

CLINICAL ARTICLE

Obstetrics

Gluten-free diet during pregnancy and pregnancy outcome: A retrospective cohort study

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Abstract

Objective: A gluten-free diet (GFD) is becoming increasingly popular, especially among young females, and including those without diagnosed celiac disease (CD). Whether a GFD is appropriate during pregnancy remains unclear. Our primary aim was to evaluate the association of a GFD and neonatal birthweight and incidence of large for gestational age (LGA) and small for gestational age (SGA). Secondly, we sought associations with other obstetric outcomes.

Methods: The data was collected retrospectively from the Tampere University Hospital database. The study period was from January 2015 to April 2021. The diet information was obtained from self-reported questionnaires. All women following a GFD were included. A total of 79 had CD and 291 followed a GFD without CD diagnosis. The latter are referred to here as people without CD avoiding gluten (PWAG). A total of 456 omnivores were randomly chosen to constitute a control group. Outcomes were analyzed by comparing gluten-free groups to a control group.

Results: The median birth weight was higher in the GFD group compared to the controls (3533 vs. 3440g, $P < 0.003$), but the incidences of SGA or LGA did not differ between the study groups. The incidence of pregnancy complications was comparable between the groups. Induction of labor was more frequent (aOR 1.52; 95% CI: 1.12–2.08), and the duration of labor was longer (aOR 1.56; 95% CI: 1.18–2.06) in the GFD group, especially among PWAG. However, no difference in the cesarean section rate were found between the groups.

Conclusion: In the present retrospective cohort study, a GFD did not appear to be associated with adverse pregnancy or neonatal outcomes.

KEYWORDS

celiac disease, gluten-free diet, pregnancy, pregnancy outcome

Abbreviations: AGA, appropriate for gestational age; BMI, body mass index; CD, celiac disease; CS, cesarean section; DF, dietary fiber; GF, gluten-free; GFD, gluten-free diet; LGA, large for gestational age; PWAG, people without celiac disease avoiding gluten; SGA, small for gestational age.

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1 | INTRODUCTION

Celiac disease (CD) is an intestinal inflammatory disease that is triggered by dietary gluten derived from wheat, rye, and barley. Without treatment it causes symptoms due to malabsorption, including diarrhea, abdominal pain, bloating and weight loss.¹ In women, untreated CD may have implications on menstrual and reproductive health, such as delayed menarche, early menopause, secondary amenorrhea, infertility and recurrent miscarriages.^{2–4} Furthermore, untreated CD in pregnant women increases the risk of miscarriage, preterm birth, labor induction, intrauterine growth restriction, and newborns with a low birth weight.^{2,5–9}

Clinical studies have shown that a gluten-free diet (GFD) is important in reducing the risk of adverse pregnancy outcomes in women with CD, making their pregnancies comparable to those of women without CD.^{10–12} However, a GFD among people without CD diagnosis has also become increasingly popular.¹³ In the US population it has increased from an estimated 0.5% in 2009 to 1.7% in 2014. In people without CD, claims of the health benefits of a GFD have spread more rapidly than evidence of its potential adverse effects. However, in one observational study, obstetric and fetal outcomes did not differ in women without CD avoiding gluten, compared with control women.¹³

Gluten-free food, being richer in carbohydrates and less rich in fiber and protein, may have an impact on fetal growth in women with CD.¹⁴ In one study, women with CD and gestational diabetes had much the same pregnancy outcomes as women with gestational diabetes alone, but children born from women with CD had significantly higher birth weight and were more likely to be large for gestational age (LGA).¹⁴ Furthermore, a GFD may have some adverse effects, even in patients with CD, such as micronutrient deficiencies and weight gain.¹⁵

Only a few studies previously have been concentrated on a GFD and pregnancy outcomes—especially in women without CD. Our hypothesis was that GFD may affect fetal growth, and the primary outcome was neonatal weight. The secondary aim was to seek other pregnancy, delivery, and neonatal outcomes in women with GFD. We also performed subanalyses of patients with diagnosed CD and PWAG.

2 | MATERIALS AND METHODS

We collected data retrospectively from the hospital medical registry at Tampere University Hospital. The period studied was between January 2015 and April 2021. The medical registry has information on maternal demographic data, pregnancy complications, delivery data and neonatal health during the first 7 days after birth. Dietetic habits or dietetic restrictions of all parturients were routinely asked in advance and recorded in maternal files. All gluten free diets were picked, regardless of the possible diagnosis of the patient. Concomitant vegetarian diets were excluded. Altogether, 826 pregnant women were included in the study. During the study period

370 women followed a GFD, and of these, 79 women had been diagnosed with CD and they constituted the celiac disease group. A total of 291 women voluntarily followed a GFD without CD diagnosis, and they constituted the PWAG group. We randomly selected 456 women following an omnivorous diet and they constituted the control group.

Maternal and pregnancy outcomes of interest in these three groups were recorded and compared. We evaluated the baseline characteristics of the women, including age, body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters), parity, smoking during the pregnancy, pre-pregnancy diabetes, thyroid disease, previous cesarean sections (CS) and if the pregnancy had begun spontaneously or assisted by infertility treatments. Data concerning possible pregnancy complications, and the characteristics of labor and delivery were gathered, as well as data on the newborns, including birth weight, Apgar scores, umbilical artery pH and possible treatment at a neonatal ward. Maternal anemia during pregnancy was defined as a hemoglobin value below 110 g/L.

Newborns who were small for gestational age (SGA) were defined as having a birth weight of 2 standard deviations (SD) or below national sex-specific standard means, and LGA newborns were defined as having a birth weight of 2SD or more above these means.¹⁶

The Ethics Committee of Tampere University Hospital, Finland (R21632) approved the study.

Mother-related characteristics (age, BMI, primipara, earlier cesarean section, smoking during pregnancy, pre-pregnancy diabetes and thyroid disease) were compared between diet groups calculating Cohen's standardized difference $d = (p_1 - p_2) / \sqrt{[(p_1(1-p_1) + p_2(1-p_2))/2]}$, where p_1 and p_2 denote the proportion of binary factors in the gluten free versus control (or CD vs. PWAG) diet group. Confidence interval was calculated using function `cohen.d.ci` in `psych` package of the statistical program R version 4.4.2 (2024), from the R Foundation for Statistical Computing.¹⁷ For continuous factors, d was calculated, as well as other statistics, using the statistical program IBM SPSS Statistics version 29.0.1.0 software (IBM SPSS, Chicago, Illinois). Associations of diet groups on (1) characteristics of pregnancies, (2) characteristics of deliveries, and (3) pregnancy outcomes were modeled as unadjusted and mother-related characteristics adjusted logistic regression showing results using odds ratios (OR) with 95% CIs. Missing values gestational age ($n=2$), staying in hospital more than 4 days ($n=13$), both Apgar 1 and 5 min ($n=2$) were recorded in unknown categories and those categories were included in analyses. Due to the very few cases, their results are not shown. In more detailed tables, differences between CD and PWAG groups were tested using the Fisher-Freeman-Halton exact or the Mann-Whitney U -test. Two-tailed P values under 0.05 were considered statistically significant in all analyses.

TABLE 1 Characteristics of mothers on a gluten-free diet (celiac disease or women without celiac disease avoiding gluten) and women on an omnivorous diet as the control group during pregnancy ($N=826$). Standardized differences between groups are shown using Cohen's d point estimate with 95% CIs.

	Gluten-free ($n=370$)		Control ($n=456$)		Gluten-free vs. control	
	Mean	(SD)	Mean	(SD)	Cohen's d	(95% CI)
Age, years	30.7	(5.1)	30.6	(5.5)	-0.14	(-0.15-0.12)
BMI (kg/m^2)	24.9	(5.3)	25.2	(5.7)	0.06	(-0.07-0.20)
	N	(%)	n	(%)	Cohen's d	(95% CI)
Primipara	168	(45)	180	(40)	0.12	(-0.02-0.26)
Earlier cesarean section	45	(12)	49	(11)	0.05	(-0.09-0.18)
Smoking during pregnancy	24	(7)	71	(16)	-0.29	(-0.43 to -0.15)
Pre-pregnancy diabetes	12	(3)	10	(2)	0.06	(-0.07-0.20)
Thyroid disease	12	(3)	6	(1)	0.13	(-0.01-0.27)
Basedow's disease	7	(2)	3	(1)		

Note: BMI, calculated as weight in kilograms divided by the square of height in meters. Cohen's d = standardized difference = difference in means or proportions divided by standard error; imbalance defined as absolute value greater than $|0.20|$ (small effect size); $|<0.40|$ effect size is small.

Abbreviations: BMI, body mass index; CI, confidence interval; SD, standard deviation.

TABLE 2 Characteristics of pregnancies associated with the occurrence of gluten-free (celiac disease or voluntary gluten-free) diets compared to omnivorous diet (control group) during pregnancy ($N=826$). Differences between groups were tested using the unadjusted and mother related characteristics (see Table 1) adjusted logistic regression showing results by OR with 95% CIs.

	Gluten-free ($n=370$)		Control ($n=456$)		Gluten-free vs. control P value	Unadjusted gluten-free vs. control		Adjusted gluten-free vs. control	
	n	(%)	n	(%)		OR	(95% CI)	OR	(95% CI)
Infertility treatment	21	(5.7)	19	(4.2)	0.332	1.38	(0.73-2.62)	1.19	(0.61-2.31)
Gestational diabetes	83	(22)	108	(24)	0.679	0.92	(0.67-1.29)	1.03	(0.72-1.48)
Insulin-treated gestational diabetes	18	(4.9)	23	(5.0)	1.000	0.96	(0.51-1.81)	1.13	(0.57-2.23)
Anemia during pregnancy	13	(3.5)	6	(1.3)	0.059	2.73	(1.03-7.26)	2.87	(1.01-8.18)
Small for gestational age	20	(5.4)	35	(7.7)	0.209	0.69	(0.39-1.21)	0.62	(0.35-1.12)
Large for gestational age	25	(6.8)	26	(5.7)	0.563	1.20	(0.68-2.11)	1.30	(0.68-2.46)
Pre-eclampsia	11	(3.0)	13	(2.9)	1.000	1.04	(0.46-2.36)	0.96	(0.41-2.21)
Gestational hypertension	14	(3.8)	27	(5.9)	0.198	0.63	(0.32-1.21)	0.70	(0.35-1.39)
Chronic hypertension	3	(0.8)	7	(1.5)	0.525	0.52	(0.13-2.04)	0.48	(0.12-1.91)
Gestational or chronic hypertension	17	(4.6)	33	(7.2)	0.142	0.62	(0.34-1.13)	0.66	(0.35-1.24)
Cholestasis of pregnancy	4	(1.1)	3	(0.7)	0.707	1.65	(0.37-7.42)	1.38	(0.30-6.30)

Abbreviations: CI, confidence interval; OR, odds ratio.

3 | RESULTS

The baseline characteristics of the women are shown in Table 1. There tended to be more primiparas and women with thyroid disease in the GFD group than in the control group, and there were fewer smokers in the GFD group than in the control group.

Anemia was more common in the GFD group, with no difference between CD or PWAG (Table 2).

Table 3 shows that moderately preterm delivery adjusted for factors related to the mother was less common in the GFD group compared to the control group. Labor induction was more common in the GFD group (Table 3), the number of inductions being especially

high among parturients with CD (Table S1). The median durations of labor, and the first and second stages of labor, were significantly longer in the GFD group, both among primiparas and multiparas. However, the longer duration of labor in GFD was totally explained by the PWAG group, as the labors among CD were comparable with those of the control group (Table S1). Vacuum extraction tended to be more common in the GFD group, with no difference between CD and PWAG (Table S1).

Birth weight and height were higher in the GFD group, but no differences between CD and PWAG groups could be found. The proportions of LGA or SGA did not differ between groups (Table 4). There was less need for newborn treatment at the neonatal ward

TABLE 3 Characteristics of deliveries in the gluten-free diet (celiac disease or voluntary gluten-free) compared to omnivorous diet (control group) ($N = 826$). Crude and mother-related characteristics-adjusted effects of gluten-free compared to control group were modeled separately for all characteristic using logistic regression showing results by OR with 95% CIs.

	Control ($n = 456$)		Gluten-free ($n = 370$)		Gluten-free vs. control		Unadjusted gluten-free vs. control		Adjusted gluten-free vs. control	
	<i>n</i>	(%)	<i>n</i>	(%)	<i>P</i> value		OR	(95% CI)	OR	(95% CI)
Gestational weeks*										
22 ⁺⁰ -31 ⁺⁶	12	(2.6)	5	(1.4)	0.155		0.50	(0.17-1.43)	0.45	(0.15-1.29)
32 ⁺⁰ -36 ⁺⁶	44	(9.6)	24	(6.5)			0.65	(0.39-1.09)	0.56	(0.33-0.97)
>42	10	(2.2)	14	(3.8)			1.67	(0.73-3.81)	1.77	(0.75-4.18)
37 ⁺⁰ -42 ⁺⁰	389	(85)	326	(88)			1.00		1.00	
Labor induction	131	(29)	136	(37)	0.017		1.44	(1.08-1.93)	1.52	(1.12-2.08)
Mode of delivery										
Spontaneous vaginal	327	(72)	265	(72)	0.058		1.00		1.00	
Vacuum delivery	22	(4.8)	35	(10)			1.96	(1.12-3.43)	1.65	(0.92-2.97)
Breech delivery	12	(2.6)	5	(1.4)			0.15	(0.18-1.48)	0.46	(0.15-1.34)
Acute cesarean section	44	(9.6)	34	(9.1)			0.95	(0.59-1.54)	0.79	(0.47-1.32)
Elective cesarean section	51	(11)	31	(8.4)			0.75	(0.47-1.21)	0.59	(0.34-1.00)
Epidural analgesia	229	(50)	207	(56)	0.107		1.26	(0.96-1.66)	1.25	(0.93-1.69)
Total bleeding over 550mL	131	(29)	91	(25)	0.207		0.81	(0.59-1.11)	0.73	(0.53-1.01)
Staying in hospital more than 4 days	192	(43)	146	(40)	0.474		0.90	(0.68-1.19)	0.78	(0.58-1.07)
Total duration* of labor (h:min), for vaginal deliveries	7:41 (4:19-10:33)	$n = 361$	8:09 (5:28-12:49)	$n = 305$	0.004					
First stage (h:min)	7:16 (4:11-10:05)		7:45 (5:02-12:15)		0.010					
Second stage (h:min)	11 (5-21)		17 (8-32)		<0.001					
Third stage (min)	10 (9-12)		10 (8-12)		0.624					
Primiparas										
First stage (h:min)	$n = 136$ 9:38 (7:00-13:28)	$n = 124$ 11:10 (8:06-16:20)	0.046							
Second stage (h:min)	20 (12-31)	27 (17-48)	<0.001							
Multiparas										
First stage (h:min)	$n = 225$ 5:28 (3:01-8:28)	$n = 181$ 6:05 (4:02-8:32)	0.028							
Second stage (h:min)	7 (4-13)	10 (4-20)	0.003							

*Bold values significances *p* value under 0.05.

Abbreviations: CI, confidence interval; OR, odds ratio.

TABLE 4 Pregnancy outcomes in the gluten-free diet (celiac disease or voluntary gluten-free) and omnivorous diet (control group) ($N=826$). Crude and mother-related characteristics—adjusted effects of gluten-free compared to omnivorous diet group were modeled separately for all outcomes using logistic regression showing results by OR with 95% CIs.

	Control ($n=456$)		Gluten-free ($n=370$)		Gluten-free vs. control <i>P</i> value	Unadjusted gluten-free vs. control		Adjusted gluten-free vs. control	
	<i>n</i>	(%)	<i>n</i>	(%)		OR	(95% CI)	OR	(95% CI)
Birth weight, g, Md (range)	3440	(475–5110)	3533	(450–4830)	0.003				
Birth weight >4500g <i>n</i> (%)	12	(2.6)	9	(2.4)	1.000				
Birth length, cm, Md (range)	50	(29–55)	50	(28–57)	0.001				
Gestational weight					0.592				
AGA	418	(92)	348	(94)		1.00		1.00	
SGA	21	(4.6)	11	(3.0)		0.63	(0.30–1.32)	0.68	(0.32–1.45)
LGA	16	(3.5)	10	(2.7)		0.75	(0.34–1.68)	0.71	(0.29–1.72)
Apgar score 1 min <7	41	(9.0)	33	(8.9)	1.000	0.99	(0.61–1.60)	0.88	(0.53–1.44)
Apgar score 5 min <7	26	(5.7)	13	(3.5)	0.186	0.60	(0.30–1.19)	0.53	(0.26–1.06)
Treatment at neonatal ward	89	(20)	55	(15)	0.081	0.72	(0.50–1.04)	0.68	(0.46–0.998)

Note: Bold values significances *p* value under 0.05.

Abbreviations: AGA, appropriate for gestational age; CI, confidence interval; LGA, large for gestational age; OR, odds ratio; SGA, small for gestational age.

in the GFD, especially in the CD group, than in the control group (Table S2).

Among the statistically significant results of our study, anemia during pregnancy achieved a higher *e*-value of 5.19. However, the *e*-value of 1.11 for the CI indicates that substantial confounder associations with gluten free and control diet could potentially move the CI to include 1. Correspondingly, *e*-values for labor induction were lower 1.77 with 1.31 for CI, and treatment at neonatal ward reached *e*-values of 1.72 with 1.03 for CI, which means that confounding may affect the results in our study.

4 | DISCUSSION

Newborns were slightly heavier and taller in the GFD group, but the proportions of LGA or SGA did not differ between groups. The immediate condition of the newborns was not different according to groups. No significant differences in pregnancy complications between the study groups were found. Thus, in our study we did not find any adverse effects of GFD on the newborns, neither on the mothers with CD or PWAG.

The slightly higher birth weight among GFD might be related to the diet, as GFD typically may be rich in carbohydrates and its fiber content may be low, predisposing to accelerated fetal growth.¹⁴ However, the mean weights in both groups were within normal limits, and the numbers of SGA or LGA did not differ

between groups. There were no differences in pregnancy complications that predisposed to low birth weight, such as gestational hypertension or pre-eclampsia. On the other hand, there were no differences in factors that predisposed to high birth weight, such as high maternal BMI, incidence of GDM or need for medication in the case of GDM. In our study, the GFD could be assumed rather healthy diet in respect of fetal growth. Our results also support the finding in the previous study.¹³

The tendency of more thyroid diseases in women with CD was not surprising, as CD is characterized as an autoimmune condition.¹³ Autoimmune diseases also tended to be more common in the PWAG group compared with the control group. Although, to our knowledge, the PWAG group did not include patients with CD, some CD patients may have inadvertently fallen within this category. There may have been some CD patients without appropriate CD diagnosis in the PWAG group, or a diagnosis had not been properly recorded in the pregnancy files or diagnosis had not yet been confirmed.¹⁸

Smoking was more common in the control group. Possibly women having CD or PWAG generally aim to follow a healthier lifestyle, which is reflected also in the smaller number of smokers. Anemia was slightly more common in the GFD group, but the proportions of anemic women were low in all groups.

Our finding of a longer duration of labor in the GFD group, especially in the PWAG group, is novel, and it was noticed in both multiparous and primiparous women. Obesity is known to

increase labor length,¹⁹ but it cannot explain the result, as BMI values did not differ between groups. Labor induction was more common in GFD group, which might be associated with the longer duration of labor. However, the greatest proportion of labor inductions was in the CD group, which was not characterized by longer labor. The greater number of primiparas among GFD and especially among PWAG might lead to longer durations of labor, but the labor was longer among GFD also when primiparas and multiparas were analyzed separately. A longer duration of labor was not clinically important, as the relative number of operative deliveries was not different between groups, and women in the PWAG group were discharged from hospital sooner than women in the control group.

Within GFD there were some differences between CD and PWAG groups. As expected, the number of autoimmune conditions tended to be more frequent among CD. The number of labor inductions was greater among CD, but the duration of labor (first and second stage) was greater among PWAG. As the number of women with CD was rather small and some women within PWAG may actually have had CD no firm conclusions can be drawn.

In this study, the *e*-values of the confidence intervals did not reach high, which can be a sign that there is random variation between tested groups. This may be due to the fact that mothers on omnivorous diets, which we have used as negative controls, were not a homogeneous group. Heterogeneity also applies to the group of those on a voluntarily gluten-free diet.

The main strength of this study was a fairly large sample size without dropouts. Grouping together patients with CD and PWAG may have brought together quite different people with possibly different backgrounds and dietic habits. This can be regarded either as a limitation or a strength. Adding comparison between CD and PWAG subgroups in supplementary tables helps to characterize these groups. However, it is possible that some CD patients may have fallen within the PWAG group, lacking an appropriate CD diagnosis. As the diet was self-reported, some inaccuracies may exist.

5 | CONCLUSION

According to our study, avoiding gluten did not appear to adversely affect maternal or fetal health.

AUTHOR CONTRIBUTIONS

All authors read through, commented on, and accepted the final manuscript. J.R. was the principal investigator. J.U. and K.T. planned the study and guided its progress. T.L. was responsible for statistical analyses.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data available on request from the authors. The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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