Early Childhood Antibiotic Use Not Associated with Increased Celiac Disease Risk

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Key Findings:

- Children who receive antibiotics during the first year of life do not have an increased likelihood of celiac disease by age 6 compared to those who did not receive any antibiotics.

Celiac disease is a chronic autoimmune condition triggered by gluten ingestion.[1] Prior studies have speculated that early antibiotic use may disrupt the gut microbiome, potentially increasing susceptibility to autoimmune disorders, including celiac disease.[2,3] We aimed to understand the relationship between antibiotics given in early childhood and subsequent diagnoses of celiac disease.

We studied 597,531 children from birth through age 6 and categorized them based on the number of antibiotic courses the child received in the first year of life. We limited our analysis to antibiotics in the first year of life to avoid potential conflation with antibiotics often prescribed in later childhood as part of an assessment for celiac disease. We included patient demographics, gestational age and delivery method, frequency of outpatient care, number of first year infections, and maternal history of celiac disease in our analysis.

Overall, while antibiotic use was associated with a lower likelihood of being diagnosed with celiac disease by age 6, this result was only significant for those who had 3-5 prescriptions, as seen in Figure 1.

Celiac Disease Likelihood by Antibiotic Course Count

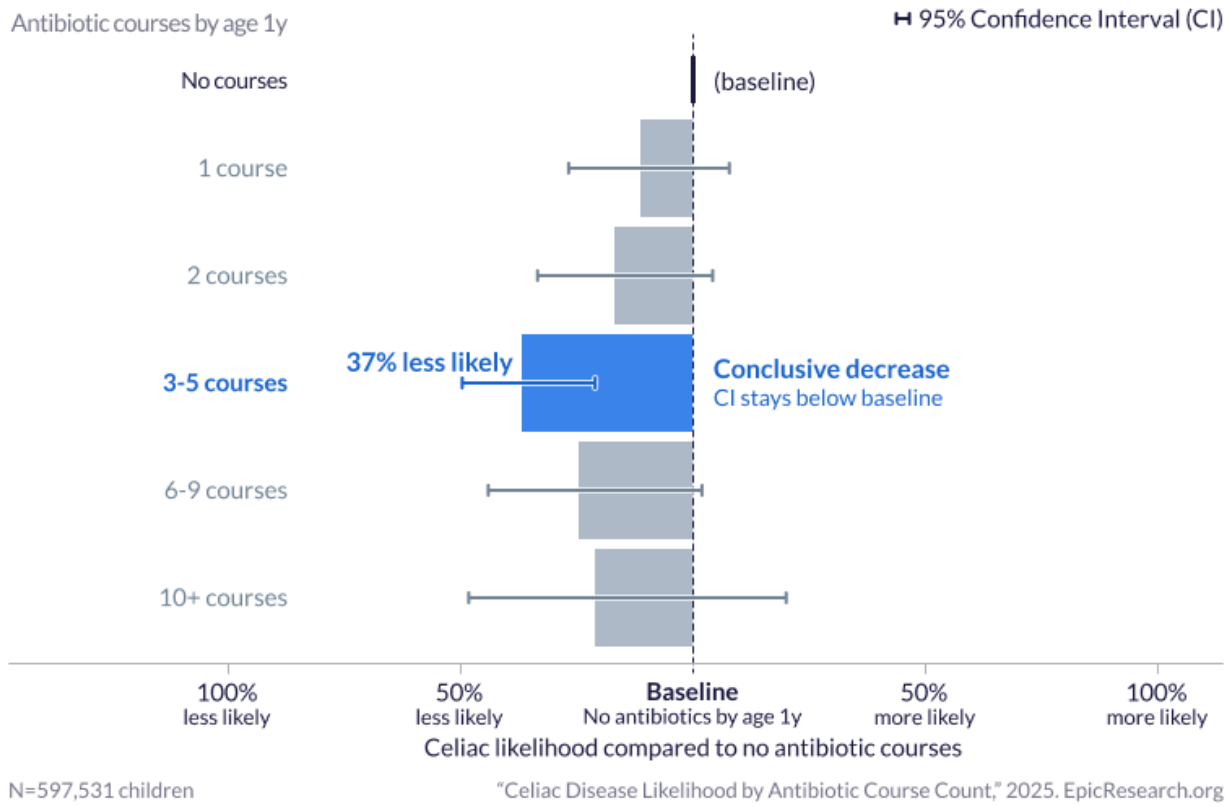

Figure 1. The likelihood of a child being diagnosed with celiac disease by age 6 by the number of antibiotic courses they had during the first year of life.

We found similar results when assessing antibiotic use before age 3, celiac disease by age 3, and in patients without a history of surgery.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 300 million patient records from 1,700 hospitals and more than 40,000 clinics from all 50 U.S. states, Lebanon, and Saudi Arabia. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

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3. Kamphorst K, Van Daele E, Vlieger AM, Daams JG, Knol J, van Elburg RM. Early life antibiotics and childhood gastrointestinal disorders: a systematic review. BMJ Paediatr Open. 2021;5(1):e001028. Published 2021 Mar 3. doi:10.1136/bmjpo-2021-001028

Data Definitions

Term	Definition
Study period	Patients with a birth documented who were born between 1/1/2000 and 3/1/2022
Study population	Patients with: • A gestation age at birth between 28 and 45 weeks • A legal sex of male or female • At least one **outpatient care visit** each year of life between birth and age 6
Exposures	The number of orders for **systemic antibiotics** the patient received in the first year of life.
Outcomes	**Celiac disease** documented before the child's sixth birthday
Confounders	Legal sex Gestational age: 28-36 weeks or 37+ weeks **Race and ethnicity** **RUCA:** Metropolitan, Micropolitan, Small Town, Rural **Social Vulnerability Index** quintiles for the child, or for the mother if none is recorded for the child Mother history of **celiac disease** Number of antibiotic orders: 0, 1, 2, 3-5, 6-9, 10+ Number of **outpatient care visits** by first birthday: 1-6, 7-9, 10-13, 14+ **Infections before first birthday**: 0, 1, 2+ **GI infection** before first birthday: 0, 1+ C-section delivery
Outpatient care visit	Encounter of type "Well child," "Office Visit," "Well Child," "Follow-Up," "Telemedicine," "Urgent Care," or "Walk-In," or with a diagnosis of ICD-10-CM code Z00.1*, or with a procedure of CPT code 99381-99383 or 99391-99393
Celiac disease	A diagnosis with ICD-10-CM code K90.0
Systemic antibiotics	A medication order with pharmaceutical class "Penicillin antibiotics;" "Cephalosporin antibiotics - 1st generation;" "Cephalosporin antibiotics - 2nd generation;" "Cephalosporin antibiotics - 3rd generation;" "Cephalosporin antibiotics - 4th generation;" "Cephalosporins - 5th generation;" "Macrolide antibiotics;" "Tetracycline antibiotics;" "Periodontal collagenase inhibitors;" "Quinolone antibiotics;" "Aminoglycoside antibiotics;" "Amebicides;" "Absorbable sulfonamide antibacterial agents;" "Chloramphenicol antibiotics and derivatives;" "Vancomycin antibiotics and derivatives;" "Lincosamide antibiotics;" "Antibiotics, miscellaneous, other;" "Polymyxin antibiotics and derivatives;" "Betalactams;" "Carbapenem/Penem Antibiotics;" "Anaerobic antiprotozoal-antibacterial agents;" "Antiprotozoal drugs,miscellaneous;" "Antiparasitics;" "Cyclic lipopeptides;" "Streptogramin antibiotics;" "Oxazolidinone antibiotics;" "Rifamycins and related derivative antibiotics;" "Ketolide antibiotics;" "2nd gen. Anaerobic antiprotozoal-antibacterial;" "Glycylcyclines;" "Lipoglycopeptide antibiotics;" "Nitrofuran derivatives antibacterial agents;" "Antibiotic, antibacterial, misc.;" or "Antitubercular antibiotics" and a route of "combination," "injection," "intramuscular," "intravenous," "oral", "buccal", or "transdermal"

Race and ethnicity	**How were race and ethnicity used?** Distinct categories for Black and Hispanic categorizations for either the child or the mother
Infections before first birthday	Occurrences of the following diagnoses where we ignored diagnoses if the same infection type was documented on the patient in the 14 days prior: • Strep throat: ICD-10-CM code J02.0, J03.00, J03.01 • Ear infection: ICD-10-CM code H65* • Influenza: ICD-10-CM code J09*-J11* • RSV: ICD-10-CM code J12.1, J20.5, J21.0, B97.4 • COVID-19: ICD-10-CM code U07.1, U00, U49, U50, J12.82 • Hand, foot, and mouth disease: ICD-10-CM code B08.4
GI Infection	A diagnosis with ICD-10-CM code A04*, A08*, or A09*
Model specifications	Logistic regression

Table 1: Celiac Disease Likelihood by Antibiotic Course Count

Number of Courses	Odds Ratio	95% CI Low	95% CI High
1	0.89	0.73	1.08
2	0.83	0.66	1.04
3-5	0.63	0.50	0.79
6-9	0.75	0.56	1.02
10+	0.79	0.52	1.20