



RESEARCH ARTICLE

THE ASSOCIATION OF ADULT MALE AND FEMALE INFERTILITY WITH CELIAC DISEASE PATIENTS IN YEMEN

Al-Anesi Mohsen¹, Qiping Hu¹, Ekram Al-Eryani², Mansour Al-Amrani², Hassan Al-Shamahy³

¹Department of biochemistry and molecular biology, Guangxi Medical University, China.

²Department of biochemistry, Faculty of Medicine and Health Sciences, Sana'a University, Yemen.

³Faculty of Medicine and Health Sciences, Sana'a University, Yemen.

Article Info:



Article History:

Received: 3 October 2017

Reviewed: 12 November 2017

Accepted: 25 December 2017

Published: 15 January 2018

Cite this article:

Al-Anesi M, Hu Q, Al-Eryani E, Al-Amrani M, Al-Shamahy H. The association of adult male and female infertility with celiac disease patients in Yemen. *Universal Journal of Pharmaceutical Research* 2017; 2(6): 21-23.

<http://doi.org/10.22270/ujpr.v2i6.R5>

*Address for Correspondence:

Dr. Hu Qiping, Guangxi Medical University, China. E-mail: huqiping@gxmu.edu.cn

Abstract

Objectives: Celiac disease's potentially destructive effect on reproductive health is among the most vital matters associated with progress awareness. Men and women with unexplained infertility, women with recurrent abortions, intrauterine growth retardation, low birth weight babies and menstrual disorders are not often screened for celiac disease (CD) despite scientific studies that point to a correlation. The aims of the present study were to examine the evidence of the correlation between CD and infertility by measuring sex hormones in CD comparing healthy controls (HC).

Methods: The study was carried out in Autoimmune Unit, AL-Thowra Hospital Sana'a city, Yemen. The study included 32 CD patients, and 32 HC. Blood samples were collected then examined for sex hormones in both.

Results: There was highly significant low down level of the mean±SD of sex hormones among male and female CD than HC: for male CD FSH=1.96±1.4 IU/ml vs 3.3±1.27 IU/ml of HC, LH=3.9±3.3 IU/ml vs 6.5±2.03 IU/ml of HC; and the testosterone=1.03±0.76 IU/ml, vs 3.8±1.4 IU/ml of HC. For CD females the mean ± SD of FSH, for CD females was 4.37±2.46 IU/ml vs 4.92±2.35 IU/ml of HC, Estradiol (40.7±30.8 IU/ml vs 7.1±76.66 IU/ml of HC), and Progesterone (1.2±1.15 IU/ml, vs 6.4±4.38 IU/ml of HC).

Conclusion: In conclusion, there was significant association between CD and infertility among Yemeni CD patients in which it indicated by low sex hormones in CD patients.

Keywords: Celiac disease, infertility, sex hormones, Sana'a, Yemen.

INTRODUCTION

Celiac Disease (CD) is an autoimmune condition activated by the ingestion of gluten, the protein fraction of wheat, barley and rye. As in other autoimmune diseases, celiac disease is the result of an immune response to self-antigens leading to tissue destruction and the auto antibodies production¹. It is important to consider that not all gluten T-cell epitopes are equally immunogenic and that many parts of gluten do not stimulate CD⁴⁺ T cells. In HLA-DQ 2.5-positive individuals, T-cells response directed against α - and ω -gliadins are clearly immune-dominant². Some gluten peptides efficiently elicit inflammatory T-cell responses whereas others do not. It is inclined by at least three factors knowing: (a) resistance to proteolytic degradation, (b) substrate affinity to TG2 and (c) specificity to bind HLA molecules³. Celiac disease's potentially destructive result on reproductive health is among the most urgent matters

associated with progress awareness. Men and women with unexplained infertility, women with recurrent abortions, intrauterine growth retardation, low birth weight babies and menstrual disorders are rarely screened for celiac disease despite scientific studies that specify a correlation⁴. Not less than ten percent of the reproductive age population in the developed and developing countries suffers from infertility^{5,6}. Infertility is normally diagnosed when people are incapable to regard after 6-12 months without using birth control, depending on several factors, such as age. Women with recurrent spontaneous abortions are also considered infertile⁷. In an attempt to have children, couples seek various treatments, such as surgery or artificial insemination. The average couple spends about \$10,000 per attempt on Assisted Reproductive Technology (ART). On the other hand, nearly one third of all pregnancy losses are the result of undiagnosed, and/or treatable diseases⁸. The aims of this study were to determine the relationship between infertility among

Yemeni CD, by estimating the level of female/male sex hormones in CD comparing with their level in HC.

source for sex hormones was Roche diagnostics, Germany.

SUBJECTS AND METHODS

Study area and Study population

This cross-sectional study was conducted among 32 CD patients whom diagnosed from patients attending Autoimmune Unit, AL-Thowra Hospital Sana'a city, Yemen, starting in June and ending in August 2017. All CD and HC were older than 14 years. Also the study included 32 HC selected from community resembling cases in sex, age group and socioeconomic status. Blood samples were collected from both groups then investigated for sex hormones.

Sample size

The sample size of our study was determined by Epi-Info version 7. For the population of Sana'a city (2,000,000) and expected frequency of 2% of CD in Yemen (CD in Middle East 2% according to Rostam *et al.*,⁹ with acceptable margin of error equal to 3.5%, at least 32 CD patients and 32 healthy controls in confidence level equal to 95% for 2 clusters were needed.

Data collection

All participants gave oral consent, completed a questionnaire, and had blood drawn for sex hormones.

Laboratory methods

Ten ml whole blood was collected by vein puncture; then sera were separated and tested for male hormones and female hormones. The testes reagents porches from well known sources and procedures for every test were done according to the manufacturer's direction. The

RESULTS

There was significant different between the mean \pm SD of male sex hormones of celiac patients group comparing with healthy controls in which very low values recorded in CD patients. The mean \pm SD of FSH for CD patients was 1.96 ± 1.4 IU/ml, lower than 3.3 ± 1.27 IU/ml of healthy controls, and LH for CD patients was 3.9 ± 3.3 IU/ml, lower than 6.5 ± 2.03 of healthy controls. The mean \pm SD of testosterone for CD patients was 1.03 ± 0.76 IU/ml, lower than 3.8 ± 1.41 U/ml of healthy controls. The variations were highly significant in which *p* values were less than 0.05 for all results (Table 1).

There was significant different between the mean \pm SD of Estradiol and progesterone hormones of celiac patients group comparing with healthy controls in which very low values recorded in CD patients, while no difference occurred for FSH.

The mean \pm SD of FSH for female CD patients was 4.37 ± 2.46 IU/ml, roughly similar to 4.92 ± 2.35 IU/ml of healthy controls, while Estradiol for female CD patients was 40.7 ± 30.8 IU/ml, lower than 137.1 ± 76.66 IU/ml of female healthy controls (3.4-folds). The mean \pm SD of progesterone for female CD patients was 1.2 ± 1.15 IU/ml, lower than 6.4 ± 4.38 IU/ml of female healthy controls (4-folds). The variations were highly significant in which *p* values were less than 0.05 for all results (Table 2).

Table 1: The FSH, LH and TO of CD group comparison with control group.

Hormones	Celiac disease Group (n=10)	Control Group (n=10)	<i>p</i> -value
FSH (IU/ml)	$1.96 \pm 1.4^*$	3.30 ± 1.27	0.001
LH (IU/ml)	$3.90 \pm 3.30^*$	6.50 ± 2.03	0.0001
Testosterone (IU/ml)	$1.03 \pm 0.76^*$	3.80 ± 1.41	0.0001

Data are expressed as means \pm SD, vs. control (**p* < 0.001)

Table 2: The FSH, Estradiol and progesterone of CD group comparison with control group

Hormones	Celiac disease Group (n=22)	Control Group (n=22)	<i>p</i> -value
FSH (IU/ml)	4.37 ± 2.46	4.92 ± 2.35	0.1
Estradiol (IU/ml)	$40.70 \pm 30.8^*$	137.10 ± 76.66	0.0001
Progesterone (IU/ml)	$1.20 \pm 1.15^*$	6.40 ± 4.38	0.0001

Data are expressed as means \pm SD, vs. control (**p* < 0.0001)

DISCUSSION

When we compared between the serum level of sex hormones among our CD females as shown in Table 2, there was no difference in the mean \pm SD of FSH for CD females (4.37 ± 2.46 IU/ml) comparing with (4.92 ± 2.35 IU/ml) of the healthy control females. However, there was highly significant low level of estradiol in CD patient group in which the mean \pm SD Was 40.7 ± 30.8 IU/ml while for healthy controls estradiol was 137.1 ± 76.66 IU/ml. Furthermore, there was highly significant low level of progesterone in CD

patient group in which the mean \pm SD Was 1.2 ± 1.15 IU/ml while for healthy controls it was 6.4 ± 4.38 IU/ml. Our previous results confirmed the negative effect in fertility of CD in female CD patients. It is recognized that while infertility in 27 % of infertile couples is the result of ovulation disorders and 25% the result of identified male disorders¹⁰. Pellicano *et al.*, have found the rate of celiac disease to be 2.5 to 3.5 times greater in women with unexplained infertility than in women with normal fertility¹¹. The possible relationship between proper nutrition in females and the capacity to regard is an additional worthy note. It has been

recommended that positive energy balance, as well as increased fat storage in females as a result of proper nutrition, produces an environment within the reproductive system that enhances a female's potential to consider. A range of ovarian function has been proposed; signifying that ovarian function and associated fruitfulness may be subject to minor alters in energetic environment, creating changes below the "clinical horizon" of menstruation. The rates of ovarian steroid genesis in women with positive energy stabilities are significantly higher than in those in negative energy stabilities who are subject to follicular suppression^{10,12}. Those females with undiagnosed celiac disease and who do not follow a gluten-free diet may intensify unfavourable conditions for conception within the body and, more specifically, within the reproductive system¹³. Once we compared between the serum level of sex hormones among males as shown in Table 1, there is highly significant low down level of sex hormones among male CD patient group in which the mean±SD of FSH was 1.96±1.4 IU/ml while for healthy controls FSH was 3.3±1.27 IU/ml. As well, there is highly significant low down level of LH in CD patient group in which the mean±SD of LH was 3.9±3.3 IU/ml whereas for healthy controls LH was 6.5±2.03 IU/ml. What's more there is highly significant low down level of testosterone in CD patient group in which the mean±SD of the testosterone hormone was 1.03±0.76 IU/ml, at the same time as for healthy controls testosterone was 3.8±1.4 IU/ml higher than that of CD group. Obtained results of current study confirmed the destructive effect in fertility of CD in male patients. It is recognized that men also suffer from infertility stemming from undiagnosed celiac disease^{13,10}. The increases of follicle-stimulating hormone and prolactin may indicate an imbalance at hypothalamus-pituitary level¹⁴. Endocrine dysfunction unaccompanied by other features of hypogonadism was found commonly and 19% of male celiac were infertile¹⁴. The majority outstanding endocrine findings in a study of 41 newly diagnosed men with celiac disease was increased plasma testosterone. When jejunal morphology improved, hormone levels restored to normal^{12,13}. These higher rates of infertility among victims of celiac disease, both the male and female partners with unexplained infertility¹².

CONCLUSION

The current study is the first study of celiac disease and its association with infertility among Yemeni, the CD appear to be relatively common in Yemen. There was low level of male and female sex hormones in CD patients, comparing with normal level in Yemeni healthy adults which indicate infertility negative effect of CD.

ACKNOWLEDGEMENT

This work has been supported by Sana'a University, Sana'a, Yemen and Guangxi Medical University,

Republic of China with grant number: 432-A-2017. All authors express their great thanks to both Universities.

AUTHOR'S CONTRIBUTION

Al-Anesi M: writing, review. **Hu Q:** writing, review and editing. **Al-Eryani E:** formal analysis, writing, review, and editing. **Al-Amrani M:** writing, review, and editing, conceptualization. **Al-Shamahy H:** writing, review, and editing, methodology. All the authors approved the finished version of the manuscript.

DATA AVAILABILITY

The data and material are available from the corresponding author on reasonable request.

CONFLICT OF INTEREST

None to declare.

REFERENCES

- Torres MI, Lorite P, Palomeque T. Celiac disease and other autoimmune disorders Editors In: autoimmunity, pathogenesis, clinical aspects and therapy of specific autoimmune disease. Intech. 2015; 6: 131-151. <https://doi.org/10.5772/60695>
- Tye-Din JA, Stewart JA, Dromey JA, Beissbarth T, Van Heel DA, Tatham A, et al. Comprehensive, quantitative mapping of T cell epitopes in gluten in celiac disease. Sci Transl Med 2010; 2: 41-51. <https://doi.org/10.1126/scitranslmed.3001012>
- Du Pre, MF, Sollid LM. T-cell and B-cell immunity in celiac disease. Best Practice Res Clin Gastro 2015; 29: 413-423. <https://doi.org/10.1016/j.bpg.2015.04.001>
- Trigoni Evagelia, Alexandra Tsirogianni, Elena Pipi, et al. Celiac disease in adult patients: specific auto-antibodies in the diagnosis, monitoring, and screening; 2014. <https://doi.org/10.1177/2050640619844125>
- WHO. Sexual and reproductive health. Available at <http://www.who.int/reproductive-health/en>.
- CDC. Women's Reproductive Health | Reproductive Health | Available at <https://www.cdc.gov/reproductivehealth/womensrh/index.htm> Accessed December 21, 2017
- ACOG (American College of Obstetricians and Gynecologists). Infertility page. Available at http://www.acog.org/publications/patient_education/bp136.cfm. Accessed December 21, 2017.
- Collins JA, Crosignani PG: Unexplained infertility: a review of diagnosis, prognosis, treatment efficacy and management. Int J Gynaecol Obstet 1992; 39: 267-75. 6. [https://doi.org/10.1016/0020-7292\(92\)90257-J](https://doi.org/10.1016/0020-7292(92)90257-J)
- Rostom A, Dubé C, Cranney A et al. The diagnostic accuracy of serologic tests for celiac disease: a systematic review. Gastroenterol 2005; 128 (4): S38-S46. <https://doi.org/10.1053/j.gastro.2005.02.028>
- Freeman HJ. Reproductive changes associated with celiac disease. World J Gastroenterol 2010; 14, 16(46): 5810-5814. <https://doi.org/10.3748/wjg.v16.i46.5810>
- Pellicano R., Astegiano M, Bruno M, Fagoonee S, Rizzetto M. Women and celiac disease: Association with unexplained infertility. Minerva Med 2007; 98:217-219. PMID: 21682114
- Bast Alice, Tom O'Bryan, Elizabeth Bast. Celiac disease and reproductive health. Practical Gastr 2009; 5: 10-21.
- Farthing M, Rees L, Edwards C, Dawson A. Male gonadal function in coeliac disease: 2. Sex hormones. Gut 1983; 24, 127-135. <https://doi.org/10.1136/gut.24.2.127>
- Stazi A, Trinti A. Reproductive aspects of celiac disease. Ann Ital Med Int 2005; 20(3):143-157. PMID: 16250182