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Predictors of Allergic Airway Disease in Children Under Two Years of Age

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Author`s Contribution

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ABSTRACT

Objective: To determine the frequency of factors responsible for allergic airway disease among children under 2 years of age.

Methodology: This descriptive cross-sectional study was conducted at the Department of Pediatrics, LUMHS, Jamshoro, from October 2022 to April 2023. Children under 2 years of age diagnosed with allergic airway disease were included. Both male and female children with a disease duration of at least 3 months were enrolled. Participants were assessed for various factors, including family history of asthma, protein milk allergy, allergic rhinitis, low socioeconomic status, maternal education, respiratory tract infections (RTIs), and prematurity. All collected data were entered into an Excel file and subsequently analyzed using SPSS version 23.

Results: A total of 121 children were enrolled, with a male predominance (69.4%) and a mean age of 12.28 ± 3.40 months. Protein milk allergy was identified in 48.8% of participants, allergic rhinitis in 43.8%, and recurrent RTIs in 40.5%, while 25.6% had a history of prematurity.

Stratification analysis revealed that RTIs were the most statistically significant predictor across both disease duration (p = 0.004) and exclusive breastfeeding status (p = 0.049). RTIs were considerably more frequent among non-breastfed children (33.1%) compared to exclusively breastfed infants (7.4%).

Furthermore, prematurity was the only factor demonstrating a statistically significant association with gender (p = 0.013).

Conclusion: Lack of exclusive breastfeeding and recurrent RTIs were identified as the most significant modifiable predictors of allergic airway disease. Other contributing factors included protein milk allergy, allergic rhinitis, prematurity, and low socioeconomic status.

Keywords: Allergic airway disease, asthma, children, risk factors

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Introduction

Allergic airway diseases are considered as the major health concerns that affect nearly 10–20 percent of children around the world, representing a substantial pediatric morbidity. Among these disorders, asthma and allergic rhinitis remain highly prevalent, effecting nearly 10% and 40% of school-aged children respectively.[1] Allergic diseases have become significantly prevalent globally during recent decades, mainly in urbanized and developing regions, due to environmental pollution, lifestyle changes, reduced microbial exposure, and altered dietary patterns.[2]

Allergic airway diseases often begin during early years of life, wherein several factors may lead to allergic inflammation in certain infants. These factors include immune system, digestive tract microbiome, respiratory tract development, and environmental exposures. [3]

Early-life exposures to the internal and external factors during perinatal periods and underdeveloped immune

systems in newborns, make neonates and children aged below 5 years vulnerable to allergic airway diseases, which may persist in future.[4,5] A number of factors, including prenatal, perinatal, genetic, epigenetic and environmental factors, play their role in development and progression of allergic airway disease. Children with family history of atopic diseases, such as asthma, eczema, or allergic rhinitis, are more likely to develop allergic disease. Additionally, genetic predisposition has also been seen to increase susceptibility to allergic sensitization through immune responses.[5] Maternal psychological and physical health and exposures to smoking, air pollution, infections, and high-fat diets during pregnancy may compromise fetal immune development and lung growth, potentially altering the inflammatory pathways and airway structure, leading to increased likelihood of adverse respiratory outcomes during early childhood.[6] Mode of delivery has also been associated with altered neonatal microbiota and immune development. Children delivered through cesarean section have been shown to have increased risk of allergic conditions, such as idiopathic arthritis, asthma, and gastroenteritis.[7]

Environmental exposures during infancy, including air pollution, tobacco smoke, and household allergens, can further contribute to airway inflammation.[8] Moreover, respiratory viral infections in the first three years of life have been associated with recurrent wheezing and an increased likelihood of developing asthma later on.[9] On the other hand, some studies suggest that early exposure to diverse microbial environments may have a protective effect by promoting better immune tolerance.[10]

As the allergic airway diseases in early childhood represent an increasing public health concern, yet the predictors driving their onset in children under two years of age remain inadequately identified. To the best of our knowledge, no study has previously investigated the frequency of these predictors within the local pediatric population, and the available international literature on this specific age group also remains limited.

Hence this study was aimed to generate local evidence, regarding risk factors association with allergic airway disease among children under 2 years old, which may helpful to develop targeted strategies for the early detection and prevention of childhood asthma in the limited resources regions at local level.

Methodology

This descriptive cross-sectional study was conducted at the Department of Pediatrics, Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, from October 2022 to April 2023. The study was initiated after obtaining approval from the College of Physicians and Surgeons Pakistan (CPSP) (Ref No: CPSP/REU/PED-2019-164-5459).

A total sample size of 121 patients was calculated using the OpenEpi calculator, taking the prevalence of prematurity among uncontrolled asthma cases as 5.3%, with a margin of error of 4% and a 95% confidence interval. A non-probability consecutive sampling technique was employed.

All children under 2 years of age, of either gender, diagnosed with allergic airway disease for at least 3 months were included in the study. Children with comorbid conditions such as congenital anomalies, severe acute malnutrition (SAM), tuberculosis, meningitis, and those whose parents did not consent to participate were excluded.

Informed consent was obtained from the parents or guardians after explaining the purpose and procedures of the study. Relevant demographic and clinical data—including age, gender, residential status, duration of disease, age at diagnosis, weight, length, and history of exclusive breastfeeding during the first six months—were recorded using a pre-designed proforma.

All participants were evaluated for potential risk factors, including family history of asthma, protein milk allergy, allergic rhinitis, low socioeconomic status, maternal education, respiratory tract infections (RTIs), and prematurity.

Allergic airway disease was defined clinically as recurrent wheezing, characterized by three or more episodes of wheezing within the first two years of life. Diagnosis was confirmed or supported by a consultant pediatrician with at least five years of clinical experience, based on history, physical examination, and relevant investigations such as complete blood count (CBC), absolute eosinophil count, serum total IgE levels, and chest X-ray.

All collected data were entered and analyzed using SPSS version 23. Post-stratification, the Chi-square test or Fisher's exact test was applied where appropriate, with a p-value of <0.05 considered statistically significant.

Results

A total of 121 children under two years of age were enrolled in the study. The most common age group was 13–18 months (36.3%). There was a clear male

predominance (69.4%), with the majority of participants belonging to urban areas (66.9%) and lower socioeconomic backgrounds (52.9%).

More than half of the children (59.5%) were not exclusively breastfed during the first six months of life. Protein milk allergy was observed in 48.8% of participants, while allergic rhinitis was present in 43.8%. Recurrent respiratory tract infections (RTIs) were identified in 40.5% of children, 25.6% had a history of prematurity, and 17.4% had a positive family history of asthma. Anthropometric assessment showed a relatively high mean body mass index (BMI) of 29.19 ± 3.23 kg/m², while the mean duration of disease was 7.16 ± 2.9 months (Table I).

Table I: Analysis of demographic and clinical data n=121

Age (in months)		**No**	**%**
< 6		28	23.1
6 – 12		23	19.0
13 – 18		44	36.3
18 – 24		26	21.5
Gender	Male	84	69.4%
	Female	37	30.6%
Residence	Rural	40	33.1%
	Urban	81	66.9%
Exclusive breast feeding	Yes	49	40.5%
	No	72	59.5%
Family history of asthma	Yes	21	17.4%
	No	100	82.6%
SES	Lower class	64	52.9%
	Middle class	29	24.0%
	Upper class	28	23.1%
Protein milk allergy	Yes	59	48.8%
	No	62	51.2%
Allergic rhinitis	Yes	53	43.8%
	No	68	56.2%
RTI	Yes	49	40.5%
	No	72	59.5%
Premature birth history	Yes	31	25.6%
	No	90	74.4%
Height		23.22±5.3 inches	
Weight		11.64±2.0 kg	
BMI		29.19±3.23 kg/m^2	
Disease duration		7.16±2.9 months	

Stratification of risk factors by age group and gender revealed no statistically significant associations for most variables. However, older infants (>12 months) showed relatively higher frequencies of protein milk allergy (28.9%), allergic rhinitis (26.4%), and RTIs (25.6%). Similarly, males exhibited higher frequencies across most risk factors. Notably, prematurity was the only variable that demonstrated a statistically significant association with gender (p = 0.013), highlighting its potential clinical relevance as a predictor of allergic airway disease (Table II).

Further stratification based on disease duration and exclusive breastfeeding status showed that RTIs were the only factor significantly associated in both analyses (p = 0.004 and p = 0.049, respectively). RTIs were more frequent among children with shorter disease duration (21.5%) and those who were not exclusively breastfed (33.1%), compared to exclusively breastfed children (7.4%). This finding supports the protective role of exclusive breastfeeding against early respiratory infections. Other variables did not show statistically significant associations (p > 0.05) (Table III).

Discussion

The allergic airway disease among children under two years of age represents a growing clinical concern, with its multifactorial etiological pattern. This study enrolled 121 patients to assess the responsible factors with an overall mean age of 12.28±3.40 months, majority of boys (69.4%), urban residents (66.9%), (52.9%) had lower socioeconomic class, overall mean disease duration 7.16±2.9 months and 40.5% were exclusively breastfed. Similar demographic findings were documented in the study of Tsai YC et al[11] found higher prevalence of asthma in 59.4% of children. Likewise, in the study of Bhalla K et al.[12] out of all bronchial asthma cases (n=121), males (69.4%) were more affected than females (30.6%) and urban residents (n=106) were more common than rural (n=15). Correspondingly, in the study of Hu Y et al.13male gender (16.2%) was more affected than females (11.4%), with higher participation from urban-rural junction (14.3%) and urban residents (14.2%), and more frequent participation from higher socioeconomic class (15.2%) compared to lower-SES (10.1%).

In the present study, several risk factors for allergic airway disease were identified among children under two years of age. Prematurity was observed in 25.6% of children, while 17.4% had a positive family history of asthma. Protein milk allergy was identified in 48.8% of participants, allergic rhinitis in 43.8%, and respiratory tract infections (RTIs) in 40.5% of children.

These findings are comparable with those reported in previous studies. For instance, Kim K et al.[14] reported a higher prevalence of asthma among preterm children, with 32.7% of preterm infants affected compared to 26.9% of term infants. They also noted a higher frequency of family history of asthma (23.2%) than observed in our study. Similarly, Alhadi S et al.[15] reported a lower proportion of protein milk allergy (10%) compared to our findings,

indicating possible regional or population-based differences.

Table II: Stratification factors of allergic airway disease according to age groups. (n=121)

FACTORS		Age Groups		P-(value	GENDER		p-value
		5 – 12 months	>12 months		Male	Female	
Family h/o Asthma	Yes	9(7.4%)	12(9.9%)	0.942	11(9.1%)	10(8.3%)	0.062
	No	42(34.7%)	58(47.9%)		73(60.3%)	27(22.3%)	
Protein Milk Allergy	Yes	24(19.8%)	35(28.9%)	0.749	40(33.1%)	19(15.7%)	0.705
	No	27 (22.3%)	35(28.9%)		44 (36.4%)	18(14.9%)	
Allergic Rhinitis	Yes	21(17.4%)	32 (26.4%)	0.619	33(27.3%)	20 (16.5%)	0.131
	No	30(24.8%)	38(31.4%)		51(42.1%)	17(14.0%)	
RTI	Yes	18(14.9%)	31(25.6%)	0.320	32(26.4%)	17(14.0%)	0.418
	No	33(27.3%)	39(32.2%)		52(43.0%)	20(16.5%)	
Prematurity	Yes	13(10.7%)	18(14.9%)	0.978	16(13.2%)	15(12.4%)	0.013
	No	38(31.4%)	52(43.0%)		68(56.2%)	22(18.2%)	

Table III: Stratification factors of allergic airway disease according disease duration and exclusive breast-feeding. (n=121)

FACTORS		Duration of disease		P-value	Exclusive breast feeding		p-value
		3 – 6 months	>6 Months		Yes	No	
Family h/o Asthma	Yes	16(13.2%)	5(4.1%)	0.262	8(6.6%)	13(10.7%)	0.262
	No	66(54.5%)	34(28.1%)		26(21.5%)	74(61.2%)	
Protein Milk Allergy	Yes	36(29.8%)	23(19.0%)	0.121	17(14.0%)	42(34.7%)	0.865
	No	46(38.0%)	16(13.2%)		17(14.0%)	45(37.2%)	
Allergic Rhinitis	Yes	35(28.9%)	18(14.9%)	0.719	13(10.7%)	40(33.1%)	0.440
	No	47(38.8%)	21(17.4%)		21(17.4%)	47(38.8%)	
RTI	Yes	26(21.5%)	23(19.0%)	0.004	9(7.4%)	40(33.1%)	0.049
	No	56(46.3%)	16(13.2%)		25(20.7%)	47(38.8%)	
Prematurity	Yes	21(17.4%)	10(8.3%)	0.997	11(9.1%)	20(16.5%)	0.289
	No	61(50.4%)	29(24.0%)		23(19.0%)	67(55.4%)	

In another study, Motey MA et al.[16] found that 38% of children had a positive family history of asthma, which is notably higher than our results. Furthermore, Morata-Alba J et al.[17] demonstrated that preterm infants had a higher incidence of bronchiolitis (56.9% vs. 37.1%) and recurrent wheezing (44.8% vs. 31.0%) compared to term infants. These findings support the observation that prematurely born children are more susceptible to respiratory infections and related complications.

Children under two years of age represent a particularly vulnerable group, as this critical period of growth and development plays a key role in shaping long-term respiratory health outcomes.

In our study, prematurity was significantly associated with gender, with higher frequency of prematurity in 13.2% of male children compared to 12.4% of females (p=0.013). In agreement, in the study conducted by Zhang J et al.[18] 12% of children were born preterm, with significantly higher risk of asthma in these children compared to term children (OR 1.64; 95% CI 1.45–1.84). They also reported a higher prevalence of asthma among males (51%) than females (49%), with a male-to-female ratio of 1.26:1, suggesting that prematurity is an important factor for the development of allergic airway diseases in childhood. Closely aligning with our findings, the study of Su YY et al[19] reported that prematurity significantly increased the risk of asthma, with hazard ratios (HR) of 1.19 in males and 1.17 in females.

Additionally, a higher risk of allergic rhinitis was noted among premature infants (HR 1.03), suggesting potential role of impaired lung development and altered immune maturation in increased susceptibility to allergic airway diseases among premature infants.

In this series, respiratory tract infection was significantly associated with duration of disease (p=0.004), with higher proportion of respiratory tract infection among children with disease duration of 3-6 months (21.5%) compared with those with disease duration >6 months (19%). In line with these findings, in the study of Bønnelykke K et al[20] found that respiratory tract infections in the first 3 years of life were associated with increased risk of asthma by the

age of 7 years, as the risk of asthma significantly increased among children with rhinovirus infections and respiratory syncytial virus (P <0.05). Additionally, exclusive breast feeding was significantly associated with respiratory tract infection (p=0.049), as children without exclusive breast feeding (33.1%) were more inclined to respiratory tract infection than those without (7.4%). Aligning with these findings, in the study conducted by Sobeih AA et al[21] exclusive breastfeeding was linked to a substantially lower risk of acute respiratory infections, with significantly lower rates of exclusive breastfeeding noted among 20.8% of children with acute respiratory infections compared to 92.3% of children without acute respiratory infections.

Overall the allergic airway disease in early childhood is a growing public health concern, driven by a complex interplay of genetic, environmental, nutritional, and socioeconomic factors. The child population under two years represent the most vulnerable population, as recurrent respiratory tract infections promote airway inflammation and allergic sensitization during this critical developmental window. In this population, exclusive breastfeeding has been firmly established as the single most potent and accessible protective factor against early allergic sensitization. It provides a unique immunological protection through its rich constituents, including secretory IgA, anti-inflammatory cytokines, and prebiotics, which collectively promote healthy immune maturation, gut colonization, and tolerogenic responses against allergens in environment. However, such condition in early childhood remains a vast, highly debatable, and extensively researchable subject, certifying continued scientific investigations and clinical attention. This study possesses certain limitations, like its single-center design and relatively limited sample size study, which may limit the findings generalizability. Hence, further large-scale, multicenter studies are strongly recommended to confirm these findings and more comprehensive exploration of the multifactorial predictors for better understanding the respiratory health of children.

Conclusion

Findings of the study revealed that the recurrent respiratory tract infections, lack of exclusive breastfeeding, protein milk allergy, allergic rhinitis, prematurity, and lower socioeconomic status are the key predictors of allergic airway disease among children under two years of age. Specifically, the RTI and lack of exclusive breastfeeding were observed as the most significant modifiable predictors, emphasizing the protective role of breastfeeding in early childhood. Additional large-scale studies are recommended to validate the findings to utilize this evidence to implement early identification, targeted screening, and preventive strategies in high-risk infants, thereby reducing the growing burden of childhood asthma in the limited resources regions.

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