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Antenatal Exposure to Antibiotics and the Risk of Childhood Celiac Disease: A Population-Based Study

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Background:

Celiac disease is characterized by immune reaction to ingested dietary gluten and villous atrophy. The composition of pioneer microbiota is vital in the immune development and studies have indicated that the infant microbiota has a maternal signature. Antibiotics during pregnancy could alter the infant the gut microbiota, thereby predisposing them to celiac disease development.

Objective:

The aim of our study was to evaluate the association between maternal antibiotic exposure during pregnancy and development of childhood celiac disease in their offspring.

Methods:

We performed a population-based cohort study using prescription records, hospitalization records and physician billing claims from mother-child dyads born in Manitoba between 1996 and 2012. Childhood celiac disease was defined as any hospitalization or ≥1 physician diagnosis identified using the ICD codes. Cox-regression was used, and the analysis was adjusted for a priori covariates to determine the association between exposure and outcome. Sensitivity analysis was used to determine the exclusivity of association by comparison against pre-pregnancy and post-pregnancy exposures.

Results:

Linkage was obtained between 213,661 mother-infant dyads among which 2,540 children had a diagnosis of Celiac disease. The incidence rate ratio (IRR) of celiac disease in children born to mothers who had prenatal exposure in comparison to non-exposed was 1.23 (95%CI:1.14-1.33). There was an evident dose-response relationship (1 course aHR: 1.45; 95%CI:1.32-1.59 vs. ≥3 courses aHR:2.40; 95%CI:2.08-2.77), but temporal gradient was absent (trimester 1 aHR:1.44; 95%CI:1.30-1.60 vs. trimester 3 aHR:1.33; 95%CI:1.19-1.48). Compared to the non-exposed group, children whose mothers were exposed to antibiotics during pre-pregnancy (aHR:1.68; 95%CI:1.55-1.82), pregnancy (aHR:1.59; 95%CI:1.46-1.71) and post-pregnancy period (aHR: 1.77; 95%CI:1.63-1.92) had a significantly higher event-rate for celiac disease development.

Conclusion:

The ambiguity in the risk associated with antibiotic exposure around the time of pregnancy and the lack of a temporal gradient indicate lack of association between maternal prenatal antibiotic exposure and childhood celiac disease.