celiac disease product which is known as (IgA-tTG) has no implicated with factors that responsible for infertility in male thus, celiac disease as autoimmune disease may not produce any effectiveness on male reproductive system activity.

Recommendations:

1. Investigate other autoimmune disease products that may be contributing to this disease.

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