CE 2.1 ANCC Contact Hours

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Celiac Disease and Preterm and/or Low Birthweight Births

Abstract

Celiac disease (CD) is a genetically determined autoimmune condition, with an estimated worldwide prevalence of 1%. CD may be diagnosed or undiagnosed, but is usually identified through tests of specific antibodies and duodenal endoscopy. Treatment is the elimination of gluten from the diet. This article reviews six studies examining the relationship between CD and preterm (PTB) and/or low birth weight (LBW) births. Women previously identified with CD had pregnancy outcomes similar to women without CD. Undiagnosed CD, however, was associated with LBW in four of the six studies, and PTB in two studies. No increase in PTB or LBW birth was found in two studies. In these review of the literature, undiagnosed CD was most likely to result in increased risk of PTB or LBW. Nurses, nurse midwives, and nurse practitioners can play an important role in identifying and educating women with CD in the preconception and prenatal periods as well as during well woman health visits to potentially reduce PTB and LBW births in women with CD.

Key words: Celiac disease; Gluten; Low birthweight; Preterm birth; Small for gestational age.

Preterm (PTB) and low birth weight (LBW) births continue to be major factors in high rates of infant mortality and morbidity. One potential predisposing factor, identified in several studies from throughout the world but rarely discussed is celiac disease (CD), particularly undiagnosed CD. The purpose of this article is to

- Describe CD
- Provide current information about symptomatology, diagnosis, and treatment challenges
- Describe studies linking CD with PTB and LBW births
- Discuss strategies that nurses might utilize to identify and assist women with CD, to have an improved pregnancy outcome
- Widespread screening
- The role of nurses, nurse practitioners, and nurse midwives

What is CD?

CD is an autoimmune disorder in which the immune system mistakenly attacks and destroys healthy body tissue, the lining of the duodenum in the instance of CD, when wheat, barley, or rye is ingested (Kurppa, Collin, Mäki, & Kaukinen, 2011). As a result there is atrophy of the intestinal villi and subsequently the loss of the ability to absorb nutrients. As in all autoimmune diseases, there is a link between autoimmune disease factors and the environment. The gene will not be expressed unless it is triggered by something in the environment. For this reason, although the gene is present in an individual it may not be expressed for many years.

CD is twice as frequent in women as men (Megiorni et al., 2008). Throughout the world, it is estimated that approximately 1% of the population has CD, many of whom are undiagnosed. (Catassi & Fasano, 2008). Certain groups are at increased risk. In a study in the United States of 13,145 patients, prevalence was 1:22 in first-degree relatives (parents, siblings); 1:39 in second-degree relatives (cousins aunts, uncles) of persons with CD; and 1:56 in persons who were symptomatic. The prevalence was 1:33 for persons in none of these categories (Fasano et al., 2003).

CD is an example of the "iceberg model" of disease in that classical symptoms represent the tip of the iceberg and less typical, more subtle symptoms are often unrecognized (Rubio-Tapio et al., 2009). The iceberg effect makes the estimation of prevalence, as well as diagnosis, more difficult.

Symptoms, Diagnosis, and Treatment

Symptoms are diverse (Table 1) and many are associated with a number of conditions other than CD. Symptoms vary widely among individuals; an individual may have a single symptom or several. Some symptoms such as chronic diarrhea or foul smelling stools may bring women to a nurse, midwife, nurse practitioner, or physician. Other symptoms, such as anemia and weight loss, may be recognized during health visits through history and/or laboratory studies.

It is estimated that approximately 1% of persons in the world have CD.

The definitive diagnosis of CD is made through blood tests for the specific antibodies, followed by duodenal biopsy for confirmation if the blood test(s) is positive. There are two blood tests, one for anti-tissue transglutaminase antibodies (fTGA) and one for antiendomysial antibodies (EMA), which are most commonly used. Between 2% and 3% of persons with CD are deficient in IgA. Serum tests for CD utilize IgA, therefore IgA screening tests for CD will be negative in IgA-deficient persons even if CD is present. If CD is still suspected because of symptoms, blood IgG-ftG or DGP-IgG can be measured (National Institutes of Health Celiac Disease Awareness Campaign, 2009).

Treatment for CD is the total elimination of the damaging gluten found in wheat, rye, and barley from the diet. The presence of these food substances is often unrecognized without a careful reading of food ingredients on labels. Corn and rice also contain gluten but it is of a different biochemical structure and is not harmful to

Table 1: Potential Symptoms of CD

- Abdominal pain and bloating
- Pale, foul smelling stool
- Chronic diarrhea
- Vomiting and/or constipation
- Weight loss
- Iron deficiency anemia
- Osteoporosis, bone pain, arthritis
- Chronic fatigue
- Depression and/or anxiety
- Reproductive symptoms in women
  - Delayed menarche
  - Early menopause
  - Secondary amenorrhea
  - Unexplained infertility
  - Recurrent early pregnancy loss
  - Fetal growth restriction/lower birthweight
  - Menstrual cycle irregularities

This table includes information from the following sources, Walker and Murray (2011); National Center for Clinical Excellence Guidelines (2009); Martinelli, Fortunato, Tafuri, Germinario, and Prato (2010).

Table 2: Summary of Studies Included in Review

GRECO ET AL. (2004) Italy

Design: Prospective

Purpose: To examine the relationship between undiagnosed CD and unfavorable pregnancy outcome

Sample: 5,055 obstetrical patients in a regional network (95% of population); 12 additional women with known CD to give prevalence rate of 1:80

Methods: All subjects received antibody testing to identify previously undiagnosed CD

Results: 51 women positive for CD; 4,997 negative. Undiagnosed CD was not associated with an increase in PTB, small birthweight, or IUGR

KHASHAN ET AL. (2010) Denmark

Design: Retrospective population-based cohort study

Purpose: To assess the effect of treated and untreated CD during pregnancy on birthweight, SGA, and PTB

Sample: All singleton births in Danish Medical Birth Registry, 1979–2004

1,105 women with diagnosed (treated) CD; 346 women with undiagnosed (untreated) CD at the time of pregnancy; 1,502,821 women without CD

Methods: Record review

Results: Infants born to women undiagnosed at the time of pregnancy but diagnosed postbirth: SGA, OR = 1.31; 95% CI = 1.06–1.68; VSGA, OR = 1.54; 95% CI = 1.17–2.03; PTB OR = 1.33; 95% CI = 1.02–1.72. Women with CD diagnosed before birth had outcomes similar to women without CD.

LUDVIGSSON ET AL. (2005) Sweden

Design: Retrospective cohort study

Purpose: To resolve inconsistencies due to low power in previous study

Sample: 2,087 women diagnosed with CD (1964–2001); 1,149 diagnosed prior to pregnancy; 929 diagnosed after birth (undiagnosed CD)

Methods: Record review using the Swedish National Birth Registry

Results: Undiagnosed CD associated with IUGR (OR = 1.62; 95% CI = 1.22–2.15); LBW (OR = 2.13; 95% CI = 1.32–2.17); VLBW (OR = 2.45; 95% CI = 1.35–4.43); PTB (OR = 1.71; 95% CI = 1.32–2.17). CD diagnosed before pregnancy not associated with these outcomes.

MCCARTHY ET AL. (2009) Ireland

Design: Retrospective cohort study

Purpose: To assess magnitude of LBW infants (<10th percentile) in women with undiagnosed CD

Sample: 270 women patients , Cork University Hospital, with CD confirmed by duodenal biopsy; a reference group of 214 women without CD attending gynecologic and family practice clinics in Cork

Methods: Women completed structured postal questionnaire; 63% response rate

Results: Women with undiagnosed CD had increased rate of LBW infants compared to reference group (OR = 2.45; 95% CI = 0.98–6.10).

OZGÖR, SELIMOĞLU, TEMEL, SEÇKIN, AND KAFKASLI (2011) Turkey

Design: Prospective

Purpose: To investigate the frequency of CD in mothers and fathers of PTB and LBW newborns

Sample: 316 parents of 164 PTB and LBW newborns and 246 parents of 123 healthy newborns

Methods: Antibody testing of parents postbirth; duodenal endoscopy, if positive

Results: CD in parents of PTB or LBW newborns not statistically higher than in the general population

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SALVATORE ET AL. (2007) Italy

Design: Prospective

Purpose: To examine the potential relationship between CD and PTB and SGA births

Sample: 1,714 parents: 868 mothers and 846 fathers

Methods: Review of 905 consecutive PTB infants; identify CD through antibody tests and duodenal biopsy

Results: Undiagnosed CD associated with increase in SGA births (OR = 6.97; 95% CI = 1.11–43.55) in comparison with mothers without CD. No increase in PTB

The definitive diagnosis of CD is made through blood tests for specific antibodies and duodenal biopsy for confirmation if blood tests are positive.

persons with CD. Gluten is also found in some herbal preparations, medications, and supplements as well as in certain nonfood substances including some toothpaste, lipstick, and other cosmetics.

Studies of the Association Between CD and PTB/LBW

The review question was: Is there a relationship between diagnosed and/or undiagnosed CD and PTB and/or LBW birth? Studies as well as review articles addressing the question were sought, first using the PubMed database and subsequently CINAHL. Search terms were celiac disease, celiac disease and pregnancy outcome, preterm birth, and low birthweight birth. Both review articles and research studies were examined for additional references. No additional references were found. Six studies were ultimately found that addressed the review question. Four studies found an association; two did not. These studies are summarized in Tables 2 and 3.

Table 3: Summary of Findings

Outcome Measured	Results
PTB	Two studies found increased rates of PTB in women with undiagnosed CD (Khashan et al., 2010; Ludvigsson et al., 2005) Two studies found no difference (Greco et al., 2004; Ozgör et al., 2011)
LBW, IUGR, SGA, VLBW, VSGA	Three studies found increases in LBW, IUGR, or SGA in women with undiagnosed CD (Ludvigsson et al., 2005; McCarthy et al., 2009; Salvatore et al., 2007). However, with CI of 0.98–6.10 the McCarthy study does not reach significance. One study found increase in VLBW (Ludvigsson et al. 2005); one study found increase in VSGA (Khashan et al., 2010), both in women with undiagnosed CD.
Other subjects	No increases in PTB or decreased birthweight were found in women diagnosed prior to pregnancy.

Acronyms: LBW, low birthweight; IUGR, intrauterine growth restriction; SGA, small for gestational age; VLBW, very low birthweight; VSGA, very small for gestations age.

Studies defined the term undiagnosed CD (also latent, untreated) differently to describe CD that is present but unrecognized. Several studies used existing data bases. Other studies began with PTB or LBW birth and then screened the mother using antibody testing followed by endoscopy if the antibody test was positive.

As Tables 2 and 3 indicate, both methodology and findings differ in these studies. In no study did women previously identified with CD experience an excess rate of LBW/PTB. One weakness in the retrospective studies that used data bases was the assumption that all previously diagnosed patients maintained a gluten-free diet. In a review of 38 studies in the United Kingdom, Hall, Rubin, & Charnock (2009) found rates for adherence to a gluten-free diet ranged from 42% to 91%. A study to assess compliance with a gluten-free diet in childbearing women previously diagnosed with CD would be useful.

None of the studies reviewed address the issue of how CD is related to pregnancy outcome. Freeman (2010) stated that there is limited information about this question. Possible answers include injury to maternal and fetal parts of the placenta, with placental compromise. This does not address the question of why the risks of pregnancy outcome differ between women with diagnosed and undiagnosed CD, clearly one for continuing research.

Screening for CD: A Viable Option?

Because four studies have indicated differences in outcomes in women with undiagnosed CD, principally in growth restriction and in PTB in one instance, the potential value of screening has been proposed in order to identify patients with undiagnosed CD. Duggan and Duggan (2009) believed that patients with unexplained symptoms related to CD (Table 1) should be considered for screening, as should patients who are at risk because of family history or associated conditions. Norström, Lindholm, Samdstrom, Nordyke, and Ivarssom (2011) in a Swedish study using a cross-sectional questionnaire of 1,560 randomly selected members of the Swedish Society for Celiacs, the mean delay from first symptoms to diagnosis was 9.7 years and from first doctor visit to diagnosis was 5.8 years, leaving a potentially large number of persons with undiagnosed CD. Identifying women

Suggested Clinical Applications

Although little has been said about nursing in any of the papers that were reviewed, a nurse, nurse practitioner, or midwife who cares for women has a unique opportunity to identify women with both diagnosed and undiagnosed CD and to assure that women with CD have the best of care. What can nurses and midwives do?

- Be knowledgeable about print and online resources for patients, their families, and healthcare providers (Table 4).
- Initiate discussions with colleagues of all disciplines to develop a plan of assessment and referral, in order to identify women with undiagnosed CD.
- When obtaining a health history, ask if there is a family history of CD. Not every patient will have or know of a family member with CD. However, the high prevalence rates for women with first-order or second-order relatives make it particularly important to identify them. Changing health history forms in an office or agency requires consensus among colleagues, but nurses can present the rationale for this change.
- Screening via blood tests may be indicated in women from high prevalence groups or women with symptoms (Duggan & Duggan, 2009).
- Women already diagnosed with CD should be assessed for any problems they may have in maintaining their diet. Nurses can be helpful to women with CD by knowing the resources available in the community, such as celiac support groups and stores with gluten-free products, as well as Web sites related to CD and/or gluten-free diets.
- A one page information sheet outlining important resources could be developed and made available to women.
- To aid clinical care, nurse researchers might choose to interview women with CD, both newly diagnosed and those with a long history of the condition to gather data that will increase the understanding of CD. Studies are needed to identify the length of time from earliest symptoms to diagnosis and the experiences of women during that time, as well as the experiences of women with a history of CD, both within the healthcare system and in their quality of life.

with a family history or symptoms can be rapid and cost-effective. There is not a consensus about screening, however. Greco et al. (2004) noted that screening has large public health significance, and as his study did not find CD associated with unfavorable outcomes, did not recommend screening. However, mass screenings are far different from targeted screenings of persons with symptoms and/or a strong family history.

Table 4: Resources for Healthcare Providers and Families with CD

National Organizations

Gluten Intolerance Group of North America
www.gluten.net

Celiac Disease Foundation
www.celiac.org/

Celiac Sprue Association
www.csaceliacs.org/

National Institute of Diabetes and Digestive, and Kidney Diseases, National Institutes of Health
http://niddk.nih.gov

Celiac Disease Awareness Campaign
www.digestive.niddk.nih.gov

Gluten Free Registry
www.glutenfreeregistry.com

The Role of Nurses and Nurse Midwives

Women previously diagnosed with CD should review their eating patterns with their nurse or nurse midwife as should newly diagnosed women. The basic dietary directions, to avoid foods and other products containing wheat, rye, or barley by carefully reading labels, can be provided by nurses as well as nutritionists. Printed materials, written at no more than the fourth grade level, and illustrated with pictures of food labels, are valuable. Once gluten ingestion is eliminated, symptoms often improve in 2–4 weeks. In most instances, the mucosa of the intestine heals in 6–12 months after the start of a gluten-free diet (Hancock & Koren, 2004).

Self care of persons with CD requires the ability to read, making limited health literacy a major challenge for women with low literacy. In 2003, approximately 80 million adults (36%) in the United States were reported to have limited literacy skills (Berkman et al., 2011). To help persons understand the importance and interpretation of food labels, the principles of healthcare literacy are essential. One of the most valuable tools is the "teach back." After discussing the identification of foods, ask the woman to tell you how she would identify foods at her grocery store or in a restaurant. A toolkit, Health Literacy Universal Precautions Toolkit (2010), published by the Agency for Healthcare Research and Quality, can be downloaded from www.ahrq.gov/qual/literacy

Limited economic resources are also a problem for some women. Gluten-free foods often cost more than other foods, whether in a grocery store or ordered over the internet. Accessibility of markets and restaurants can limit food choices for both women who live in rural areas or in inner city communities. If women with CD have access to the internet, gluten-free foods can be ordered that way. Whether in a restaurant, a church supper, or at the house of family or friends, eating away from home can

Currently the only treatment is the total elimination of the damaging gluten found in wheat, rye, and barley from the diet.

pose special difficulties. An increasing number of restaurants, both national chains and local restaurants, now have gluten-free menus. A Web site www.glutenfreeregistry.com, provides a map of the United States on which one can click first on a state and then on a city, and appropriate restaurants with gluten-free menus are listed. One can eat successfully in almost any restaurant, even fast food restaurants, by asking questions of the server or asking the server to check with the chef if they are unsure of the answer. Many restaurants have menus on their Web sites, which may assist women with CD in making decisions about where to eat before leaving for a restaurant.

Nurses, nurse midwives, and nurse practitioners have a major role to play in the care of women who have risk for CD or who have been diagnosed with the disease. Teaching women and their families about the illness and its consequences, as well as the dietary treatments necessary are two of the most important nursing interventions for women. ✣

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