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Gluten-free Adherence Triples While Celiac Disease Prevalence Remains Stable

Bianca Nogrady

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The number of people adhering to a gluten-free diet more than tripled between 2009 and 2014, despite the fact that the prevalence of celiac disease has remained largely stable over the same period, according to data from the National Health and Nutrition Examination Survey.

Hyun-seok Kim, MD, MPH, and colleagues from Rutgers New Jersey Medical School noted that the popular trend of gluten-free diets exceeds the numbers that would be solely attributable to an increasing prevalence of celiac disease.

In a recent report published online in *JAMA Internal Medicine*, researchers noted that of 22,278 persons ages 6 and older for whom data were available on celiac disease status and gluten-free diet status, 106 (0.69%) had a diagnosis of celiac disease, and 213 (1.08%) followed a gluten-free diet but did not have celiac disease.

At a US population level, this would correspond to an estimated 1.76 million individuals with celiac disease, and 2.7 million individuals without celiac disease who follow a gluten-free diet.

The prevalence of celiac disease ranged from 0.70% during 2009-2010 to 0.77% during 2011-2012 and 0.58% during 2013-2014 (*JAMA Intern Med.* 2016 Sept 6. doi: 10.1001/jamainternmed.2016.5254).

In contrast, the prevalence of a gluten-free diet without celiac disease increased from 0.52% during 2009-2010 to 0.99% during 2011-2012 and 1.69% during 2013-2014, although the increase was even greater among non-Hispanic whites.

"The two trends may be related because gluten consumption has been identified as a risk factor for celiac disease, such that steady or even decreasing gluten consumption may be contributing to a plateau in celiac disease," they reported.

The authors suggested that there were

VIEW ON THE NEWS
Gluten free without celiac should not be dismissed

Part of what may be driving this gluten-free diet trend is simply a belief, fueled by marketing and media, that these foods are healthier. However, surveys suggest that many individuals who adhere to a gluten-free diet believe that the exclusion of gluten has resulted in subjective health benefits, ranging from weight loss to reduced symptoms of inflammation and gastrointestinal distress. Because a gluten-free diet may have negative social, financial, and health repercussions, it is important for clinicians to understand whether the elimination of the protein gluten is responsible for symptom improvement, or whether following a gluten-free diet is simply a marker of other dietary choices that are creating positive effects. Although the choice to be gluten free may be driven in part by marketing and a misperception that gluten free is healthier, it is important that this choice not be dismissed as an unfounded trend except for those with celiac disease and wheat allergy.

Dr. Daphne Miller is from the Department of Family and Community Medicine at the University of California, San Francisco. The comments are taken from an editorial (*JAMA Intern Med*. 2016 Sept 6. doi: 10.1001/jamainternmed.2016.5271).

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a number of reasons why individuals without celiac disease might choose to follow a gluten-free diet. "The public perception is that gluten-free diets are healthier and may provide benefits to nonspecific gastrointestinal symptoms," they wrote, pointing out that gluten-free products are now also more widely available in supermarkets and online.

"There is also an increasing number of individuals with self-diagnosed gluten sensitivity, but not the typical enteropathic or serologic features of celiac disease, who have improved gastrointestinal health after avoidance of gluten-containing products."

The numbers of individuals in the survey with celiac disease or adhering to a gluten-free diet were relatively small, and diagnosis of celiac disease was not confirmed by intestinal biopsy, but instead based on serologic tests and prior diagnosis by a health professional.

Fluoxetine Appears Safer for Bone Health in At-risk Older Patients

Amy Karon

Older patients prescribed citalopram had almost 12-fold higher odds of hip osteoporosis compared with those prescribed fluoxetine, according to a large retrospective study at a tertiary bone health clinic.

Patients taking fluoxetine also had the lowest levels of C-terminal cross-linked telopeptide of type 1 collagen (CTX), a biochemical marker of bone turnover, reported Dr. Clodagh Power and associates at St. James's Hospital in Dublin.

Credit: Crevis / Shutterstock

Fluoxetine causes less bone resorption than other selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors, or tricyclic antidepressants and "may be a safer choice for a cohort already predisposed to poorer brain health," the researchers concluded in a poster presented at the 18th Congress of the International Psychogeriatric Association.

Poor bone health correlates with both antidepressant therapy and depression itself. In the case of antidepressants, tricyclics might increase the risk for falls and fractures by blocking α-adrenergic, H_1, and M_3 receptors, while SSRIs are thought to reduce bone mass through selective blockade of 5-HTT. To evaluate the relative effects of individual antidepressants, the investigators compared bone mineral densities, T-scores, fracture histories, and CTX levels among 522 patients on antidepressants with 1,056 randomly selected controls from the same bone health clinic who were not taking antidepressants. Average age of the entire cohort was 67, and 79% were female. Compared with controls, patients taking antidepressants tended to be older, had a 1.0 kg/m^2 greater average

mean BMI, and were more often women, the researchers noted.

Even after controlling for these differences, patients taking antidepressants had a 0.03 g/cm^3 lower average bone mineral density than controls, and 2.2-fold greater odds of prior hip fracture (odds ratio, 1.7-2.8). Even patients taking antidepressants who had never had a hip fracture had lower bone mineral density of the hip than controls (mean difference, 0.121 g/cm^3). No relationship, however, was found between antidepressant therapy and spinal bone mineral density.

Analyses of T-scores suggested that individual antidepressants have different effects on bone health. Mirtazapine had the highest estimated odds of hip osteoporosis (2.3), compared with controls. In descending order, the remaining odds ratios were 2.0 for citalopram, 1.5 for tricyclic antidepressants, 1.4 for sertraline, and 1.3 for escitalopram, but only the odds ratio for citalopram reached statistical significance. No apparent relationship was found between hip osteoporosis and exposure to paroxetine, venlafaxine, or duloxetine, while fluoxetine actually showed a protective effect (OR, 0.16).

Additional analyses supported the hypothesis that fluoxetine poses the least risk to bone health. In a head-to-head comparison, the odds of hip osteoporosis were 11.9 times higher among patients taking citalopram than those taking fluoxetine. Also, patients on fluoxetine had average CTX levels of 0.06, compared with 1.17 for controls.

These findings "add to prior data that implicate antidepressants as adversely impacting bone health," the researchers concluded, but the results also merit cautious interpretation, as "no single drug was identified as clearly causing a greater reduction in bone mineral density or increased risk of fracture."

Disclosures: The investigators disclosed no external funding sources or conflicts of interest.

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High Free T4 Levels Linked to Sudden Cardiac Death

Mary Ann Moon

Higher levels of free thyroxine (T4) are associated with an increased risk for sudden cardiac death, even in euthyroid adults, according to a recent report.

Thyroid dysfunction, even in the subclinical range, is known to correlate with increased cardiovascular disease, but a possible link between free T4 levels and sudden cardiac death (SCD) had never been explored in the general population until now. Any factors that could improve prediction of SCD in the general population would be helpful because almost half of these cases are the first indication that the patient had heart disease, said Layal Chaker, MD, of the Rotterdam Thyroid Center and the Departments of Internal Medicine and Epidemiology, Erasmus University, Rotterdam, and her associates.

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They assessed SCD among 10,318 participants in the Rotterdam Study, a prospective population-based cohort study examining endocrine, cardiovascular, neurologic, ophthalmologic, and psychiatric diseases

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in middle-aged and older adults in the Netherlands. Men and women ages 45 to 106 who had thyroid testing at baseline were followed for a median of 9.2 years (range, 4 to 21 years) for the development of SCD. There were 261 cases of SCD, and 231 of these occurred in euthyroid participants.

Higher levels of free T4 were associated with an increased risk for SCD, with a hazard ratio of 1.87 for every 1 ng/dL increase in free T4. When the analysis was confined to the 231 euthyroid participants, this correlation was even stronger (HR, 2.26) (*Circulation.* 2016 Sept 6. doi: 10.1161/CirculationAHA.115.020789).

The findings were similar in several sensitivity analyses, including one that excluded participants who had an unwitnessed SCD. Adjustment of the data to account for the presence or absence of diabetes, as well as exclusion of patients who had heart failure, did not significantly alter the risk estimates. The results were consistent across all age-groups and both sexes.

The exact mechanism for the association between free T4 and SCD is not yet known, but it appears to be independent of traditional cardiovascular risk factors. "Bigger sample size and more detailed data are needed to determine whether these associations share the same or have distinct pathways," Dr. Chaker and her associates concluded.

Disclosures: The Netherlands Organisation for Health Research and Development and Erasmus Medical Center supported the study. Dr. Chaker and her associates reported having no relevant financial disclosures.

Morning Sickness Linked to Lower Risk for Pregnancy Loss

Bianca Nogrady

Nausea and vomiting in early pregnancy were associated with a substantially reduced risk for pregnancy loss in a prospective preconception cohort of almost 800 pregnant women.

Although it has long been suggested that nausea is a sign of a healthy pregnancy, evidence supporting this idea has been limited.

"Much of the published literature reports on studies that enrolled women after a clinically recognized pregnancy, thereby failing to include women with early pregnancy losses or relying on participant recall of nausea and/or loss," wrote Stefanie N. Hinkle, PhD, of the Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, Maryland, and her colleagues.

In this study, the researchers examined data from 797 women with one or two prior pregnancy losses and a current pregnancy confirmed by an HCG pregnancy

VIEW ON THE NEWS
Valuable contribution to the literature

This study's contribution to the existing literature is valuable because investigators were able to compare nausea and vomiting among women who experienced an early pregnancy loss with those whose pregnancies continued. By collecting daily urine samples, it was possible to identify all pregnancies very early in gestation and thus definitively quantify the losses that occurred around the time of implantation, in addition to those that occurred after ultrasonography. As common as nausea and vomiting are in the first trimester, researchers and clinicians should be cautious about deeming it to have a protective effect against pregnancy loss. Although such a designation may provide reassurance to some women, they should not be discouraged from seeking treatment for a condition that can have a considerable negative effect on their quality of life.

Siripanth Nippita, MD, and **Laura E. Dodge,** ScD, are with the Department of Obstetrics and Gynecology at Beth Israel Deaconess Medical Center, Boston. These comments are adapted from an accompanying editorial (*JAMA Intern Med.* 2016 Sep 26. doi: 10.1001/jamainternmed.2016.6101).

test. They were all enrolled in a randomized clinical trial on the effects of aspirin on gestation and reproduction (*JAMA Intern Med*. 2016 Sep 26. doi: 10.1001/jamainternmed.2016.5641).

Participants kept a daily record of nausea and vomiting symptoms for gestational weeks 2-8 and then monthly after that. At week 12, 86% of the women reported nausea and 35% reported nausea with vomiting at least once a week in the previous four weeks.

Overall, women with nausea and vomiting in any given week had a 75% lower risk for pregnancy loss during that week (hazard ratio, 0.25), while those with only nausea had a 50% reduction in pregnancy loss (HR, 0.50), compared with women with neither symptom.

The researchers found a similar association among women who had a peri-implantation pregnancy loss, but it did not reach statistical significance. The hazard ratio was 0.59 for women who had nausea only and 0.51 for women who experienced nausea with vomiting.

In women who did not experience a peri-implantation pregnancy loss, nausea only and nausea with vomiting were associated with a 66% (HR, 0.44) and 80% (HR, 0.20) reduction in risk for pregnancy loss, respectively, compared with women with neither symptom. These reductions in risk were similar when the analysis was limited to first-trimester pregnancy loss and persisted even after accounting for lifestyle and fetal factors, such as number of prior pregnancy losses, BMI, fetal karyotype, and multiple fetal gestations.

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"These findings overcome prior analytic and design limitations and represent the most definitive data available, to our knowledge, indicating the protective association of nausea and vomiting in early pregnancy on the risk for pregnancy loss and thus may provide reassurance to women experiencing these difficult symptoms in pregnancy," researchers wrote.

Disclosures: The study was supported by the National Institutes of Health. The researchers reported having no financial disclosures.

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Anxiety, Depression May Precede Parkinson's by 25 Years

Amy Karon

Prodromal anxiety and depression are common in Parkinson disease and may develop years earlier than conventionally thought, according to data presented at the 2016 Congress of the International Psychogeriatric Association.

"In some cases, the psychiatric prodrome can appear 25 or more years earlier than the onset of motor symptoms," said Andreea Seritan, MD, a geriatric psychiatrist at the University of California, San Francisco (UCSF). Psychiatrists need to keep this fact in mind when treating patients with anxiety or depression, and refer them to a

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neurologist if they notice or are informed of motor symptoms, she emphasized.

Patients with Parkinson disease often have developed anxiety or depression before the onset of motor symptoms. Historically, this psychiatric prodrome was thought to begin anywhere from five to 10 years before motor symptoms, "depending on which expert you ask," Dr. Seritan said. But after observing that some of her Parkinson's patients reported decades-long histories of anxiety or depression, she and her colleagues reviewed medical charts for 39 patients ages 50 and older with confirmed Parkinson disease who were referred for psychiatric evaluation at the UCSF Movement Disorder and Neuromodulation Center in 2015 or 2016. A total of 28 patients (72%) were men, mean age at referral was 65, and the patients had been diagnosed with Parkinson disease an average of 12 years previously.

At referral, a total of 34 (87%) patients met *DSM-5* criteria for major depressive disorder, dysthymia, or an unspecified depressive disorder, while 68% met *DSM-5* criteria for generalized anxiety disorder, panic disorder, social anxiety disorder, or other anxiety disorders, Dr. Seritan said. About two-thirds of patients had comorbid depression and anxiety. Other *DSM-5* diagnoses included impulse control disorders (15% of patients), substance abuse disorders (13%), and mild (21%) or major (13%) neurocognitive disorders.

Exactly 50% of patients had depression preceding their Parkinson disease diagnosis, while 43% of patients had prodromal anxiety, Dr. Seritan and her colleagues determined. The average age of onset of psychiatric symptoms was in the 30s, but this ranged from childhood or adolescence into the 60s. Mean ages at Parkinson diagnosis were much later—58 for patients whose primary prodrome was anxiety and 56 for patients whose primary prodrome was depression.

The findings suggest that a decades-long prodrome of anxiety or depression is common in Parkinson disease. Psychiatrists should be alert to the possibility of Parkinson disease in patients with depression or anxiety, because individuals with movement disorders can be very susceptible to the side effects of antidepressants and antipsychotics, Dr. Seritan stressed. **CR**

Disclosures: Dr. Seritan reported no funding sources and had no conflicts of interest.

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