International Journal of Population Data Science

Journal Website: www.ijpds.org

Longitudinal trajectories of asthma exacerbations from infancy to school age.

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Introduction

Previous studies which used data-driven methodologies have reported the existence of an exacerbation-prone asthma subtype, which is independent of asthma severity. However, longitudinal patterns of asthma exacerbations during childhood have not been studied.

Objectives and Approach

We sought to investigate whether there are distinct longitudinal trajectories of asthma exacerbations from infancy to school-age that could facilitate better understanding of the heterogeneity of asthma syndrome. We used longitudinal k-means modelling (an unsupervised data-driven method), to analyse linked primary care data from 916 participants in a population-based birth cohort study (Manchester Asthma and Allergy Study), to ascertain clusters of children with similar trajectories of asthma exacerbations during childhood (n=160). We tested the validity of these clusters in relation to lung function, airway hyperreactivity and inflammation, allergic sensitisation, and the use of asthma medication.

Results

A two-cluster model provided the optimal solution for our data set. Based on the pattern of exacerbations from infancy to age 8 years, we assigned the clusters as: "Early-onset frequent exacerbations (FE)" (n=10) and "Infrequent exacerbations (IE)" (n=150). Shorter duration of breastfeeding was the strongest risk factor for FE (median weeks 0 (IQR: 0-1.75) vs IE, median weeks 6 (IQR: 0-20), p<0.001). Children in the FE cluster were more likely to exhibit persistent wheeze (90% vs 47%, p=0.03) and have poorer lung function, more airway hyperreactivity, and more airway inflammation throughout childhood (Table 1). In a post-hoc analysis, when we compared children in the exacerbation clusters with those who have wheezed only (n=389), and those that wheezed but had no exacerbations (n=338), other early life risk factors such as atopic sensitisation (IE - RR: 3.2 (95%CI: 2.1-5.1), p<0.001) (FE - RR: 10.9 (95%CI: 2.1-57.7), p=0.004), exposure to tobacco smoke at birth (FE - RR: 2.8 (95%CI: 1.3-6.3) ,p=0.02), position in sibship (IE - RR: 1.5 (95%CI: 1.0-2.3), p=0.03), and day care attendance (IE - RR:0.6 (95%CI: 0.4-0.9), p=0.01) were significantly associated with exacerbations.

Conclusion/Implications

We have identified two distinct patterns of asthma exacerbations during childhood with different outcomes, early-life risk factors, and lung function when compared to children who wheeze, but have no exacerbations. These results indicate that exacerbations represent an independent susceptibility phenotype.

http://dx.doi.org/10.23889/ijpds.v3i3.614
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