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The Kingston Allergy Birth Cohort

Exploring parentally reported respiratory outcomes through the lens of the exposome

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ABSTRACT

Background: The Kingston Allergy Birth Cohort (KABC) is a prenatally recruited cohort initiated to study the developmental origins of allergic disease. Kingston General Hospital was chosen for recruitment because it serves a population with notable diversity in environmental exposures relevant to the emerging concept of the exposome.
Objectives: To establish a profile of the KABC using the exposome framework and examine parentally reported respiratory symptoms to 2 years of age.
Methods: Data on phase 1 of the cohort (n = 560 deliveries) were compiled, and multivariate Cox proportional hazards regression models were used to determine associations with respiratory symptoms.
Results: The KABC exhibits diversity within the 3 exposome domains of general external (socioeconomic status, rural or urban residence), specific external (cigarette smoke, breastfeeding, mold or dampness), and internal (respiratory health, gestational age), as well as significant associations between exposures from different domains. Significant associations emerged between parental reports of wheeze or cough without a cold and prenatal cigarette smoke exposure, mold or dampness in the home, and the use of air fresheners in the early-life home environment. Breastfeeding, older siblings, and increased gestational age were associated with decreased respiratory symptoms.
Conclusion: The KABC is a unique cohort with diversity that can be leveraged for exposomics-based studies. This study found that all 3 domains of the exposome had effects on the respiratory health of KABC children. Ongoing studies using phase 1 of the KABC continue to explore the internal exposome through allergy skin testing and epigenetic analyses and the specific external domain through in-home environmental analyses, air pollution modeling, and ultimately potential convergences within and among domains.

Introduction

Developmental Origins of Allergic Disease and the Exposome

Allergic diseases are common in childhood.[1–4] The increase in prevalence remains poorly understood, and a substantial environmental contribution has been recognized.[1–4] Progress in research on the developmental origins of health and disease (Barker hypothesis) has revealed that many noncommunicable diseases (NCDs), including allergies and asthma, are likely to arise from cumulative gene-environment interactions.[5,6] The exposome has been introduced as a conceptual framework encompassing

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exposures encountered by an individual throughout life, and their changes over time.[7,8] Three exposome domains are recognized: internal, specific external, and general external.[7] The internal domain encompasses host factors, such as age, metabolism, microbiome, and epigenetics.[7] Specific external exposures are individual level, such as cigarette smoke and air pollution, whereas general external include wider socioeconomic and geographic factors, such as income and urban or rural residence, which also have effects on the individual.[7] Examining the exposome over time necessitates that birth cohort studies play a key role in exploring this new concept and applying it to gain a deeper understanding of the causes of NCDs.[8,9]

Studying Children With Varied Exposomes

The Kingston Allergy Birth Cohort (KABC) is the first prospective study of allergic disease to be established at Kingston General Hospital (KGH). By offering access to a small Canadian city plus surrounding rural areas, it complements larger Canadian cohort efforts, such as the Canadian Healthy Infant Longitudinal Development (CHILD) study.[1,4,10,11] The KGH catchment also includes notable diversity in socioeconomic status (SES). Mean incomes in certain neighborhoods are well above the provincial average, whereas others are archetypes of multigenerational poverty.[12,13] Environmental health issues also disproportionately affect Kingston, such as prenatal smoking, which at 21.2%, is significantly higher than the rate in Ontario (12.4%) and the nearby city of Ottawa (7.7%).[14]

The KABC cohort includes the collection of umbilical cord blood, skin prick testing of the mothers and children, home visits for blood collection, and indoor and outdoor environmental sampling. In the present study, questionnaire data collected during the third trimester and at 6, 12, and 24 months of age were analyzed (Fig 1). We present the first study, to our knowledge, to examine early childhood respiratory symptoms from the perspective of the exposome. We found that urban or rural residence and SES were associated with prenatal and postnatal environmental exposures. Respiratory symptoms were significantly associated with prenatal cigarette smoke exposure, indoor mold, and air fresheners. Breastfeeding, siblings, and gestational age were negatively associated with respiratory symptoms.

Methods

Recruitment

Participants were 18 years or older, in the second or third trimester, not banking umbilical cord blood, without preeclampsia or insulin-dependent diabetes, able to communicate in English, and able to provide written informed consent before any study-specific procedures. Ethical clearance was provided by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board. Participants were recruited via posters and invited to participate at clinic appointments, before scheduled cesarean sections, or in early labor, if they responded positively to a query from a health care professional regarding speaking with study staff. Because of factors surrounding the delivery, cord blood was not collected from 26% of participants.

Prenatal and Postnatal Questionnaires

The first 51 participants were administered a less detailed pilot survey at enrollment. The pilot survey included questions regarding parental allergies and asthma and prenatal smoke exposure. The full questionnaire was administered to all women who enrolled subsequently and included additional questions regarding the home and other environmental exposures. Efforts were made to harmonize the information gathered in the full questionnaire with the CHILD study by adapting questions from Takaro and colleagues.[1]

Survey responses, such as maternal smoking, sex of the child, siblings, and mode of delivery, were validated against medical records wherever possible, and all exposures except maternal smoking were found to be consistent. Maternal smoke exposure

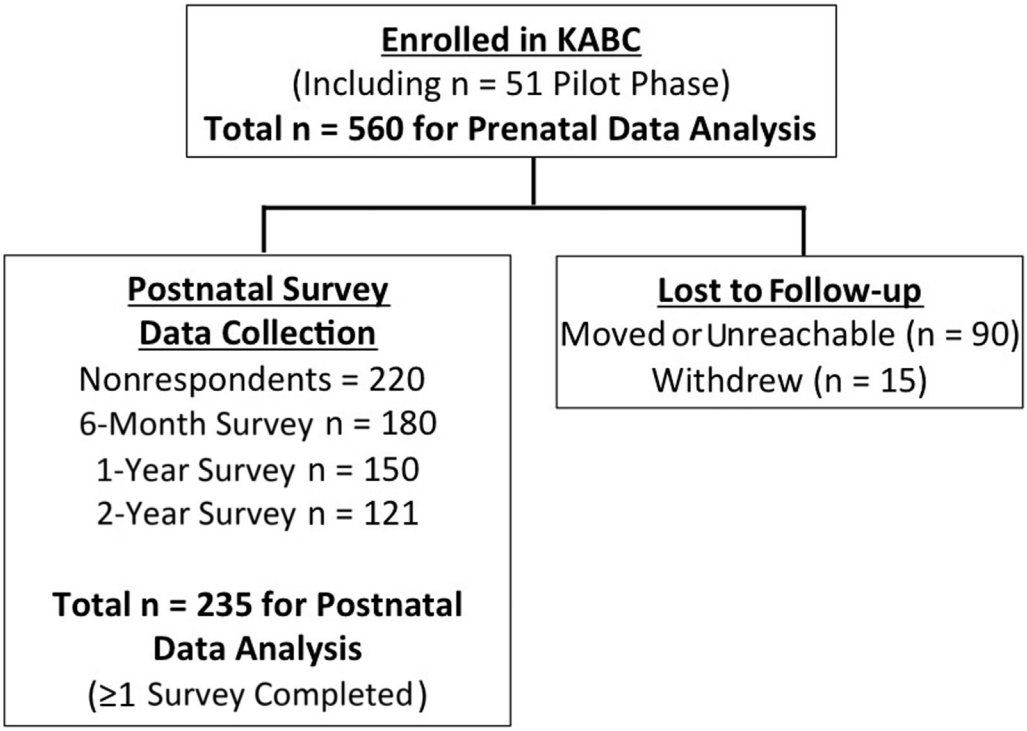

Figure 1. Flowchart of Kingston Allergy Birth Cohort (KABC) enrollment, withdrawal, loss to follow-up, and follow-up questionnaire completion relevant to this study.