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Allergic Disease Prevalence in School Children in Bengaluru, India: A Cross-Sectional Survey

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The authors confirm contribution to the paper are as follows:

1. *Parthasarathi Ashwaghosha:*

- Acquisition of data, analysis, interpretation of the data
- Drafting the manuscript for intellectual contents
- Managing Submission Process: Responding and making changes to reviewers' feedback
- Author approved the final version of the manuscript

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The authors are in Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Key Messages:

1. 'We surveyed over 7500 schoolchildren in Bengaluru; Rates of self-reported wheeze (15%), rhinitis (15%) and eczema (3%) were documented; Asthma and rhinitis are higher than previously reported for India, eczema is similar'
2. Male gender, low birth weight and kindergarten attendance were associated with an enhanced risk of allergic rhinitis and asthma, whilst pet ownership reduced risk in this cohort.
3. A significantly high proportion of asthmatic children in this cohort showed evidence of poorly controlled asthma

To the Editor,

India is a Low-Middle Income Country (LMIC) with a population of ~1.3bn. It is the second most populous country comprising 20% of the global population. Whilst India has not faced an 'allergy epidemic' as in High Income Countries (HICs), there is some evidence that the burden of allergic diseases has gradually risen¹, and is greatly magnified by the absolute numbers and is compounded by the unmet demand for allergy services^{2,3}. Data regarding epidemiology, risk factors and natural course of allergic diseases in India are relatively sparse. By virtue of considerable diversity in culture, breast feeding, infections including parasitic, diet, environmental conditions such as weather, aero-allergens, and unacceptably high levels of particulate matter $\leq 2.5\mu\text{m}$ (PM_{2.5}), India offers an invaluable platform to study immune-mediated diseases^{3,4}.

The aim of this study was to investigate the prevalence and risk factors of allergic diseases amongst children resident in Bengaluru. A cross-sectional cohort study was conducted in 2018 involving 40 schools, randomly selected from 226 schools from 5 wards (randomly selected from 198 wards). This study was approved by the Institutional Ethics Committee of JSS Medical College, Mysuru (Approval number: JSSMC/IEC/2017/Aca study 05/ 2018-19). A written informed consent was obtained from the parents of all participants. The cohort comprised 9,085 children, Children of all ages >6years were included and their parents were invited to complete the ISAAC questionnaire (demographics in supplementary table 1). All parents had competency in English language and filled the questionnaire. Briefly, the questionnaire had 21 items, including core questions to assess the

prevalence of rhinitis, asthma and eczema. Each question required either a 'yes' or 'no' response or the question sought a numerical answer. Questionnaire response rate was 86% (n= 7803).

Multinomial logistic regression analyses using SPSS v.23 was conducted to generate odds ratios and 95% confidence intervals for multiple variables recognized to be associated with allergic diseases. Chi-square test was employed to investigate differences among various categorical variables. Data on prevalence and regression analysis are summarized in Table-1 and Figure 1.

The mean age ($\pm$ SD) of the cohort was 9.6 ($\pm$ 2.6) years with an equal representation of gender; 6.3% were pre-term and 12.5% were low birth weight. 39% had siblings (birth order was not investigated), 79% were exclusively breastfed and 55.5% had attended kindergarten. Lifetime prevalence of wheeze (surrogate for asthma) was 16%, with a relatively greater proportion of males. A very low proportion (3.8%) of those with a lifetime prevalence of wheeze were on any type of medication while only 1.6% were on an asthma action plan/ management plan. Only 10% and 15% of the cohort had a physician-diagnosed asthma and rhinitis respectively. 22% of children had rhinitis, with a slightly greater female preponderance. Only 4% of cohort had eczema, also with a female preponderance. Almost all (95%) children with eczema had a physician confirmed diagnosis.

Multinomial regression analysis revealed that children with siblings and those that attended kindergarten had significant odds of having all the three allergic conditions, with the impact of kindergarten attendance being 2-3-fold. Male gender and low birth weight enhanced the odds of rhinitis and asthma but not eczema. Interestingly pet ownership protected against airways diseases and not eczema. A UK birth cohort study reported that pet ownership during pregnancy and early childhood reduced the risk of atopic sensitization and atopic asthma but enhanced risk of non-atopic asthma⁵. Exclusive breast feeding protected against eczema but not airways diseases. This is in contrast with findings of a systematic review and meta-analysis that reported a protective effect on asthma.⁶ Exposure to environmental tobacco smoke (ETS) and recurrent upper respiratory infections during the first 3months of life increased the odds of wheeze and rhinitis by nearly 4-fold but not eczema. ETS is a recognized risk factor affecting asthma control and antenatal exposure significantly enhances risk of wheeze in the child^{3,7}. The median hair nicotine levels in Indian women have been reported to be greater⁸ than in western countries and the nature of ETS in India is different, as 72%

smoke 'bidi's'³. Presence of a co-existing allergic disease enhanced the odds of another allergic disease, which is a well-recognized phenomenon and serves as an internal validation for our dataset.

This is the largest and most comprehensive study from India thus far that not only generated data on prevalence but also analyzed risk factors. The prevalence of wheeze and rhinitis from this paediatric cohort in Bengaluru, is much higher than the overall prevalence reported as a part of previous multinational ISAAC studies³. Other prevalence data from India have shown wide range in prevalence that could at least in part be explained by geographical location, rural *versus* urban differences, varying sample sizes and differences in study methodology. The prevalence of eczema was however approximately the same as that reported previously as a part of multinational ISAAC studies. Bengaluru is a metropolitan city with a higher socio-economic status of residents compared to other Indian cities in Eastern and Northern states. Furthermore, it has high levels of particulate matter (PM_{2.5}), mainly from traffic pollution. There is a significant migrant population from other Indian states into Bengaluru due to the IT industry.

A significant proportion of children in this cohort showed evidence of poorly controlled asthma, with nearly 40% experiencing acute exacerbations >12 times per year (Figure-1). Compliance to therapy was only 54%, with only 65% on inhaled corticosteroids. 89% reported use of inhaled devices, suggestive of excessive use of rescue therapy (further details in supplementary figure 1). The AP-AIM study reported that nearly 90% of asthmatics in India had uncontrolled asthma with recurrent oral corticosteroid use (~10.5 times/year), although this study did not report data separately in children⁹. The AP-AIM study highlighted that Indian patients had a preference to oral medications as opposed to inhaled therapies⁹.

This study has limitations. First, it was questionnaire-based with only a small proportion of children having a physician diagnosed allergic disease and no data on allergen sensitisation, peripheral blood eosinophil counts and serum total IgE. Second, other recognised variables that are relevant to allergic diseases such as birth order, weaning and complementary foods, maternal smoking during pregnancy, family history, mode of childbirth, details of pet ownership, sources of indoor air pollution, stool examination, BCG scar size, history of tuberculosis etc., were not captured in the questionnaire. Third, the study was conducted in Bengaluru, one of the most urbanised and polluted

cities of India. Fourth, all the parents who participated in this study had proficiency in English language, i.e., those who lacked proficiency were not included. This makes our dataset not fully representative for the paediatric population in Bengaluru.

In conclusion, the prevalence of asthma and rhinitis in this Bengaluru cohort is higher than the previously reported overall prevalence in India. A high proportion of children in Bengaluru had uncontrolled asthma. Hence there is an urgent need for a strategic multipronged approach to address this issue consisting of parent and physician education, availability of trained specialists along with efforts to reduce indoor and outdoor air pollution and ETS. Larger prospective and longitudinal multi-center studies investigating phenotypes, risk factors and natural course of disease are needed to pave

Legend for Figure-1: Self-reported prevalence and clinical characterisation of allergic rhinitis, eczema and asthma in the study population of n=7804 with a mean age of $9.61 \pm (2.582)$ in the city of Bengaluru, India in the year 2018

the way for primary and secondary prevention strategies.

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Table 1: Multinomial logistic regression analysis to determine the factors contributing to the development of Asthma, Allergic rhinitis and Eczema individually in the study population of the city of Bengaluru, India (2018)

Parameters	Asthma		Allergic Rhinitis		Eczema	
	Adjusted OR	p-value	Adjusted OR	p-value	Adjusted OR	p-value
	(95% CI)		(95% CI)		(95% CI)	
Age less than 10 years	0.93 (0.81-1.08)	0.37	0.96 (0.85-1.08)	0.53	0.92 (0.72-1.16)	0.49
Male gender	1.46(1.27-1.68)	<0.01	1.22 (1.09-1.38)	<0.01	1.18 (0.93-1.49)	0.16
Low birth weight ¹	1.21 (1.01-1.45)	0.03	1.2 (1.07-1.45)	<0.01	1.19 (0.89-1.59)	0.23
Pre-term delivery ²	0.99 (0.75-1.32)	0.98	1.42 (1.13-1.80)	<0.01	1.00 (0.63-1.61)	0.97
Presence of siblings	1.28 (1.08-1.51)	<0.01	1.37 (1.20-1.57)	<0.01	1.96 (1.49-2.58)	<0.01
Parents/Relatives smoke ³	3.99 (3.19-4.98)	<0.01	0.99 (0.79-1.26)	0.99	1.40 (0.84-2.33)	0.19
Attending kindergarten	2.34 (1.97-2.77)	<0.01	2.46 (2.14-2.82)	<0.01	2.96 (2.22-3.97)	<0.01
Breastfed exclusively ⁴	0.86 (0.72-1.03)	0.11	0.93 (0.80-1.09)	0.38	0.66 (0.49-0.90)	<0.01
Recurrent URI ⁵ in the first three months of birth	3.09 (2.54-3.77)	<0.01	1.04(0.83-1.30)	0.69	0.97 (0.60-1.55)	0.9
Presence of pets ⁶ in the house	0.53(0.46-0.63)	0.02	0.74(0.58-0.94)	<0.01	0.91 (0.84-1.12)	0.97
Co-existence with Allergic rhinitis	7.33(6.41-8.39)	<0.01	N/A	N/A	5.39 (4.12-7.06)	<0.01
Co-existence with Asthma	N/A	N/A	7.33 (6.41-8.39)	<0.01	3.22 (2.49-4.16)	<0.01
Co-existence with Eczema	3.22 (2.49-4.16)	<0.01	5.39 (4.12-7.06)	<0.01	N/A	N/A

Note: The above is a multinomial logistic regression analysis of the study population of n=7804 children with mean age $9.61 \pm (2.582)$ in the city of Bengaluru, India in the year 2018. ¹Low birth weight is defined as the neonate weighing <2.5 Kg at birth. ²Pre-term birth is defined as the child being born before 3 weeks of expected date of delivery. ³Parents/relatives smoke is defined as mother, father or any close relative smokes. ⁴Exclusive breast feeding is defined as the only diet for the infant is breastmilk up to 6 months of age. ⁵URI is an abbreviation for Upper Respiratory tract Infection. ⁶pets include both animals and birds.

Accepted Article

PREVALENCE OF ALLERGIC DISEASES IN THE STUDY POPULATION

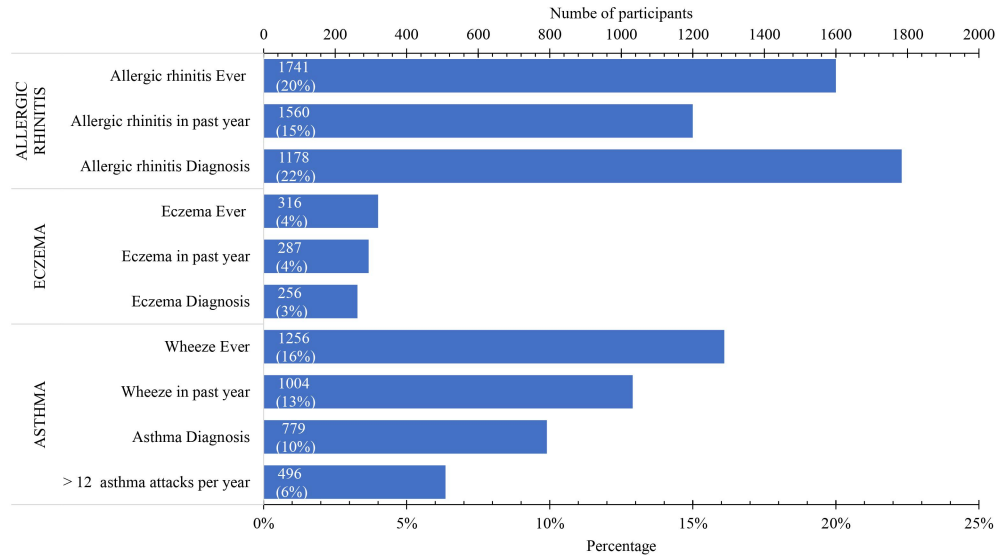
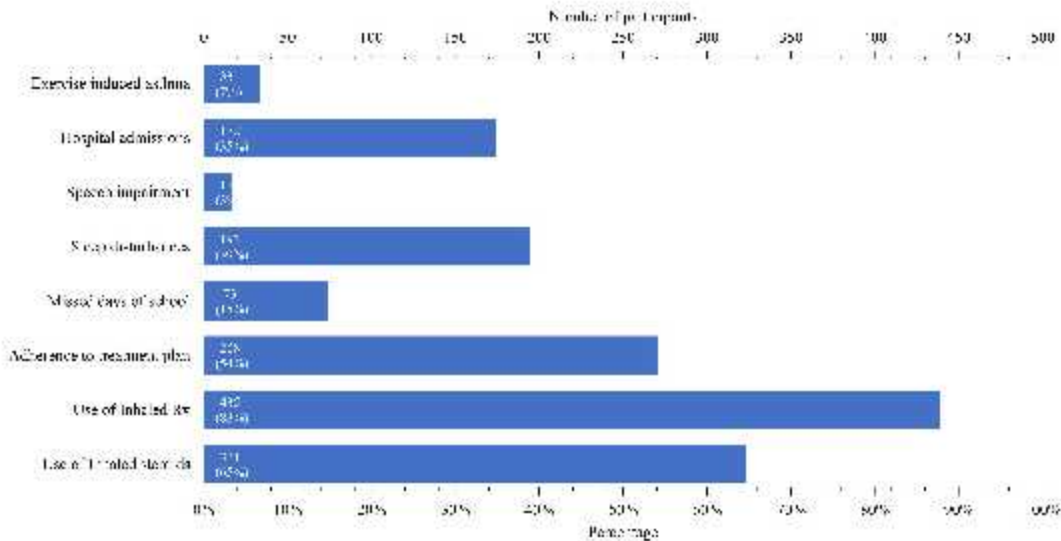


Figure-1: Self reported prevalence and clinical characterisation of allergic rhinitis, asthma and eczema in the study population of n=7804 with a mean age of $9.61 \pm (2.582)$ in the city of Bengaluru, India in the year 2018

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REPORTED VARIABLES IN THE STUDY POPULATION WITH >12 ATTACKS OF WHEZZE PER YEAR



Supplementary Table 1. Reported frequency of admissions, medications and other variables in the study population with >12 attacks of wheeze per year (i.e. n=156) in the city of Bengaluru, India in the year 2018

E-Table 1: Demographic factors of the study population consisting of both males and females in the city of Bengaluru, India in the year 2018

	Female	Male	Total
	n=3906 (50.1%)	n=3897 (49.9%)	n=7803 (100%)
Age *	9.61 ± (2.582)		
Age group			
less than 10 years	1934 (49.50%)	2033 (52.20%)	3967 (50.80%)
10 years and older	1972 (50.50%)	1864 (47.80%)	3836 (49.20%)
Pregnancy duration: Pre-Term ¹			
Yes	174 (6.00%)	178 (6.7%)	352 (6.3%)
No	2736 (94.0%)	2475 (93.3%)	5211 (93.7%)
Low Birth Weight ²			
Yes	514 (13.20%)	460 (11.80%)	974 (12.50%)
No	3392 (86.80%)	3437 (88.20%)	6829 (87.50%)
Presence of Siblings			
Yes	1316 (45.20%)	847 (31.90%)	2163 (38.90%)
No	1594 (54.80%)	1806 (68.10%)	3400 (61.10%)
Exclusive breast feeding done ³			
Yes	2304 (79.20%)	2079 (78.40%)	4383 (78.80%)
No	606 (20.80%)	574 (21.60%)	1180 (21.20%)
Attended Kindergarten			
Yes	2246 (58.60%)	1963 (52.40%)	4209 (55.50%)
No	1589 (41.40%)	1786 (47.60%)	3375 (44.50%)

Note: Demographic factors for the study population of n=7804 children with mean age 9.61 ± (2.582) in the city of Bengaluru, India in the year 2018. ¹ Pre term birth is defined as the child being born before 3 weeks of expected date of delivery. ² Low birth weight is defined as the neonate weighing <2.5 Kg at birth. ³ Exclusive breast feeding is defined as the only diet for the infant is breastmilk up to 6 months of age. *Age describes the age of mean age ± SD for the entire population inclusive of both males and females.

