

Risk Factors Exposure during the First Life Year and Asthma Development among Albanian Children

Case Study

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Abstract

Background: Different environmental factors are accused as risk factors (RF) in the development of allergic respiratory diseases. This study aimed to investigate the role of exposure to suspected RFs during the first life year in the development of childhood asthma among Albanian capital residents with a provincial or suburban origin.

Method: Parental reports about own asthmatic children (276, m 160, f 116, aged 1-14, mean age 5.6) were collected regarding conduction of cesarean delivery, breast feeding, exposure to high house humidity, pets, or to passive tobacco smoke, and presence of familiar atopy or atopic dermatitis during the first life year. These results were compared with a sample of non-allergic children (100, m 49, f 51, mean age 5.7), diagnosed with common upper respiratory infections.

Results: Conduction of cesarean section (OR = 9.8, p = 0.0002), exposure to high humidity at home (OR = 3.77, p = 0.0001), or to passive tobacco smoke (OR = 4.78, p < 0.0001), as well as presence of atopic dermatitis (OR = 10.37, p = 0.0001) was significantly associated with asthma development. Familiar atopy (OR = 1.07) and exposure to pets (OR = 1.66) resulted insignificant, whereas breast feeding resulted in protective factor (OR = 0.48, p = 0.0134).

Conclusion: Cesarean section during birth, increased humidity level at home, atopy and passive tobacco smoke during the first life year could be RFs regarding the asthma development. The avoidance of mentioned factors at least during the mentioned period may reduce the development risk of this disease.

Keywords: Asthma; First Life Year; Risk Factors.

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Introduction

Asthma is one of the most common chronic respiratory disorders [1]. Many epidemiology studies have suggested an increasing trend of asthma especially in industrialized world, and that perinatal exposure to several risk factors and genetic predisposition have been associated with development of childhood asthma or

other respiratory allergic diseases [1-4]. The identified risk factors of asthma and other respiratory allergic diseases include maternal smoking and environmental tobacco smoke, traffic-related pollution, antibiotics, home dampness, etc [1, 5-8]. To further investigate the regional role of some of these environmental factors and their contribution to the first year of life in asthma development, we conducted a retrospective study in asthmatic subjects and the control group presented in a multidisciplinary clinic of Tirana (capital city of Albania).

Methodology

This study is focused on presence of familiar history for atopic diseases, development of atopic dermatitis and exposure to indoor risk factors during the first year of life on asthmatic children who were visited in our clinic during 2008-2010. The parents of each child respectively have provided written informed consent and completed self-administered questionnaires. They included questions about two optional answers yes or no regarding the mode of delivery (cesarean or natural), breast feeding, and exposure to high humidity in their dwellings, pets, or environmental passive smoking as well as presence of family atopic history or atopic dermatitis. The study consisted of 276 asthmatic children aged 1-14 years (m 160, f 116, mean age 5.6±1.1), and a control group composed of 100 children (m 49, f 51, mean age 5.7±1.4), diag-

nosed with acute common upper respiratory infections. Diagnosis of asthma was confirmed or excluded due to clinical examination, ISAAC questionnaire, presence or absence of obstruction during spirometry (including salbutamol reversibility test), and results of skin prick tests with Mediterranean aeroallergens. The same questions were addressed to parents of control group children after exclusion of respiratory allergic symptoms. The study group and the control group matched in regard to age and sex indexes. The comparative data were shown as odd ratio (OR) and confidence interval (CI), and chi2-test was used to evaluate the significance level. Statistical significance was settled for $p < 0.05$.

Results

Our study shows a significant association of bronchial asthma with cesarean delivery (46/276 vs. 2/100, OR 9.8, CI 2.33-41.17, $p = 0.0002$), high indoor humidity exposure (164/276 vs. 28/100, OR 3.77, CI 2.29-6.2, $p = 0.0001$), environmental tobacco smoke (105/276 vs. 12/100, OR 4.78, CI 2.49-9.17, $p = 0.0001$), as well as the presence of atopic dermatitis (67/276 vs. 3/100, OR 10.37, CI 3.18-33.78, $p = 0.0001$). Breastfeeding on the other part resulted a protective factor (194/276 vs. 83/100, OR 0.48, CI 0.27-0.87, $p = 0.0134$). Both, family atopic history (38/276 vs. 13/100, OR 1.07, CI 0.54-2.1, $p = 0.84$) and pet exposure findings (43/276 vs. 10/100, OR 1.66, CI 0.8-3.45, $p = 0.17$) were statistically insignificant (see Table 1 and Figure 1).

Discussion

Asthma in itself is a disease depended on the interplay between

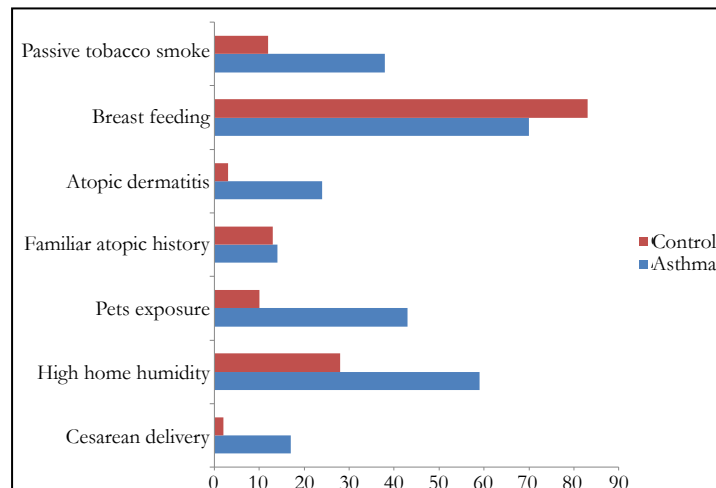
genetic and environmental factors [1, 2, 9]. The main impact on both factors originates in intrauterine and early extra-uterine life that corresponds to increased plasticity period during novel immune maturation [5, 10, 11]. Specifically, it is estimated that period from mid-gestation until 2 years after birth is one of a particular concern relative to allergic diseases and asthma [5, 11]. Although most published studies are underpowered to study interactions between genetic polymorphisms and ambient exposures, the identified risk factors play an active role in biologic mechanisms of immunologic balance and responsiveness [9, 12]. The emerging data onto our study demonstrated that especially developments of atopic dermatitis, and to a lesser extent, a familiar history for atopic diseases are non-environmental risk factors in the development of childhood asthma. Similarly to this, a recent German cohort evidenced an augmented asthma incidence of offspring up to adulthood in subjects with parental asthma and nasal allergy [13]. Developing dynamically through childhood, co-morbidity of atopic pathologies in children increases with age, reaching a higher frequency and persistence among subjects with parental atopy [4]. These findings indicate that allergy-related diseases should be neither seen nor studied as isolated entities.

In a previous study, we have found that younger generations of atopic respiratory patients report a family history of allergic disease about half as frequently as older ones, indicating for the existence of environmental factors in the development of asthma and allergic rhinitis [14]. Several observations in the past decades have clearly shown a mark difference in the prevalence between urban and rural regions, indicating that protective effect of the rural region consists of early exposure to microbes or microbial products

Table 1. Perinatal risk factors, atopy, and development of asthma.

Risk factors	Asthma (%), n = 276	Control (%), n = 100	OR	(CI 95%)	P
Cesarean delivery	46 (17)	2 (2)	9.80	(2.33-41.17)	0.0002
Breastfeeding	194 (70)	83 (83)	0.48	(0.27-0.87)	0.0134
High home humidity	164 (59)	28 (28)	3.77	(2.29-6.20)	0.0001
Pets	43 (16)	10 (10)	1.66	(0.80-3.45)	0.17
Passive tobacco smoking	105 (38)	12 (12)	4.78	(2.49-9.17)	0.0001
Familiar atopic history	38 (14)	13 (13)	1.07	(0.54-2.10)	0.84
Atopic dermatitis	67 (24)	3 (3)	10.37	(3.18-33.78)	0.0001

Figure 1. Frequency (%) of exposure to risk factors in control and asthma group during first life year.



Breast feeding resulted as protective factor, pet exposure and familiar atopy were non-significant risk factors, whereas atopic dermatitis, cesarean delivery, high house humidity, and passive exposure to tobacco resulted as important risk factors.

and modulating of the immune system so as to reduce the future risk of asthma and allergies [1]. It should be taken into account that the vast majority of our subjects originates from suburban regions that nowadays reside in the Albanian metropolis. Consequently, these subjects are generally exposed to a novel environment, even if asthma prevalence remains relatively low [14, 15].

In the present study, most of children are successors of the above-mentioned population, and during their first life year they are exposed to outdoors and mostly indoors allergens inside their dwellings [5]. Therefore, this might support the estimation, that many of these indoor and outdoor triggers have strong driving power over immature airway, toward "asthma battle" risk in later phases of their lives. With respect to indoor factors, our proper data evidenced a strong role in the pre-and perinatal exposure to environmental tobacco smoke. This agrees with little published data that emphasize the role of environmental tobacco smoke and other ambient air pollutants in the interaction with genetic polymorphism in asthma [6, 9, 11]. This exposure, with time leads to deficits in lung function, early onset of asthma, and respiratory-related school absenteeism among children [16-18]. In concert with other measures, avoiding tobacco smoke exposure to pregnancy, might prevent or delay the development of asthma [11, 13].

Home dampness during first life year is also reported on risk factors of the present survey. Independently to familiar history for atopy, associations between home dampness and respiratory diseases among children is proven through the protective influence of opening windows of the child's room at night and cleaning the child's room frequently [6, 19]. Similarly to our study, early exposure to visible mould and/or dampness has been associated with an increased asthma risk [20]. These findings stress out the fact that modern hermetical and air conditioning environment leads to increased allergic burden indoors, and therefore, to high rates of persistent childhood asthma [21].

In contrast to environmental tobacco smoke and home dampness, our study suggested for a protective role in breastfeeding. It is postulated that breastfeeding provides immunological protection when the infant's immune system is immature and a modest protective effect against asthma in early childhood, while induction of epigenetic mechanism by colonizing bacteria results in a functional immune phenotype and no expression of disease [3, 22]. This protective effect has been evidenced in our study even though generally the breastfeeding in our country is very common, independently to the subsequent health outcome of the respiratory system [11, 22]. Emerging data onto ISAAC multi-centric study also denied the consistent association with breastfeeding in the first life year and either a history or current symptoms of wheezing, rhino-conjunctivitis or eczema in 6-7 year old children [23]. Similarly to our study, breastfeeding for longer than four months among populations of certain industrialized countries have shown protective effects, especially among preschool age children with allergic heredity [6, 24, 25]. According to this evidence, the authors found out that introduction to preventive guidelines with regard to breastfeed (and other risk factors) during pre- and peri-natal age is associated with an important reduction of recurrent wheezing and asthma at 2 years of age [6].

Pet exposure (as a marker of infant exposure to distinct microbioma) revealed in present study as an insignificant risk factor of the development of childhood asthma, indicating that suburban origin and actual metropolitan life play a complex role on the

genetic-environment relationship. Nevertheless, several studies have shown controversial or insignificant results in development of asthma and allergic sensitization [26-28]. Children originating from atopic parents living in households with indoor dogs at birth were less likely to develop frequent wheezes than those without indoor dogs' presentation, whereas this effect has been not proven in children exposed to cats [26, 29]. Although perinatal exposure to pets might show a weak protective effect, sensitization to perennial household furry pets were associated with increased asthma risk [26, 28]. In summary, these findings indicated that pet ownership in early life did not appear to either increase or reduce the risk of asthma or allergic rhinitis symptoms in children [27-30].

Similarly to pet exposure, delivery mode is considered a potential marker for infant exposure to distinct microbioma [28]. It is believed that premature and cesarean delivery can lead to inadequate intestinal colonization, resulting in the absence of adequate bacterial-epithelial "crosstalk" and an increased incidence of immune-mediated diseases like asthma [11, 22, 31]. The strong effect of cesarean delivery of the development of childhood asthma has been observed both in our study and in further surveys [22, 31-33]. Thus, analyses of first-borns demonstrated that elective caesarean section was associated with an increased risk of dispensed inhaled corticosteroids in children aged between 2 and 5 years [32]. However, recent studies point out first, the presence of confounding factors, and second, they don't support the role of inadequate bacterial colonization during cesarean delivery and its association with childhood asthma [31, 32]. In this context, Nathan et al. reported that children delivered through caesarean sections did not have higher IgE levels nor were they more sensitized to aeroallergens, while multiple logistic regression show that asthma was significantly associated with a positive family history of atopy [33]. In turn, Kolokotroni et al. concluded from adjusting to potential confounders that association between cesarean delivery and asthma diagnosis in children indicates that family history of allergies may modify the effect of cesarean delivery on atopy [34]. Specifically, these authors observed a two-fold increase in the odds of being atopic among children with a familiar heredity if born by cesarean section, but any association was evidenced in children without a family history for allergic pathologies. Furthermore, Almqvist et al. observed that only emergent obstetrical intervention accounted for increased asthma diagnosis and medication during year of follow-up in children born with cesarean delivery, whereas elective section was insignificant [31]. Concluding that vaginal microflora plays no casual effect of the association with delivery mode and childhood asthma, these authors postulated that a more probable explanation should be sought in the indications for emergency cesarean section. Possibly, emergency cesarean delivery is a marker for cumulative maternal and prenatal stress, as long as these mothers are more likely to have asthma and higher stress is associated with increased IL-13 and decreased IFN-gamma [10]. If true, an additional adjusting for the stress would have suppressed the association between emergency cesarean delivery and the development of asthma [31]. Especially in developing countries, it is likely that expensive elective cesarean delivery is actually preferred by mothers with high socioeconomic status, whereas among mothers with low socioeconomic status emergency cesarean sections are generally applied to unexpected complications and constitutes a supplemental stressor. In fact, maternal cumulative adversity and lower maternal childhood socioeconomic status is also associated with increased cord blood IgE levels, asthma and repeated wheeze through both direct and indi-

rect effects [35-37]. The association of elective cesarean delivery with childhood asthma observed in previous surveys may account for the confounding role of family atopy background, which in fact, should be associated with deviation from traditional life [15, 32, 34]. After adjustment for interfering confounding factors, the elective cesarean section seems to play no causative effect of the development of childhood asthma [31].

Conclusion

This study supports the idea that atopic dermatitis is better indicator of a potential asthma development during childhood as compared to family history for atopic disease; however, they seem to be only an evident externalization of what lies in the genes. Moreover, our data indicate that children with suburban origin, but in the same time metropolis residents of a developing country like Albania, are subjects of *de novo* exposure to a wide variety of risk factors of asthma development, such as cesarean delivery, high humidity inside the dwellings and passive tobacco smoke during the first life year. Consequently, the avoidance of these factors during this immunologically fragile period may prevent this scenario [6, 38]. Nevertheless, the role of protective factors of breast feeding, respiratory infections in early life, and a "healthy" indoor environment needs further evaluation. Additional detailed studies are necessary for the detection of real asthma triggers, which could be hidden behind the well-determined risk factors.

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