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ORIGINAL ARTICLE

# Characteristics and Maternal–Fetal Outcomes of Pregnant Women Without Celiac Disease Who Avoid Gluten

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## Abstract

**Background** Gluten avoidance among patients without celiac disease has become increasingly popular, especially among young and female demographics; however, no research has explored gluten avoidance during pregnancy, when nutrition is particularly important.

**Aims** To determine whether avoiding gluten in pregnancy is associated with any medical, obstetric, or neonatal characteristics.

**Methods** In this single-center retrospective cohort study, we identified women with singleton pregnancies who avoid gluten based on antenatal intake questionnaire responses and inpatient dietary orders, excluding those with celiac disease. Certain demographic, medical, obstetric, and neonatal characteristics were compared to matched controls who do not avoid gluten.

**Results** From July 1, 2011 to July 1, 2019, 138 pregnant women who avoid gluten were admitted for delivery of singleton gestations. Compared to controls, gluten-avoidant women had fewer prior pregnancies ($p=0.005$), deliveries ($p<0.0005$), and living children ($p<0.0005$), higher rates of hypothyroidism (OR = 3.22; $p=0.001$) and irritable bowel syndrome (OR = 6.00; $p=0.019$), higher second trimester hemoglobin ($p=0.018$), and lower body mass index at delivery ($p=0.045$). Groups did not differ in any obstetric or fetal characteristics.

**Conclusions** Gluten avoidance in pregnancy is common and, in women without celiac disease, is associated with higher rates of hypothyroidism and irritable bowel syndrome, fewer pregnancies, term births, and living children, and lower peripartum BMI, but is not associated with any obstetric or neonatal comorbidities. Avoiding gluten does not appear to adversely affect maternal or fetal health, but reasons for gluten avoidance, as well as long-term maternal and pediatric outcomes after gluten avoidance in pregnancy, warrant further study.

**Keywords** Gluten-free · Gluten avoidance · Non-celiac · Obstetric · Pregnancy · PWAG

## Introduction

Celiac disease (CD), characterized by an autoimmune response in the small intestine to the protein gluten, is treated with a long-term gluten-free diet (GFD). From 2009 to 2014, the prevalence of CD remained stable (at

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approximately 0.7% of Americans) while adherence to a GFD increased markedly, due to a rapid rise in "*p*eople *w*ithout celiac disease *a*voiding *g*luten" (PWAGs) [1]. PWAGs, who lack known biomarkers of CD, may avoid gluten for self-diagnosed CD, non-celiac gluten sensitivity, other medical conditions, or perceived wellness benefits.

With a greater than threefold increase from 2009 to 2014, PWAGs now outnumber people with CD, at nearly 2% of the US population [1]. More likely to be non-Hispanic, Caucasian, female, and of reproductive age [1–3], PWAGs differ from the general population in certain health metrics, including: lower BMI and waist circumference; lower rates of hypertension and diabetes; higher rates of irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), thyroid disease, lupus, and autism spectrum disorder; higher HDL; and lower iron, folate, and hemoglobin [2–5].

Compared to gluten-containing counterparts, gluten-free products contain more fat and refined starches (added to enhance flavor) and less protein, fiber, whole grains, certain vitamins (thiamine, riboflavin, niacin, folate, cobalamin, vitamin D), and some minerals (iron, zinc, magnesium, calcium) [6]. Substituting gluten-containing with gluten-free products may yield a diet with nutritional deficiencies (e.g., protein, folate, magnesium), and people on a GFD consume more calories and fat and less fiber and folate [7].

During pregnancy, nutrition is particularly crucial to support fetal development and maternal physiological changes. The Institute of Medicine and Centers for Disease Control recommend micronutrient supplements for women on certain diets; however, a GFD is not among those listed. No professional societies endorse a GFD in pregnancy in the absence of CD, and only one explicitly recommends against a GFD, citing the micronutrient deficiencies outlined above [8]. Maternal gluten intake has been associated with development of type 1 diabetes in offspring; [9] otherwise, whether pregnant PWAGs or their children are predisposed to or protected from any comorbidities, either from underlying disease processes or gluten avoidance, is unknown. We therefore aimed to identify pregnant PWAGs admitted for delivery and compare their medical, obstetric, and neonatal characteristics to matched controls who do not avoid gluten.

## Methods

We performed a retrospective cohort study of pregnant PWAGs admitted for delivery. We obtained all data from the hospital's electronic medical record (EMR).

We included all patients during the eight-year period spanning 7/1/2011 to 7/1/2019 who (a) requested a GFD during admission to Labor and Delivery (L&D) at Columbia University Irving Medical Center or (b) indicated gluten restriction on an open-ended dietary restrictions question on the antenatal intake form at a Columbia Maternal–Fetal Medicine (MFM) practice in midtown Manhattan. We excluded patients with a known diagnosis of CD (identified by chart review), positive CD serologies (anti-gliadin, anti-tissue transglutaminase, or anti-endomysial antibodies), or duodenal biopsy consistent with CD, as well as patients with documented wheat allergy or dermatitis herpetiformis. We also excluded patients with multiple gestations. We matched each subject to an age-, race-, and ethnicity-matched control, excluding any patients with: history, serology, or biopsy suggestive of CD; a GFD order during L&D admission; or antenatal intake form indicating gluten restriction.

We performed an EMR query for demographic characteristics (age, race, ethnicity, insurance type, length of stay, dietary orders) and conducted manual chart reviews to evaluate for medical characteristics (chart-listed diagnosis of hypertension, diabetes, lupus, hypothyroidism, IBS, IBD, autism, depression, anxiety, chronic anemia), obstetric characteristics (gravidity, parity, pregravid and peripartum BMI), obstetric comorbidities (gestational hypertension, preeclampsia, gestational diabetes mellitus, and postpartum blood transfusion, postpartum depression), neonatal outcomes (gestational age at birth, birth weight, APGAR scores), and neonatal comorbidities (including neural tube defects, major fetal malformation, small for gestational age, neonatal intensive care unit admission). Weight gain during pregnancy was calculated and categorized according to the American College of Obstetricians and Gynecologists' guidelines [10]. Laboratory values included hemoglobin during the first trimester (< 14 weeks), second trimester (14–28 weeks), and delivery admission, along with mean corpuscular volume (MCV) and red cell distribution width (RDW) at delivery. Iron, ferritin, total iron binding capacity, folate, and cobalamin labs were included when available.

We compared categorical variables in PWAGs and controls using the Pearson $\chi^2$ test or Fisher exact test where appropriate, and continuous variables using the Student $t$ test. We used conditional logistic regression to compare odd ratios of PWAGs versus matched controls, with a significance level of $\alpha = 0.05$ and two-sided $p$ values. Statistical analysis was performed with Stata 16.0 (StataCorp; College Station, Texas). The Institutional Review Board at Columbia University Irving Medical Center approved this study.

## Results

Between July 1, 2011 and July 1, 2019, 2223 pregnant women received obstetric care at the Manhattan MFM practice, of whom 1725 (77%) responded to the intake form's dietary restrictions question. The most common responses were: no dietary restriction ($n = 1127$; 66%); gluten-/wheat-/starch-free ($n = 106$; 6.2%); lactose-/milk-/

dairy-free ($n=101$, 5.9%); kosher ($n=73$, 4.3%); and vegetarian ($n=72$; 4.2%).

Review of these antenatal intake forms, along with dietary orders during L&D admission, yielded 245 women with gluten restriction: 38 women by intake form only, 69 by dietary order only, and 138 by both. Upon chart review, 37 were excluded for CD and one for dermatitis herpetiformis; an additional 58 were excluded for history, serology, or biopsy that did not definitively rule out CD. Of these 149 PWAGs admitted for L&D, ten were excluded for twins and one for triplets, yielding 138 PWAGs with singleton gestations.

PWAGs and their age-, race-, and ethnicity-matched controls were predominantly white (67%) and non-Hispanic (67%), with a mean age of 36.6 years (SD 5.3) at admission (Table 1). Most PWAGs and controls had commercial insurance (93.5 vs. 95.7%), with no differences in overall insurance type or length of stay. Compared to matched controls, PWAGs were more likely to adhere to a lactose-/milk-/dairy-free diet (36 vs. 0%; $p<0.0005$), and less likely to adhere to a vegetarian (4.0 vs. 15%; $p=0.013$) or Kosher diet (4.0 vs. 12%; $p=0.041$).

Among PWAGs, BMI was marginally lower pre-pregnancy (24.0 vs. 25.2; $p=0.072$) and significantly lower peripartum (28.3 vs. 29.6; $p=0.045$) than controls. Pregravid weight, peripartum weight, weight gain, and appropriateness of weight gain were similar.

PWAGs had fewer pregnancies, ($p=0.005$), term births ($p<0.0005$), and living children ($p<0.0005$), with no differences in preterm births, spontaneous abortions, or elective abortions.

PWAGs were more likely than controls to have hypothyroidism (25% vs. 10%; $p=0.001$) and IBS (8.7% vs. 1.5%; $p=0.019$), with similar but nonsignificant trends for lupus (2.2% vs. 0.7%; $p=0.34$) and IBD (2.9% vs. 0%; $p=0.12$; Table 2). Rates of obesity, hypertension, diabetes, depression, anxiety, and chronic anemia did not differ.

There were no differences between groups in any obstetric characteristics (Table 3), although PWAGs had a lower rate of postpartum depression that neared statistical significance ($p=0.056$). Delivery type and indication were similar between groups.

Hemoglobin was similar between groups during the first trimester (12.6 vs. 12.4; $p=0.36$), higher among PWAGs during the second trimester (11.5 vs. 11.2; $p=0.018$), and again similar at delivery (12.1 vs. 12.0; $p=0.31$; Table 4). Compared to controls, PWAGs had higher MCV (90.1 vs. 88.7; $p=0.043$) and marginally lower RDW (13.9 vs. 14.1; $p=0.097$).

There was no difference between groups for any neonatal characteristics or outcomes, nor for a composite of neonatal complications (44.2% in PWAGs vs. 42.8% in controls, $p=0.85$; Table 5).

## Discussion

In this retrospective cohort study, gluten was the most common dietary restriction in pregnancy, and most pregnant women who avoided gluten (61%) did not have CD. Compared to pregnant women of the same age, race, and ethnicity, PWAGs had fewer pregnancies, term births, and living children, lower delivery BMI, and higher rates of hypothyroidism and IBS, but no differences in obstetric or neonatal characteristics, suggesting that a GFD may be safe in pregnancy.

Of women completing antenatal intake forms at the MFM practice, 6.2% reported gluten restriction—more than triple recent estimates in the general population [1]. This cohort's high rate of gluten avoidance may reflect a continued rise in the popularity of the GFD, obstetric patient affiliations with our institution's Celiac Disease Center, or the pervasiveness of the GFD in New York City, particularly among patients seeking medical care in midtown Manhattan.

At delivery, subjects' mean age was 36.6 years, and for first-time mothers was 36.2 years, which is considerably older than the age at first birth nationally (26.8) [11] and in Manhattan (31.1) [12]. Specialty MFM centers attract women with more comorbidities, which correlate with increasing age, but the mean age among PWAGs was greater than our center's average L&D age (30.4), suggesting that women who avoid gluten become pregnant later, similar to women with CD [13].

In this same time period, the makeup of our hospital's L&D patients was 34% white and 36% non-Hispanic, compared to 67 and 67% of PWAGs admitted to L&D, respectively. This concurs with Choung et al.'s analysis of National Health and Nutrition Examination Surveys [1], Blackett et al.'s study of hospitalized patients [2], and Laszkowska et al.'s investigation of online search trends [14] that PWAGs are disproportionately white. Commercial insurance, a proxy for higher socioeconomic status in the USA, was similar between PWAGs and controls. Similarly, Choung et al. found no correlation between GFD adherence and socioeconomic status; in contrast, Blackett et al. reported higher rates of commercial insurance among PWAGs than controls, but they matched by age and sex only. By using race and ethnicity to match our PWAGs, who were predominantly white and non-Hispanic and therefore more likely to be commercially insured, we likely inflated the rate of commercial insurance among controls.

Remarkably, more than one-third of PWAGs reported other dairy restrictions, compared to zero controls. Undiagnosed CD could produce secondary lactose intolerance in some PWAGs; more likely, these patients' gastrointestinal symptoms led them to restrict multiple foods. Gluten avoidance has been associated with restriction of other

**Table 1** Demographic characteristics for PWAGs versus controls

| Characteristic | PWAGs ($n=138$) | Control ($n=138$) | $p$ value |
|---|---|---|---|
| Age (years) | 36.6 (STD 5.3) | 36.6 (STD 5.3) | 0.99 |
| Race | | | |
| Asian | 5 (3.6%) | 5 (3.6%) | 1 |
| Black | 6 (4.4%) | 6 (4.4%) | |
| White | 92 (66.7%) | 92 (66.7%) | |
| Other/decline/unknown | 35 (25.4%) | 35 (25.4%) | |
| Ethnicity | | | |
| Hispanic | 4 (2.9%) | 4 (2.9%) | 1 |
| Non-Hispanic | 93 (67.4%) | 93 (67.4%) | |
| Unknown/decline | 41 (29.7%) | 41 (29.7%) | |
| Primary insurance | | | |
| Commercial | 129 (93.5%) | 132 (95.7%) | 0.57 |
| Medicare/medicaid | 6 (4.4%) | 5 (3.6%) | |
| Self-pay/none | 3 (2.2%) | 1 (0.7%) | |
| Other dietary restrictions | | | |
| Vegetarian | 4 (4.0%) | 8 (15.4%) | 0.013 |
| Kosher | 4 (4.0%) | 7 (12.7%) | 0.041 |
| Dairy-free | 38 (36.2%) | 0 (0%) | 0.000 |
| Pregravid BMI | | | |
| Unknown | 14 (10.1%) | 17 (12.3%) | 0.35 |
| 15–19.9 | 18 (13.0%) | 17 (12.3%) | |
| 20–24.9 | 71 (51.5%) | 55 (39.9%) | |
| 25–29.9 | 23 (16.7%) | 28 (20.3%) | |
| 30–34.9 | 6 (4.4%) | 14 (10.1%) | |
| 35–39.9 | 3 (2.2% | 5 (3.6%) | |
| >40 | 3 (2.2%) | 2 (1.5%) | |
| Mean pregravid BMI | 24.0 (STD 5.1) $n=124$ | 25.2 (STD 5.3) $n=121$ | 0.073 |
| Gravidity | | | |
| 1 | 55 (39.9%) | 35 (25.4%) | 0.005 |
| 2 | 35 (25.4%) | 38 (27.5%) | |
| 3 | 31 (22.5%) | 27 (19.6%) | |
| 4 or more | 17 (12.3%) | 38 (27.5%) | |
| Term births | | | |
| 0 | 91 (65.9%) | 61 (44.2%) | |
| 1 | 39 (28.3%) | 46 (33.33%0 | 0.000 |
| 2 | 5 (3.6%) | 12 (8.7%) | |
| 3 | 1 (0.7%) | 7 (5.1%) | |
| 4 or more | 2 (1.4%) | 12 (8.7%) | |
| Preterm births | | | |
| 0 | 135 (97.8%) | 129 (93.5%) | 0.087 |
| 1 | 1 (0.7%) | 8 (5.8%) | |
| 2 | 1 (0.7%) | 1 (0.7%) | |
| 3 | 1 (0.7%) | 0 (0%) | |
| Spontaneous abortions | | | |
| 0 | 91 (65.9%) | 87 (63.0%) | 0.828 |
| 1 | 33 (23.9%) | 33 (23.9%) | |
| 2 | 8 (5.8%) | 12 (8.7%) | |
| 3 or more | 6 (4.3%) | 6 (4.3%) | |

**Table 1** (continued)

| Characteristic | PWAGs ($n=138$) | Control ($n=138$) | $p$ value |
|---|---|---|---|
| Elective abortions | | | |
| 0 | 113 (81.2%) | 111 (80.4%) | 0.835 |
| 1 | 20 (14.5%) | 19 (13.8%) | |
| 2 | 4 (2.9%) | 7 (5.1%) | |
| 3 | 1 (0.7%) | 1 (0.7%) | |
| Living children | | | |
| 0 | 94 (68.1%) | 63 (45.7%) | 0.000 |
| 1 | 35 (25.4%) | 41 (29.7%) | |
| 2 | 6 (4.3%) | 14 (10.1%) | |
| 3 | 1 (0.7%) | 9 (6.5%) | |
| 4 or more | 2 (1.4%) | 11 (8.0%) | |
| Mean length of stay (days) | 3.84 (STD 3.4) | 3.78 (STD 4.5) | 0.55 |

**Table 2** Medical comorbidities for PWAGs versus controls

| Comorbidity | PWAGs ($n=138$) | Control ($n=138$) | OR | 95% confidence interval (CI) | $p$ value |
|---|---|---|---|---|---|
| Obesity | 8 (5.8%) | 17 (12.3%) | 0.47 | 0.20–1.09 | 0.079 |
| Hypertension | 5 (3.6%) | 6 (4.4%) | 0.83 | 0.25–2.73 | 0.76 |
| Type 1 diabetes | 0 (0%) | 0 (0%) | Unable to calculate | | |
| Type 2 diabetes | 1 (0.7%) | 1 (0.7%) | 1 | 0.06–15.99 | 1 |
| Lupus | 3 (2.2%) | 1 (0.7%) | 3 | 0.31–28.84 | 0.34 |
| Hypothyroidism | 34 (24.6%) | 14 (10.1%) | 3.22 | 1.53–6.81 | 0.001 |
| IBD | 4 (2.9%) | 0 (0%) | Unable to calculate | | |
| IBS | 12 (8.7%) | 2 (1.45%) | 6 | 1.34–26.81 | 0.019 |
| Autism | 0 (0%) | 0 (0%) | Unable to calculate | | |
| Depression | 15 (10.9%) | 21 (15.2%) | 0.68 | 0.34–1.39 | 0.29 |
| Anxiety | 23 (16.7%) | 20 (14.5%) | 1.18 | 0.62–2.25 | 0.62 |
| Chronic anemia | 7 (5.1%) | 7 (5.1%) | 1 | 0.32–3.1 | 1 |

foods [15], which may reflect a growing enthusiasm for elimination diets, in which one abstains from one or more foods (such as dairy, gluten, eggs, or soy) to identify food sensitivities and avoid their perceived effects.

With PWAGs representing 61% of all pregnant women who avoid gluten, we add to a body of evidence that most people who avoid gluten do not have CD. Because this study is retrospective, we do not know patients' individual reasons for gluten restriction; however, most PWAGs had no identifiable medical indication for this diet. Some people may avoid gluten due to presumed non-celiac gluten sensitivity (NCGS), a controversial syndrome of unclear pathophysiology [16, 17], CD-like symptomatology [18], and vague diagnostic criteria [19]. Even in healthy individuals, as many as one-third of people believe a GFD can aid in weight loss, digestive health, skin health, and overall health [20], despite little evidence supporting these claims. In healthy individuals, gluten may alter the human gut microbiome [21] but, in the only double-blind randomized control trial of asymptomatic individuals to date, gluten or gluten restriction had no effect on abdominal pain, reflux, indigestion, diarrhea, constipation, or fatigue [22].

As noted previously, the well-documented nutritional differences of a GFD appear to have physiologic effects. Observational studies link a GFD to higher HDL, lower iron, and lower BMI [4, 5], lower serum folate and hemoglobin, higher CRP, lower rates of hypertension, and higher rates of thyroid disease [5]. From randomized controlled trials, results are mixed, with: no impact on healthy athletes' performance, gastrointestinal symptoms, well-being, intestinal injury or inflammatory markers; [23] reduced waist circumference and improved glycemic control and triglyceride levels among patients with metabolic syndrome; [24] and increased hemoglobin, MHC, MCHC, HDL, and total cholesterol, and decreased RDW, B12, and systolic blood pressure in healthy subjects [25].

We investigated many of these factors in pregnancy, finding that hypothyroidism was three times more common

**Table 3** Pregnancy characteristics for PWAGs versus controls

| Characteristic | PWAGs ($n=138$) | Control ($n=138$) | $p$ value |
|---|---|---|---|
| Pregravid BMI | 24.0 (STD 5.1) $n=124$ | 25.2 (STD 5.3) $n=121$ | 0.072 |
| Delivery BMI | 28.3 (STD 4.9) $n=137$ | 29.6 (STD 5.6) $n=134$ | 0.045 |
| Pregravid weight (kg) | 64.8 (STD 14.3) $n=124$ | 66.7 (STD 13.6) $n=121$ | 0.30 |
| Delivery weight (kg) | 76.7 (STD 14.0) $n=137$ | 78.5 (STD 15.2) $n=134$ | 0.30 |
| Mean gestational weight gain (kg) | 12.4 (STD 4.5) $n=124$ | 11.9 (STD 6.1) $n=118$ | 0.51 |
| Appropriate weight gain | | | |
| Inadequate | 37 (29.8%) $n=124$ | 44 (37.3%) $n=118$ | 0.30 |
| Appropriate | 50 (40.3%) $n=124$ | 37 (31.4%) $n=118$ | |
| Excessive | 37 (29.8%) $n=124$ | 37 (31.4%) $n=118$ | |
| Type of delivery | | | |
| NSVD | 78 (56.5%) | 80 (58.0%) | 0.78 |
| C-section | 55 (39.9%) | 51 (37.0%) | |
| Vacuum or forceps | 5 (3.6%) | 7 (5.1%) | |
| Indication for delivery | | | |
| Full term | 80 (58.0%) | 86 (62%) | 0.11 |
| Fetal | 25 (18.1%) | 20 (14.5%) | |
| Maternal | 10 (7.2%) | 16 (11.6%) | |
| Maternal/fetal | 14 (10.1%) | 9 (6.5%) | |
| Placental | 3 (2.2%) | 5 (3.6%) | |
| Preterm labor | 6 (4.3%) | 2 (1.4%) | |
| Obstetric comorbidities | | | |
| Gestational hypertension | 4 (2.9%) | 6 (4.4%) | 0.52 |
| Preeclampsia | 9 (6.5%) | 8 (5.8%) | 0.80 |
| Gestational diabetes | 10 (7.3%) | 16 (11.6%) | 0.22 |
| Postpartum depression | 1 (0.7%) | 6 (4.4%) | 0.056 |
| Postpartum transfusion requirement | 5 (3.6%) | 10 (7.3%) | 0.18 |

**Table 4** Maternal laboratory findings for PWAGs versus controls

| Laboratory finding | PWAGs ($n=138$) | Control ($n=138$) | $p$ value |
|---|---|---|---|
| Hemoglobin | | | |
| At first trimester | 12.6 (STD 1.07) $n=116$ | 12.4 (STD 1.01) $n=111$ | 0.36 |
| At second trimester | 11.5 (STD (0.95) $n=124$ | 11.2 (STD 1.1) $n=121$ | 0.018 |
| At delivery | 12.1 (STD 1.1) $n=138$ | 12.0 (1.2) $n=137$ | 0.31 |
| MCV at delivery | 90.1 (STD 5.7) $n=138$ | 88.7 (STD 6.3) $n=137$ | 0.043 |
| RDW at delivery | 13.9 (STD 1.2) $n=138$ | 14.1 (STD 1.5) $n=137$ | 0.097 |

and IBS six time more common in PWAGs. Blackett et al., whose study included 42 of our 138 patients, similarly reported higher rates of hypothyroidism and IBS among all hospitalized PWAGs, along with higher rates of IBD and lupus, for which our associations did not reach statistical significance [2]. The prevalence of these diseases among PWAGs may reflect a public perception that gluten intrinsically increases inflammation and gastrointestinal symptoms, prompting individuals with these issues to avoid gluten. We did not corroborate their findings that PWAGs have lower rates of hypertension and diabetes, perhaps because these diseases are comparatively uncommon in pregnancy; moreover, we found no differences in rates of gestational hypertension, preeclampsia, or gestational diabetes.

Gluten's role in mood regulation has become a popular press topic, with a recent meta-analysis demonstrating that a GFD improved, and a gluten challenge worsened, depression symptom scores among patients with NCGS [26]. In Blackett et al. PWAGs were more likely to be prescribed an antidepressant but not more likely to be diagnosed with depression. We found no difference in rates of depression or anxiety between groups. PWAGs did trend toward a lower rate of postpartum depression compared to controls (0.7% vs. 4.4%; $p=0.056$); although this may be attributable to the purported mood-modulating effects of a GFD,

**Table 5** Newborn outcomes for PWAGs versus controls

| Outcome | PWAGs ($n=138$) | Control ($n=138$) | OR | 95% CI | $p$ value |
|---|---|---|---|---|---|
| Gestational age at delivery (weeks) | 38.6 (STD 3.0) | 38.5 (STD 2.9) | | | 0.88 |
| Birth weight (kg) | 3.17 (STD 0.6) | 3.15 (STD 0.7) | | | 0.83 |
| Low birth weight | 16 (11.6%) | 18 (13.0%) | 0.87 | 0.41–1.82 | 0.71 |
| 1-min APGAR < 7 | 8 (5.8%) | 14 (10.1%) | 0.57 | 0.24–1.36 | 0.21 |
| 5-min APGAR < 7 | 3 (2.2%) | 6 (4.4%) | 0.50 | 0.13–2.00 | 0.33 |
| Neural tube defect (NTD) | 0 (0%) | 1 (0.7%) | Unable to calculate | | |
| Major fetal malformation | 4 (2.9%) | 9 (6.5%) | 0.44 | 0.14–1.44 | 0.18 |
| Stillbirth | 1 (0.7%) | 1 (0.7%) | 1 | 0.06–15.99 | 1 |
| Perinatal demise | 2 (1.5%) | 3 (2.2%) | 0.67 | 0.11–3.99 | 0.66 |
| Intrauterine fetal demise | 1 (0.7%) | 3 (2.2%) | 0.33 | 0.035–3.20 | 0.34 |
| Neonatal demise | 1 (0.7%) | 0 (0%) | Unable to calculate | | |
| Preterm birth | 21 (15.2%) | 19 (13.8%) | 1.13 | 0.57–2.27 | 0.72 |
| Intrauterine growth restriction | 4 (2.9%) | 7 (5.1%) | 0.57 | 0.17–1.95 | 0.37 |
| Small for gestational age | 5 (3.6%) | 6 (4.4%) | 0.83 | 0.25–2.73 | 0.76 |
| Large for gestational age | 6 (4.4%) | 8 (6.5%) | 0.67 | 0.24–1.87 | 0.44 |
| Macrosomia | 7 (5.1%) | 11 (8.0%) | 0.64 | 0.25–1.64 | 0.35 |
| Hypoglycemia | 4 (3.1%) $n=131$ | 6 (4.4%) $n=135$ | 0.80 | 0.21–2.98 | 0.74 |
| Hyperbilirubinemia | 16 (12.2%) $n=131$ | 15 (11.1%) $n=135$ | 1.23 | 0.59–2.56 | 0.58 |
| Jaundice | 29 (22.1%) $n=131$ | 29 (21.5%) $n=135$ | 1.09 | 0.61–1.98 | 0.76 |
| Neonatal ICU admission | 25 (18.1%) | 21 (15.2%) | 1.27 | 0.64–2.49 | 0.49 |
| Respiratory distress syndrome | 10 (7.6%) $n=131$ | 7 (5.2%) $n=135$ | 1.43 | 0.54–3.75 | 0.47 |
| Any neonatal complication | 61 (44.2%) | 59 (42.8%) | 1.05 | 0.67–1.65 | 0.82 |

basing this conclusion on a small, statistically insignificant difference would be premature.

No fetal outcomes were associated with maternal gluten avoidance. Given that the typical GFD is low in folate [7], possibly because folate fortification regulations exempt nearly all gluten-free flours [27], we hypothesized that folate consumption among PWAGs may be inadequate, which may increase the risk of neural tube defects (NTDs), a rare but highly morbid fetal malformation. Supporting this, a recent study of more than 10,000 women showed that those on a low-carbohydrate diet had 30% more NTDs among their offspring, which the authors ascribed to low fortified grain intake [28]. Our small study was unlikely to reveal differences in NTD prevalence, which affect fewer than 1 in 1000 births. We did assess for micronutrient-deficiency anemia, but too few patients had iron, folate, or cobalamin labs to draw meaningful conclusions. While rates of chronic anemia were identical between groups, PWAGs had slightly higher second trimester hemoglobin, which is surprising given previous studies linking a GFD to anemia [5, 18]. PWAGs did have greater MCV, possibly reflecting macrocytosis due to B vitamin deficiency, as may be seen with a GFD [6]. The MFM practice recommends prenatal supplements of folate and iron to all its pregnant patients, but assessment of supplement adherence may have clarified these differences.

Only one study has investigated fertility in PWAGs, reporting a case of successful conception after a woman and her partner began a GFD [29]. Interestingly, our PWAGs had significantly fewer prior pregnancies, term births, and living children than controls, but no difference in abortions. This may further distinguish PWAGs from CD patients who, compared to non-celiac controls, have been shown to have fewer pregnancies, more spontaneous abortions, and more stillbirths prior to, and similar rates after, CD diagnosis (and, presumably, initiation of a GFD) [30]. From our findings, it would be premature to conclude that gluten avoidance reduces fertility among PWAGs. Perhaps, correlating with higher education levels and socioeconomic status, PWAGs begin childrearing later in life (similar to CD patients [13]) or have fewer offspring. Alternatively, women may be less likely to restrict gluten after having multiple children.

This study is limited by its observational nature; we can merely speculate if between-group differences stem from diet or other factors underlying gluten avoidance, particularly since PWAGs evidently have greater-than-average means, education, and healthcare access. A randomized control trial would best elucidate causality between maternal–fetal variables and gluten restriction, but such a trial may be impractical and controversial to conduct in pregnant women. Our subjects were largely drawn from a single-center serving a unique demographic population, limiting

generalizability. We intentionally excluded all multiple gestations because of higher complication rates with these pregnancies, and unavoidably excluded pregnancies that were not carried to delivery (i.e., elective terminations and spontaneous abortions). We were unable to determine the duration of patients' gluten restriction, which could correlate with certain outcomes, and categorized diets using intake forms and dietary orders, which may oversimplify dietary habits. Finally, we relied on the EMR, which may be inaccurate and incomplete (for instance, if patients had positive CD testing with outside providers).

Future work may include qualitative assessment of the reasons for pregnant PWAGs' gluten avoidance to better understand this diet's popularity, as well as dietary assessment tools to better characterize nutritional intake across pregnancy. Follow-up with the PWAGs may prove valuable, particularly regarding the diets that the children of PWAGs maintain. In recent mouse and human studies, a GFD during pregnancy reduced the rate of type 1 diabetes in offspring [9, 31]; this and other long-term health outcomes should be the focus of subsequent studies.

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## Compliance with Ethical Standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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