



Contents lists available at ScienceDirect

International Journal of Hygiene and Environmental Health

journal homepage: www.elsevier.com/locate/ijheh

Asthmatic/wheezing phenotypes in preschool children: Influential factors, health care and urban-rural differences

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ARTICLE INFO

Keywords:

Allergy test
Asthma
Children
Health care
Urban-rural differences
Wheezing phenotypes

ABSTRACT

Background: Different wheezing and asthmatic phenotypes turned out to indicate differences in etiology, risk factors and health care. We examined influential factors and urban-rural differences for different phenotypes.

Methods: Parents of 4732 children filled out a questionnaire concerning children's health and environmental factors administered within the Health Monitoring Units (GME) in a cross-sectional study in Bavaria, Germany (2014/2015). To classify respiratory symptoms, five phenotype groups were built: episodic, unremitting and frequent wheeze, ISAAC (International Study of Asthma and Allergies in Children) – asthma and physician-diagnosed asthma (neither of the groups are mutually exclusive). For each phenotype, health care variables were presented and stratified for residence. Urban-rural differences were tested by Pearson's chi-squared tests. Multivariable logistic regression was performed to analyze associations between influential factors and belonging to a phenotype group, and to compare groups with regard to health care variables as outcome.

Results: Risk factors for wheezing phenotypes were male gender (OR = 2.02, 95%-CI = [1.65–2.48]), having older siblings (OR = 1.24, 95%-CI = [1.02–1.51]), and preterm delivery (OR = 1.61, 95%-CI = [1.13–2.29]) (ORs for unremitting wheeze). 57% of children with ISAAC asthma and 74% with physician-diagnosed asthma had performed allergy tests. Medication intake among all groups was more frequent in rural areas, and physician's asthma diagnoses were more frequent in urban areas.

Conclusions: In accordance with previous research this study confirms that male gender, older siblings and preterm delivery are associated with several wheezing phenotypes. Overall, low numbers of allergy tests among children with physician's diagnoses highlight a discrepancy between common practice and current knowledge and guidelines. Residential differences in health care might encourage further research and interventions strategies.

1. Introduction

Asthma is the most common chronic disease in children. About 10% of children in Western Europe have asthma (The Global Asthma Report 2014, 2014; Schlaud et al., 2007) and around 40% of children under six years of age have had at least one wheezing episode (Weiss, 2008; Mallol et al., 2010). Asthma is an umbrella term, and according to the Global Initiative for Asthma, a heterogeneous disease characterized by a variety of symptoms (Anon, 2017).

In children younger than six years it is difficult to diagnose asthma, as among other things, pulmonary function tests cannot be performed reliably before the age of six. In this age, wheezing remains one of the main symptoms of asthma, although it is not clear whether young children who wheeze will develop asthma or not. Different wheezing phenotypes have been defined and investigated in several epidemiological studies (Henderson et al., 2008; Savenije et al., 2011). Although there is increasing evidence that different forms of wheezing may be associated with different risk factors and prognosis, so far neither the

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<https://doi.org/10.1016/j.ijheh.2017.12.001>

Received 14 June 2017; Received in revised form 30 November 2017; Accepted 1 December 2017

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Table 1
Description of wheezing groups.

Groups	Definition	Prevalence
1. Episodic Wheeze (N = 438)	Ever having wheezing episodes concomitantly together with a cold with fever or rhinitis and no symptoms between those wheezing episodes	9.3%
2. Unremitting Wheeze (N = 491)	Having symptoms between distinct wheezing episodes or having wheeze without a cold with fever or rhinitis.	10.4%
3. Frequent Wheeze (N = 61)	Having more than 4 attacks (wheeze, shortness of breath, asthma or bronchitis) in the last 12 months	1.3%
4. Asthma diagnosis (ISAAC) (N = 371)	A physician's diagnosis of asthma at least once per lifetime or recurrent diagnoses of asthmatic, spastic or obstructive bronchitis	7.8%
5. Physician diagnosed asthma (N = 129)	A physician's diagnosis of asthma	2.7%

Annotation: Wheezing groups are not mutually exclusive.

pathogenesis of wheezing phenotypes nor their relation to asthma have been completely elucidated. Phenotypes in childhood may differ in the likelihood of persisting asthma in later life. Several cohort studies have followed children with respiratory symptoms into their adult life. In the Melbourne Asthma Study (Kelly et al., 1990) children with severe degrees of asthma had a higher probability of persistent asthma in adulthood than children with mild infrequent asthma. There are still deficits in asthma diagnostics. Yeatts et al. (2003), for instance, found that 28% of children between 12 to 14 years of age (North Carolina, USA) from their study had current asthma-like symptoms, and that out of this group, more than 60% had no diagnosis of asthma.

Good medical care in wheezing children is important. Insufficient medical diagnoses may lead to missing therapeutic consequences, e.g. sleep disturbances and absence from school (Yeatts et al., 2003). Tariq et al. (2000) followed a birth cohort and discovered that an early IgE sensitization to hen's egg proteins increases a later risk for asthma. As allergies are a main cause of childhood asthma, allergy anamnesis and testing are recommended (Bundesärztekammer (BÄK), 2009). If the child is allergic, an early intervention may improve children's health considerably or prevent the progression of the disease (Høst et al., 2003).

Further we were interested in comparing residences, as at the time, we were not aware of any data describing urban-rural differences in the health care situation of wheezing preschool children in Bavaria, Germany.

There are two main aims of this study: first, to describe characteristics and potential influential factors of different asthmatic/wheezing phenotypes in preschool children and second to ascertain differences in health care for those phenotypes, also with regard to urban-rural differences.

2. Methods

2.1. Data collection

Health monitoring units (GME) were first established in 2004 by the Bavarian Health and Food Safety Authority with the intention to periodically collect standardized health data of preschool children in order to develop and evaluate intervention and prevention strategies. In the course of a compulsory school entrance examination, parents of preschool children were asked to fill out a questionnaire regarding their children's health and socioeconomic issues. The data analyzed in the present study was collected in 2014/2015 from three urban (Munich, Ingolstadt, Bamberg city) and three rural (Schwandorf, Günzburg, Bamberg rural district) regions within Bavaria with the GME questionnaire. There are regular meetings with school medical assistants and consultation of all involved local health authorities to ensure a standardized data collection. The GME have the approval of the local ethics committees. Bolte et al.'s publication provides further information on the health monitoring units (Bolte et al., 2007).

2.2. Demographic and socioeconomic variables and influential factors

The following variables were analyzed: region of data collection was categorized ("rural" or "urban"), having older siblings ("yes" or "no"), parental school education refers to the highest education of mother or father (low = "Hauptschulabschluss" or no graduation, middle = "Realschulabschluss", "POS" or others, high = "Fachhochschulreife" or "Abitur"), parental smoking habits ("prenatal smoking exposure", "current smoking exposure at home" and "both prenatal smoking exposure and current smoking exposure at home"), country of birth ("Germany" versus "other countries") and underweight at birth or preterm delivery ("yes" or "no"). In addition, age and sex of the children were recorded.

2.3. Asthmatic/wheezing phenotypes and health care

In the questionnaire parents were asked whether their child had ever wheezed, had ever wheezed without having a cold with fever or sniff, wheezed in the last 12 months, had wheeze attacks during the past 12 months ("no attacks", "1–3 attacks", "4–12 attacks" or "more than 12 attacks"), had gasped for breath while talking after one or two words (dyspnea) during the past 12 months, had been symptom free between wheeze attacks, and at what age it had first wheezed. Furthermore, they were asked whether their children had medical diagnoses of asthma ("once", "several times" or "no") or asthmatic/spastic/obstructive bronchitis ("once", "several times" or "no").

Five phenotype groups were constructed similarly to the clinical phenotypes stated in a publication of 2014 by Depner et al. (2014): episodic, unremitting and frequent wheeze, asthma according to ISAAC definition (definition of Asthma according to the ISAAC study (The International Study of Asthma and Allergies in Childhood): either one time physician-diagnosed asthma or more than one time physician-diagnosed obstructive bronchitis) and medically diagnosed asthma (for details see Table 1). A healthy control group was built out of those children who were in none of the five groups. The five phenotype groups are not mutually exclusive, as a child can belong to more than one group at the same time.

Concerning health care, the questionnaire comprised questions about the use of a peak-flow-meter for the assessment of pulmonary function, the intake of medication for airway-related symptoms during the past 12 months, as well as the intake of regular or emergency medication. The parents were also asked whether an allergy test had been performed, whether it had been positive for any allergens and whether the test had been performed by a specialized physician (allergist).

2.4. Statistical analysis

Sociodemographic characteristics of phenotype groups and health care stratified by residency are summarized in two descriptive tables

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