Researchers find increased intestinal permeability is precursor of celiac disease in pediatric study

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Researchers from Mass General for Children and Italy have identified a

potential biomarker preceding the development of celiac disease autoimmunity in children.

Using blood samples and environmental and other data from the 10-year, prospective Celiac Disease Genomic, Environmental, Microbiome and Metabolomic (CDGEMM) Study, researchers found an increase in intestinal permeability in children who develop celiac disease autoimmunity, a physiological precursor to celiac disease.

In the paper, "Zonulin as a Biomarker for the Development of Celiac Disease," published in *Pediatrics*, levels of the widely used marker of intestinal permeability were higher in a cohort of children at 18 months of age who subsequently went on to develop celiac disease.

"We know that intestinal permeability, as measured by zonulin levels, is increased in certain chronic inflammatory diseases, including Crohn's disease and type 1 diabetes," says Maureen Leonard, MD, MMSc, clinical director at the Center for Celiac Research and Treatment at Mass General for Children and senior author on the study.

"We saw a significant rise in the zonulin levels of children who were identified as at-risk of celiac disease in the period before they were diagnosed with celiac disease," says Leonard. "Our findings point toward the use of zonulin as a biomarker to screen children at-risk of celiac disease."

The group, which includes pediatric researchers from Salerno, Rome, Bari, and Genova, Italy, evaluated data from 102 children at-risk of celiac disease enrolled in the CDGEMM Study; 51 children had developed celiac disease autoimmunity and 51 children had not.

Along with serum zonulin measurements from the age of 12 months to onset of celiac disease autoimmunity or the corresponding time point in

control subjects, the group studied the influence of environmental factors on the levels of zonulin, including how often infants were administered antibiotics.

In the group that went on to develop celiac disease autoimmunity, researchers found an association between a greater number of courses of antibiotics and higher zonulin levels when compared to the control group .

Their findings showed a rise in zonulin in a subgroup of at-risk infants with a higher use of antibiotics before they developed celiac disease autoimmunity. The results align with findings from researchers in Denmark and Norway. In the paper, the authors call for "continued efforts to reduce unnecessary antibiotics to aid in future disease prevention."

The CDGEMM Study was founded at MGfC in 2013 by Alessio Fasano, MD, and Leonard to study the progression from genetic predisposition to celiac disease. Since then, more than 600 children and infants from the US and Italy with a first-degree relative with celiac disease have provided blood, stool and tissue samples along with extensive environmental and in-depth clinical information.

"Our goal is to break down the early steps in celiac disease autoimmunity—before celiac disease is fully progressed—in order to prevent its development," says Fasano, director of the Center for Celiac Research and Treatment. "We can achieve that goal by predicting who will develop celiac disease autoimmunity and taking steps to prevent that from occurring."

More information: Tracey M. DaFonte et al, Zonulin as a Biomarker for the Development of Celiac Disease, *Pediatrics* (2023). DOI: 10.1542/peds.2023-063050