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Does celiac disease affect the female reproductive system? A short report

Czy celiakia wpływa na układ rozrodczy kobiet? Krótki raport

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ABSTRACT

Celiac disease is an autoimmune disorder in which gluten is the main trigger of the disorder. It enters the body through foods made from wheat, rye or barley. A patient who is positive for celiac disease suffers from several disorders after ingesting gluten, such as cramps, nausea, bloating, diarrhoea, constipation, lack of appetite. It has been shown that this disorder can affect other systems besides the gastrointestinal tract, for example, the reproductive system. It can cause complications in pregnancy, miscarriage or infertility. In this study, we focused on investigating this disease in the adult population, specifically in women who have had at least one pregnancy. We specifically investigated whether any complications occurred during pregnancy, whether the woman followed a gluten-free diet during pregnancy, and whether the baby tested positive for celiac disease after birth.

KEY WORDS

infertility, celiac disease, gluten, gastroenterology difficulties.

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INTRODUCTION

Celiac disease (gluten enteropathy) is characterized as an autoimmune disease that has a specific histological and serological profile, triggered by gluten consumption [1]. The disease has a global prevalence of around 1.40–2.00% (with a female predominance), but this is steadily increasing. The highest prevalence of seropositivity is in Europe and Asia [2]. This disease can occur at any age along with variable manifestations. Gold standard for the diagnosis of celiac disease is examination of the gastrointestinal tract using duodenal biopsy. Adherence to a gluten-free diet recommended by a specialist physician is the only possible treatment. Currently, this disease is overlooked and underestimated especially by physicians and the lack of classification of symptoms [3]. In the last survey con-

ducted, 60.00–70.00% of patients diagnosed with celiac disease were women. This may be due to more frequent use of health services [4].

Failure to detect celiac disease in a woman and to follow a gluten-free diet can result in infertility or difficulty of becoming pregnant. During pregnancy, a balanced diet is essential for both the woman and the foetus. The intake of Ca, Fe, fibre and other minerals for proper foetal development should be taken into account. As for minerals and vitamins, deficiencies have been scientifically proven. These are zinc, selenium, or folic acid [5, 6]. There is no significant problem with a single violation of a gluten-free diet, but with long-term consumption of gluten, there is a disturbance in the absorption of nutrients in the mother's body. This can affect the foetus in its organ development or growth [7, 8]. If mothers who breastfeed their babies and consume a regular diet, gluten peptides are introduced into their milk along with other substances, which may be the cause of gluten tolerance in the baby. However, some studies show that neither the duration of breastfeeding, the time of adding gluten to the diet, nor their relationship to each other are primary preventers of celiac disease [9]. It has been found that the immune system of women with celiac disease can be affected by pregnancy. Anti-tTgG (anti-transglutaminase) antibodies adhere to the membrane of the foetal trophoblast, causing damage to the future placenta. Also, anti-tTgG can damage the endometrial cytoskeleton of the mother's endometrial cells. These antibodies have been found in patients with an active form of celiac disease [10].

Many women with reproductive difficulties do not have obvious symptoms that would indicate celiac disease. Often it is anaemia. However, reduced fertility in women, absence of menstrual bleeding, early menopause, may be an early sign of celiac disease. Symptoms in women are not only more frequent, but in this disease, they appear more quickly than in men. Most often, celiac disease is diagnosed in young women. A survey conducted by a team of researchers in the UK showed that in women with treated celiac disease, the reproductive period lasts longer than in women who do not follow a gluten-free diet [8]. Other research points to the fact that celiac disease may be a factor in spontaneous abortions as well as low birth weight babies. Finnish doctors have confirmed that of all patients with celiac disease, up to 4.00% have trouble getting pregnant. In this case, women must strictly follow the diet, otherwise there may be a problem with getting pregnant, the fertility period may be shorter and earlier onset of menopause may occur [11, 12].

Women who could not conceive had symptoms characteristic of celiac disease. However, in the so-called silent form of celiac disease, no significant symptoms appear. If a woman has trouble conceiving, it is still recommended that she be tested for celiac disease, precisely because of the presence of the silent (symptomless) form of celiac disease. Once a gluten-free diet is in place and the effects of time have occur, a woman has a chance to conceive without complications [13]. One possible reason why untreated celiac disease affects a woman's fertility lies in the inadequate intake of nutrients (iron, selenium, zinc, folic acid). Taking antibodies can cause damage to the uterus or embryo. The blood vessels in the placenta are destroyed by antibodies, reducing the foetal nutritional intake, and this can result in insufficient body weight of the newborn [14]. Cases where celiac disease affects a man's fertility are rare. Studies in the UK have shown that gonadal dysfunction is related to celiac disease. Analysis of ejaculate has shown significant abnormalities in sperm morphology and motility, similar to those seen in people with Crohn's syndrome. Sperm morphology is improved by the removal of dietary gluten [8, 12].

MATERIAL AND METHODS

The research was carried out by means of anonymous questionnaires, which were recommended to patients to fill in when visiting the gastroenterology outpatient clinic in Humenne, eastern Slovakia. The questionnaire was constructed for the target group of women with celiac disease. The return rate of the questionnaires was 100%, and the patients' answers were checked by a nurse. All questionnaires were accepted. The research sample consisted of 139 women. The age of the respondents ranged from 20 to more than 51 years. The results were statistically processed by GraphPad Prism 5 and then plotted using Microsoft Office Excel spreadsheets.

RESULTS

As part of the results, we reported body weight and height values in Table 1. The body mass index (BMI) was then calculated from the data (Table 2). Even though the average BMI was within the normal range in each age category, 1.44% were underweight and 0.71% were overweight in the first category. In the 20–30 years age group, 0.71% were overweight and 3.59% were underweight. It is scientifically proven that with age there is increased fat deposition, which was pointed out in the 31–40 years age group where 1.44% suffered from overweight and 0.71% suffered from underweight. However, in the 41–50 years age group, 1.44% of the patients were underweight. This might have been due to adherence to a gluten-free diet. From the age of 51 years and above, 1.44% of patients were overweight. The findings suggest that overweight

TABLE 1. Selected anthropometric parameters

Body height									
Age cat.	***N***	**Min. [cm]**	**Max. [cm]**	**SD**	**SEM**	**Lowest CI value**	**Highest CI value**	**V %**	***P*-value**
Less than 20 years	12	148.00	176.00	7.40	2.15	160.40	169.80	4.51	ns
21–30 years	33	154.00	176.00	5.12	0.90	164.30	168.00	3.12	ns
31–40 years	45	157.00	180.00	5.50	0.82	165.10	168.40	3.30	ns
41–50 years	29	156.00	175.00	5.03	0.93	164.50	168.30	3.02	ns
More than 51 years	20	158.00	180.00	5.71	1.28	165.20	170.60	3.40	ns
Body weight									
Age cat.	***N***	**Min. [kg]**	**Max. [kg]**	**SD**	**SEM**	**Lowest CI value**	**Highest CI value**	**V %**	***P*-value**
Less than 20 years	12	32.00	85.00	13.46	3.89	51.53	68.64	2.40	ns
21–30 years	33	47.00	95.00	9.30	1.62	54.88	61.48	15.98	***
31–40 years	45	52.00	120.00	13.67	2.04	64.16	72.37	20.03	***
41–50 years	29	48.00	80.00	7.87	1.46	62.21	68.20	12.06	ns
More than 51 years	20	55.00	94.00	9.98	2.23	65.78	75.12	14.17	ns

N – numbers, min. – minimum, max. – maximum, SD – standard deviation, SEM – standard error of mean, V – coefficient of variation.

TABLE 2. Average body mass index (BMI) for each age group of women with celiac disease

Age cat.	BMI [kg/m^2]
Less than 20 years	21.97
21–30 years	21.11
31–40 years	24.49
41–50 years	23.57
More than 51 years	25.07

people are not following a gluten-free diet adequately, which may put their health at risk. However, this needs to be verified with a larger sample of respondents.

In pregnancy, several complications and difficulties arise. Since the process of ontogenesis takes place in the uterine cavity, it is influenced by various external and internal factors, as well as genetic predispositions. One of the aims of the study was to investigate whether there are complications in pregnancy that could lead to manifestations of gluten intolerance in the foetus. Our questionnaire survey shows that up to 25.89% (Table 3) of the patients surveyed experienced changes during pregnancy that could lead us to assume that the children born would suffer from celiac disease, that was confirmed in Table 4. When we investigated the association between complications during pregnancy in relation to adherence

TABLE 3. Results of an anonymous questionnaire survey of women with celiac disease

Question	Answer	*N* (%)
Did you experience any complications (such as vitamin deficiencies) during pregnancy?	Yes No I don't know	36 (25.89%) 70 (50.35%) 33 (23.74%)
Did you follow a fixed gluten-free diet during pregnancy?	Yes No I don't know	59 (42.45%) 65 (46.76%) 15 (10.79%)
Did your child suffer from celiac disease after birth or have problems with the intake of gluten in food?	Yes No I don't know	15 (10.79%) 71 (51.07%) 53 (38.13%)

TABLE 4. Spearman test to confirm/refuse the link between celiac disease and pregnancy

Variable – Celiac disease during pregnancy	Spearman correlation coefficient
Complications during pregnancy – diet	Correlation = 0.166686
Complications during pregnancy – baby	Correlation = 0.044424
Confirmation/rejection of the hypothesis	Hypothesis confirmed

to a gluten-free diet, our hypothesis was not confirmed. However, when examining the relationship whether the child suffered from problems with gluten intake after birth, the hypothesis was confirmed.

The patients saw that 50.35% did not suffer from vitamin deficiency, which is about half of the sample we studied (Table 3). Patients should clearly take care of their health especially during pregnancy. About 23.74% of them could not assess whether they suffered from any complications. The survey shows that 42.45% of the patients were following the doctor-prescribed gluten-free diet, which might have reduced complications in pregnancy. When asked if the children suffered from celiac disease, 38.13% of the mothers could not answer this question. We are of the opinion that the survey requires a deeper investigation of this issue.

DISCUSSION

Celiac disease is a disease that not only has extensive complications in the gastrointestinal tract, but also affects other organs and systems, such as the reproductive system [15]. Celiac disease in pregnancy is not an isolated case. During pregnancy, 25.89% of the respondents surveyed experienced changes. Despite warnings from doctors to follow a gluten-free diet, 50.35% of women did not follow a tented diet during pregnancy. Subsequently, the question was asked whether the children had a problem with gluten intake. 10.79% of the respondents answered that their children had a problem with the conventional diet. We compared our results with research conducted by Butler et al. demonstrating that celiac disease is related to a genetic predisposition in the child. They also reported that women experienced changes (complications) during pregnancy [16]. As confirmed by Kotze in his study, celiac disease can cause delayed onset of menarche, secondary amenorrhea, higher percentage of spontaneous abortions, anaemia and hypoalbuminemia [17]. Adherence to a gluten-free diet has been shown to be effective in studies where the ratio of miscarriages to pregnancies was found to be reduced more than fivefold [18, 19]. Research by Tosco *et al.* confirmed that most children with a presumed history of the disease remain healthy. In our trial, 10.79% of children suffered from gluten digestion problems after birth [20]. Ultimately, celiac disease spreads further and it is essential that the public is made aware of the definition, progression, and consequences of this disease, which can cause considerable problems. The diet recommended to patients has been, to date, the only known treatment that people with celiac disease can undergo to improve or fully regain their condition.

CONCLUSIONS

Celiac disease is a lifelong autoimmune disorder that significantly affects the patient's life. Due to the diet in pregnancy, the mother is depleted of a multitude of vitamins and minerals, which can result in various complications even up to miscarriage. It is important to devote more in-depth research to this topic, especially in fertility in women.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Fasano A, Catassi C. Celiac disease. N Engl J Med 2012; 367: 2419-26.
2. Makharia GK, Singh P, Catassi C, et al. The global burden of coeliac disease: opportunities and challenges. Nature Rev Gastroenterol Hepatol 2022; 19: 313-27.
3. Shah S, Leffler D. Celiac disease: an underappreciated issue in women's health. Women's Health 2010; 6: 753-66.
4. Megiorni F, Mora F, Bonamico M, et al. HLA-DQ and susceptibility to celiac disease: evidence for gender differences and parent-of-origin effects. Am J Gastroenterol 2008; 103: 997-1003.
5. Singhal N, Alam S, Sherwani R, Musarrat J. Serum zinc levels in celiac disease. Indian Pediatr 2008; 45: 319-21.
6. Yüce A, Demir H, Temizel IN, Koçak N. Serum carnitine and selenium levels in children with celiac disease. Indian J Gastroenterol 2004; 23: 87-8.
7. Ferguson R, Holmes GKT, Cooke WT. Coeliac disease, fertility, and pregnancy. Scand J Gastroenterol 1982; 17: 65-8.
8. Freeman HJ. Reproductive changes associated with celiac disease. World J Gastroenterol 2010; 16: 5810-4.
9. Hoffman I. Celiakie. Praha: Mladá Fronta 2019; 270 s. ISBN 978-80-204-5414-0.
10. Celiac disease foundation. How Celiac Disease Affect Pregnancy 2014.
11. Foschi F, Diani F, Zardini E, et al. Celiac disease and spontaneous abortion. Minerva Ginecol 2002; 54: 151-9.
12. Moleski SM, Lindenmeyer CC, Veloski JJ, et al. Increased rates of pregnancy complications in women with celiac disease. Ann Gastroenterol 2015; 28: 236-40.

13. Ghadir M, Iranikhah A, Jandaghi M, et al. Unexplained infertility as primary presentation of celiac disease, a case report and literature review. Iran J Reprod Med 2011; 9: 135-40.
14. Caja S, Mäki M, Kaukinen K, Lindfors K. Antibodies in celiac disease: implications beyond diagnostics. Cell Mol Immunol 2011; 8: 103-9.
15. Lima RF, da Silva Kotze LM, Kotze LR, et al. Gender-related differences in celiac patients at diagnosis. Arch Med Res 2019; 50: 437-41.
16. Butler MM, Kenny LC, McCarthy FP. Coeliac disease and pregnancy outcomes. Obst Med 2011; 4: 95-8.
17. Kotze LMS. Gynecologic and obstetric findings related to nutritional status and adherence to a gluten-free diet in Brazilian patients with celiac disease. J Clin Gastroenterol 2004; 38: 567-74.
18. Collin P, Mäki M. Associated disorders in coeliac disease: clinical aspects. Scand J Gastroenterol 1994; 29: 769-75.
19. Ciacci C, Cirillo M, Auriemma G, et al. Celiac disease and pregnancy outcome. Obstet Gynecol Survey 1996; 51: 643-4.
20. Tosco A, Salvati VM, Auricchio R, et al. Natural history of potential celiac disease in children. Clin Gastroenterol Hepatol 2011; 9: 320-5.