Cesarean Delivery and the Risk of Childhood Allergic Rhinitis

Megan Richards, PhD1; Jeannette Ferber, MPH2; De-Kun Li, MD, PhD2; Lyndsey Darrow, PhD1
1School of Community Health Sciences, University of Nevada, Reno; 2Division of Research, Kaiser Permanente Northern California

Cesarean delivery was not associated with allergic rhinitis at follow-up ages of 6, 8 or 10 in a large contemporary US cohort.

Background
- Allergic rhinitis (AR) is the most common allergic disease worldwide and prevalence has increased over the last century
- Vaginal delivery is one of the earliest sources of microbial exposure for infants
- Early life microbial differences may increase susceptibility to allergic rhinitis later in life
- Previous meta-analysis (Bager, 2014) reported a pooled odds ratio of 1.24 (1.08, 2.43) for the association between C-section and AR

Objectives
Examine the association between C-section and AR at ages 6, 8, and 10 in a large US cohort using electronic medical records, pharmacy dispensing data, state birth records, and prospectively collected breastfeeding surveys.

Study Population: Children born in Kaiser Permanente Northern California integrated healthcare system between 2005 and 2014 with follow-up through at least 6 years of age

Exposure: Cesarean delivery, overall and sub-classified by the following attributes for births after 2008:
1. Exposure to labor
2. Exposure to maternal vaginal microbiota
3. Medical indication for C-section

Outcome: Allergic rhinitis at ages 6, 8, and 10
1. Two AR diagnosis codes (ICD-9: 477; ICD-10: J30) at least 30 days apart
2. And either: one AR medication (nasal corticosteroid or second generation antihistamine), or a third AR diagnosis code
3. At least on diagnosis code or prescription within the last two years

Statistical Methods
- Modified Poisson regression models with robust variance estimation
- Adjusted for maternal age, education, race, pre-pregnancy BMI, smoking, prenatal antibiotics, maternal asthma and allergies, gender, gestational age, birth weight, NICU admission, birth order, and breastfeeding
- Stratification by potential effect modifiers
- Effect of C-section overall ("primary" model) and estimated separately by exposure to labor, exposure to microbiota, and indication for C-section
- Assessment of bias due to missing data, loss to follow-up, and intrapartum antibiotics

Results

![Figure 1: Demographic characteristics at age 6](Image)

![Figure 2: Risk ratios for the association between C-section and AR](Image)

Discussion
- The proportion of children meeting the AR case definition at each follow-up age was 3.8% at age 6, 6.8% at age 8, and 9.2% at age 10.
- C-section delivery accounted for about 27% of deliveries among all follow-up age groups
- Despite an unadjusted association between C-section and AR, after adjustment there was no association between C-section and AR [RR1 (CI): 0.98(0.91, 1.04); RR8 (CI): 1.00(0.95, 1.07); RR10 (CI): 1.03(0.96, 1.10)]. Stratification by potential effect modifiers yielded similar estimates.
- There was modest evidence of an increased risk of AR associated with C-section among younger siblings [RR8 (CI): 1.08(0.98, 1.19)] and children born to mothers without allergies [RR10 (CI): 1.19(1.05, 1.35)].
- Children born via C-section in the "other, labor" category were less likely to develop AR at age 8 [RR8 (CI): 0.63 (0.45, 0.87)] compared to vaginally delivered children.
- Bias analyses indicated that consideration of missing data, loss to follow-up, intrapartum antibiotics, or alternate AR case definitions yielded similar estimated associations.
- Strengths of the analysis include: (1) large sample size in a contemporary US cohort, (2) thorough examination of potential sources of bias, (3) adjustment for often excluded confounders

Abbreviations: API, Asian/Pacific Islander; AR, allergic rhinitis; BMI, body mass index; C-section, cesarean section delivery; FTP, failure to progress; ICD, International Classification of Disease; KPNC, Kaiser Permanente Northern California; L, labor; NL, no labor