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Research Protocol

Abnormalities of Fertility and Pregnancy in Celiac Disease

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Abstract

Celiac disease is associated with abnormalities of fertility and pregnancy. Untreated celiac patients have a significantly increased risk of pregnancy complications compared to non-celiac patients: repeated abortions, intrauterine growth retardation, low birth weight, premature delivery and neonatal mortality. The aim of this work was to clarify the prevalence of infertility and pregnancy abnormalities observed during celiac disease. Among the celiac population with sexual activity (n = 60), 5 (8.3%) patients (3H, 2F) are followed for infertility, including 4 patients for primary infertility (3H, 1F) and one woman for secondary infertility. Among the 41 sexually active female patients, 53.7% (22/41) presented at least one obstetric abnormality.

Keywords: *Celiac Disease; Gluten-Free Diet*

Abbreviations

MC: Celiac Disease; RSG: Gluten-Free Diet

Introduction

Celiac disease (CD) is an autoimmune enteropathy secondary to the ingestion of gluten in genetically predisposed individuals. It is accompanied by multiple disorders, in particular obstetric abnormalities in women with celiac disease. Untreated patients have a significantly increased risk of pregnancy complications compared to non-celiac patients: repeated abortions, intrauterine growth retardation, low birth weight, premature delivery and neonatal mortality [1].

Aim of the Study

The aim of this study was to clarify the prevalence of infertility in the celiac population as well as the pregnancy anomalies observed in celiac women.

Materials and Methods

Prospective multicenter study conducted between January 2013 and June 2015 including 154 adult patients (42 M, 112 F) (age ≥ 16 years) with CD meeting the diagnostic criteria of ESPGHAN (European Society for Gastroenterology, Hepatology and Nutrition) 2012 The average age is 36.1 ± 13.6 years (16 -83 years). Sterility has been investigated in this celiac population. Celiac women who attempted to procreate were selected for the study of obstetric abnormalities, while male population (n = 42) and celiac women without intention of

pregnancy or in menopause (n = 71) were eliminated. Forty-one women with celiac disease were selected for the study of abnormalities of pregnancy. The mean number of pregnancies was (4.6 ± 2.9) pregnancies/woman [range 0 - 13] pregnancies/woman. The course of the different pregnancies before and/or during the study was noted and the different types of obstetric accidents were described.

Results

Among the 154 celiac patients, 60 (39%, 19M, 41F) show sexual activity. 5 (8.3%) patients (3M, 2F) are followed for infertility including 4 patients for primary infertility (3M, 1F) and one woman for secondary infertility. Among the 41 sexually active female patients, 53.7% of these patients (22/41) presented at least one obstetric anomaly. In fact, 4 celiac patients presented during consecutive pregnancies 2 types of abnormalities: abortion - stillbirth (n = 2), abortion - death - in utero (n = 1), premature delivery - stillbirth (n = 1) and one patient presented with abortion and stillbirth (n = 1). A total of 28 obstetric anomalies were observed in the female celiac population which makes it possible to estimate the prevalence of these anomalies at 68.3% (28/41). The prevalence of the various disorders was in decreasing order: abortions at 46.3% (n = 19), neonatal mortality at 12.2% (n = 5), intrauterine mortality and premature deliveries at 4,9% respectively (n = 2) see table 1.

Obstetric abnormality	Prevalence %	Number
Abortion	46,3	19
Neonatal mortality	12,2	5
Intrauterine mortality	4,9	2
Premature delivery	4,9	2
Total	68,3	28

Table 1: *Prevalence of obstetric anomalies in the sexually active female celiac population.*

The rate of obstetric abnormalities was significantly higher in the group not adhering to the gluten-free diet (RSG) (68.2%) compared to the adherent group (31.2%) with a p = 0.02. The occurrence of abnormalities in pregnancy according to adherence to the RSG is summarized in table 2.

	Non adherence to the RSG	Adherence to the RSG	Total
Presence of obstetric anomalies	17 (68%)	5 (31,2%)	22 (53,7%)
Absence of obstetric abnormalities	8 (32%)	11 (68,8%)	19 (46,3%)
Total	25 (100%)	16 (100%)	41 (100%)

Table 2: *Rate of abnormalities in pregnancy according to adherence to the RSG.*

Discussion

Sterility is found in 8.3% of our patients; 80% of cases presented with primary infertility and 20% with secondary infertility. The risk of CD in unexplained infertility is 5 fold higher than in the general population [2]. In a controlled study of screening for CD in a female population with unexplained primary or secondary infertility, the rate of subclinical CD was significantly higher in the group with infertility, estimated at 4.1% than in the control group [3]. The prevalence of obstetric anomalies in our population is estimated at 68.3% (28 anomalies/41). The risk of pregnancy complications: repeated abortions, intrauterine growth retardation, low birth weight or premature delivery, is significantly higher in celiac women: 15% versus 6% in non-celiacs [4].

The prevalence of the various disorders is in decreasing order in our series: abortions at 46.3% (n = 19), neonatal mortality at 12.2% (n = 5), intrauterine mortality and childbirth premature babies at 4.9% respectively (n = 2). A meta-analysis [2] addressed the association of reproductive abnormalities with CD and demonstrated that patients with unexplained infertility, repeated abortions, or intrauterine growth retardation have a multiplied risk of 5, 6 and 8 respectively to be celiac compared to the general population. In this same work, it was observed that celiac women have a significantly higher risk of having an abortion (relative risk (RR of 1.39), intrauterine growth retardation (RR of 1.54), low birth weight (RR of 1.75) or premature delivery (RR of 1.37) compared to non-celiac women.

Among the 41 celiac women in our study, 46.3% had abortions, with a repeat abortion rate (≥ 2) of 24.3%. The rate of repeated abortions in celiac women is variable in the literature: 7.5% in the study by Gasbarinni [5], 5.8% in the study by Sher [6]. Thus, serological screening is strongly recommended in cases of unexplained infertility, repeated abortions or intrauterine growth retardation [2]. However, there is not enough evidence available to recommend screening for CD in women with a history of preterm birth or preeclampsia [4].

In our study obstetric abnormalities have been observed in patients prior to the diagnosis of CD and the indication for RSG. This is consistent with a meta-analysis of several studies where the risk of various complications of pregnancy in women with celiac disease were considerably reduced by adherence to the RSG [2]. In another work, the risk of obstetric abnormalities was not significantly higher in celiac patients on well-monitored RSG compared to non-celiac patients [7]. These results confirm the role of the RSG in a good outcome of pregnancies and childbirth.

Conclusion

Celiac disease is associated with a significant risk of infertility and pregnancy abnormalities including a high prevalence of abortions. The value of targeted screening for celiac disease in the event of reproductive abnormalities in the female population seems justified.

Obstetric abnormalities are related to non-compliance with the gluten-free diet.

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