Allergol Immunopathol (Madr). 2018;xxx(xx):xxx-xxx

Allergologia et immunopathologia

Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica

www.elsevier.es/ai

ORIGINAL ARTICLE

An international comparison of risk factors between two regions with distinct differences in asthma prevalence

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Received 5 July 2017; accepted 3 January 2018

KEYWORDS
Asthma;
Wheeze;
Adolescents;
Geographic variation;
International;
Under-diagnosis;
Epidemiology;
Paracetamol;
Activity

Abstract
Background and purpose: Investigation of the geographic variation in asthma prevalence can improve our understanding of asthma etiology and management. The purpose of our investigation was to compare the prevalence of asthma and wheeze among adolescents living in two distinct international regions and to investigate reasons for observed differences.
Methods: A cross-sectional survey of 13–14 year olds was completed in Saskatoon, Canada ($n = 1200$) and Skopje, Republic of Macedonia ($n = 3026$), as part of the International Study of Asthma and Allergies in Childhood (ISAAC) Phase 3 study. Surveys were self-completed by students following the ISAAC protocol. Multiple logistic regression models were used to investigate associations with reports of asthma and current wheeze. A mediation analysis was then completed.
Results: Asthma prevalence was much higher in Saskatoon than Skopje (21.3% vs. 1.7%) as was the prevalence of current wheeze (28.2% vs. 8.8%). Higher paracetamol (acetaminophen) use was a consistent risk factor for asthma and wheeze in both locations and showed dose-response relationships. In both countries, paracetamol use and physical activity mediated some of the association for both asthma and wheeze. In Saskatoon, among those with current wheeze, 42.6% reported ever having a diagnosis of asthma compared to 10.2% among Skopje adolescents.
Conclusions: The results suggest that the variation in risk factors between the two locations may explain some of the differences in the prevalence of asthma and wheeze between these two study sites. However, diagnostic labeling patterns should not be ruled out as another potential explanatory factor.

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https://doi.org/10.1016/j.aller.2018.01.002

Introduction

International variation in childhood asthma prevalence has been shown with much of the work coming from the International Study of Asthma and Allergies in Childhood (ISAAC).[1–3] Westernized regions such as North America, Australia, and Western Europe have reported relatively high rates of asthma prevalence while Eastern and Northern Europe have shown much lower prevalence.[2] Variation in asthma prevalence has also been shown more regionally in such areas as Central and Eastern Europe.[4,5]

Potential explanations for the international variation in childhood asthma prevalence include differences in environment, personal characteristics, and health behaviors. Geographic differences in these factors and their relationship with respiratory health outcomes have been shown internationally[4,6] and locally.[7] While differences in diagnostic labeling between regions have been suggested,[4,5] with evidence of asthma under-diagnosis,[8] this explanation is not well investigated.

Improved the understanding of the geographic variation in asthma prevalence can assist in our knowledge of asthma etiology, while identifying differences in diagnostic labeling will allow these to be accounted for as we study other explanations of asthma etiology (e.g. environmental or health behavior). Because there have been increases in asthma prevalence within regions of previously low asthma prevalence,[9] it is especially important to investigate the explanations for observed geographic differences to better predict and plan for potential increases that may occur with global westernization.

Our objectives were to: (1) determine if there is a difference in the prevalence of asthma or wheeze between two geographically distinct regions with potentially different environmental, health behavior, and health care service/diagnostic labeling patterns among 13–14 year olds; and (2) identify risk factors for asthma and wheeze and identify potential explanatory factors for observed differences in prevalence. We completed this using data from two participating regions of ISAAC Phase 3, one with low asthma prevalence (Skopje, Republic of Macedonia) and the other with high prevalence (Saskatoon, Canada), extending an established collaboration.[10]

Materials and methods

Study design and location

The ISAAC methodology is well described.[1,11] In brief, ISAAC Phase 3 was a worldwide cross-sectional study using standardized methods.[11] For the current analysis, we compared data from Saskatoon, Canada (completed in 2003) and Skopje, Republic of Macedonia (completed in 2002). Saskatoon (population approximately 220,000[12]) is in western Canada. These two locations were chosen based on a previous collaboration and common research interests from investigators in the two regions. The differences in asthma prevalence between the regions would allow for strong scientific comparisons of interest to the researchers. Skopje (population approximately 500,000 people[13]) is on the Balkan Peninsula in South Eastern Europe. Based on previous research, we suspected that these cities would vary greatly in asthma and wheeze prevalence, where Saskatoon and Skopje would be regions of high and low prevalence, respectively,[10,14] making their selection ideal for this analysis. Also, both cities are large, in landlocked locations, and have agricultural areas surrounding them.

This study was approved by the Biomedical Research Ethics Board at the University of Saskatoon and the Ethics Committee at the Medical Faculty and The Ministry of Education and Science (Skopje). Participating schools approved of this study. In Saskatoon, active consent was required while in Skopje, passive consent was employed.

Study population and data collection protocol

Selection of participants and data collection were performed in accordance with the ISAAC methodology.[11] Due to differences in school enrollment, most high schools in Saskatoon (62 took part) and a random sample of primary schools in Skopje (17 took part) were recruited. Within each sampled school, all 13–14 year old children attending were eligible to participate. In Saskatoon, there were 1200 participants (53.7% response rate) compared to 3026 participants in Skopje (90.9% response rate).

Data were collected through a self-completed written questionnaire completed in class. The standardized ISAAC Phase 3 written questionnaires included information on asthma, rhinitis, eczema, health behaviors, and environmental risk factors. Questionnaires in Skopje were translated then back-translated prior to use.

The main outcome measures were asthma and wheeze. The lifetime diagnosis of asthma (asthma 'ever') was based on the question: ''Have you ever had asthma?'' Current wheeze was based on a positive response to ''Have you ever had wheezing or whistling in the chest in the past 12 months?''

Additional covariates considered included sociodemographic information, home environmental exposures, weight and height, activity levels, and diet. Parental smoking was based on a positive history of currently smoking cigarettes by each parent independently. Self-reported weight and height or, where they were unknown by the respondents, their objectively measured values were used for the calculation of the BMI of each respondent as weight (kg)/height (m^2). The international cut-points for BMI for overweight and obesity by sex between 2 and 18 years, 25 kg/m^2 for overweight and 30 kg/m^2 for obesity at age 18, were used.[15] Physical activity was based on the question ''How many times a week do you engage in vigorous physical activity long enough to make you breathe hard?'' and was recorded as never/occasionally, 1–2 times per week, and 3 or more times per week. Television watching was based on the question ''During a normal week, how many hours a day (24 h) do you watch television?'' and was recorded as <1hour, 1 to <3 h, 3 to <5 h, and 5 h or more. Diet was assessed by the question ''In the past 12 months, how often, on average, did you eat or drink the following?'' with response options of never/occasionally, 1 to 2 times per week, and 3 or more times per week.

Please cite this article in press as: Madani K, et al. An international comparison of risk factors between two regions with distinct differences in asthma prevalence. Allergol Immunopathol (Madr). 2018. https://doi.org/10.1016/j.aller.2018.01.002