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Understanding the burden of food allergy among urban and rural school children from north India

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ABSTRACT

Background: There is paucity of reliable epidemiological data regarding the burden of food allergy in most developing countries, including India.

Objective: To provide current estimates of the prevalence and distribution of food allergy among urban and rural school children aged 6–14 years in Delhi and the National Capital Region (NCR) of Khekra in India.

Methods: A cross-sectional study was conducted from January 2022 to February 2023 to enroll school children, 6–14 years, from select urban and rural schools in Delhi and NCR. A questionnaire consisting of questions focused on household environment, early life factors, and pediatric food allergy characteristics was administered by a trained medical researcher to collect parent-proxy data. Univariate statistics were used to describe frequencies, percentages, and 95% confidence intervals for survey items.

Results: The estimated prevalence of parent-reported food allergy was 0.8% (95% CI: 0.4–1.5; urban: 0.4%, 95% CI: 0.1–1.1; rural: 1.7%, 95% CI: 0.7–3.5). Fruits such as mango (0.3%, 95% CI: 0.1–0.9), strawberry (0.1%, 95% CI: 0.0–0.7), orange (0.1%, 95% CI: 0.0–0.7), and custard apple (0.1%, 95% CI: 0.0–0.7) were reported only by urban children, while rural children reported yogurt (0.6%, 95% CI: 0.1–1.8) and wheat (0.3%, 95% CI: 0.0–1.3). Both groups reported brinjal (also known as eggplant) and banana, 0.1% (95% CI: 0.0–0.7) of urban and 0.3% (95% CI: 0.0–1.3) of rural, respectively. Overall, commonly reported clinical symptoms were diarrhea and/or vomiting (100%, 95% CI: 76.2–100), abdominal pain (88.9%, 95% CI: 58.6–98.8), and rash/itchy skin (66.7%, 95% CI: 34.8–89.6). Among children with parent reported food allergy, 66.7% (95% CI: 34.8–89.6) of food allergies were physician diagnosed, of which 33.3% were diagnosed via history alone (95% CI:7.7–71.4) while 66.7% (95% CI: 28.6–92.3) were confirmed via skin prick test and/or blood test.

Conclusion: The overall prevalence of food allergy is very low in Delhi and Khekra, India. Future work should focus on elucidating the complex interplay of early-life, environmental, genetic, and

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lifestyle factors to understand the reasons for India's low food allergy burden and improve epidemiological clues to prevention for the nations with higher disease burden.

Keywords: Food allergy, Prevalence, India, Children, Cross-sectional studies

INTRODUCTION

Food allergy (FA) is an immune-mediated chronic disorder that is recognized as a significant global public health burden in many countries. Most FA research carried out thus far primarily represents populations from industrialized/westernized countries.[1-7] Very little is known regarding the prevalence of FAs in developing countries, particularly India.[8,9]

Limited evidence from the EuroPrevall study shows very low prevalence of FA despite high rates of sensitization among school children aged 7–10 years from China, India (Bengaluru and Mysore regions), and Russia.[10] In the same study, probable FA as defined by appearance of food-related allergic symptoms within 2 h of ingestion of a triggering food as well as the presence of allergic sensitization to the triggering food (positive Immunoglobulin E (IgE) and/or skin prick test (SPT) result) was reported to be 0.14%, while food sensitization by sIgE was highest in India (19.1%), followed by China (ranging from 7% to 16.8%), and Russia (8%). These findings were similar to results reported by the same group in Indian adults suggesting high levels of food sensitization (26.5%) but low FA prevalence (1.2%).[11]

Growing evidence also suggests that FA is a complex trait influenced by genetics, environment, and genome-environment interactions.[12] Several risk factors have been proposed to contribute to food allergy or sensitization. These include, but are not limited to, male sex in children, positive family history of FA, co-existence of atopic dermatitis, increased hygiene, the influence of the microbiome, vitamin D insufficiency, reduced consumption of omega-3-polyunsaturated fatty acids and antioxidants, increased use of antacids, and the timing and route of exposure to foods.[13-17] Further, studies also show that children growing up in rural communities have the lowest rates of FA (independent of race/ethnicity, income, sex, age, and latitude),[18] and that the rural environment might be protective against allergic diseases.[19-21]

Given that population-based epidemiological surveys on FA are relatively few among the Indian population, it is unclear if the prevalence of FA in India will show patterns similar to the Western world as its economy grows and its population embraces a more westernized lifestyle. With the lack of information available on FA in India, this study aimed to define and compare the burden of FA among urban and rural school children in Delhi and the National Capital Region (NCR) of Khekra. We collected parent proxy-report data on FA (immediate allergic reaction after eating certain food such as itchy throat, rashes, vomiting, swelling of throat, etc.) prevalence, types of food triggers, associated symptoms, physician diagnosis, and diagnostic practices. Furthermore, we comprehensively examined the environmental and early life factors among urban and rural children in Delhi and Khekra.

METHODS

Study population and study design

A cross-sectional questionnaire-based study was conducted from January 2022 to February 2023 to enroll school children between 6 and 14 years of age from select urban and rural schools in Delhi and the NCR of Khekra. Delhi, the capital of India, is a massive metropolitan area in the country's north.[22] As of the year 2023, the population of Delhi was almost 35 million people.[23] Khekra is a town in the Baghpat district of Uttar Pradesh in India. The distinction between towns and cities in the Indian Census is based on population size, and the level of economic and social development. While a town may have some urban characteristics, it may not have the same level of infrastructure, economic activity, and population density as a city, with a significant proportion of its population engaged in agricultural activities.[24] On the other hand, an area is considered rural if it has a population of less than 5000 people and a population density of less than 400 people per square kilometer, and with more than 25% of the population engaged in agricultural activities.[24] In this study, the same definition has been used for selecting schools in urban and rural areas.

Study procedures

A stratified random sampling method was used to enroll children and their parents/caregivers in the study after receiving permission from the school authorities and the State Department of Education. Bilingual (English and Hindi) invitations to participate along with the consent forms were sent home with every fourth child enrolled in classes I to IX at select schools. The select schools were identified based on 2 criteria: (i) urban vs rural, (ii) geographic representation of 4 regions and 11 districts of Delhi. Children from 4 urban and one rural school were included. Efforts were made to recruit an equal number of parents/caregivers for each year within the age group of 6–14 years and ensure gender balance among the enrolled subjects. Children were excluded if they were suffering from any terminal illness, were immuno-compromised, or were undergoing any kind of chronic medical treatment, as reported by the parent/guardian.

A trained medical researcher conducted a formal, structured interview with parents/caregivers after receiving the signed informed consent. All interviews were conducted in the home environment in a separate room with adequate visual and audio privacy. During these interviews, parents/caregivers were briefed about the purpose of the study again and a basic understanding of FAs was shared prior to undertaking the survey. The investigators were available either in-person or remotely to respond to any inquiries from the parents/guardians or field researchers. The heights and weights of children were recorded using standardized weighing scale and stadiometer on the day the interview was conducted. The questionnaire was available in Hindi and English and was back-translated to English according to standard protocols to ensure reliability and validity.

Study instrument

A questionnaire consisting of questions focused on household environment, early life factors, current life factors, as well as pediatric FA characteristics was administered to parents/guardians to collect data about their child/children (Supplemental Appendix 1). The first section of the questionnaire was aimed at capturing demographic information, such as birth city, place of current residence, birth order, religion, family type and size. The second section focused on the socio-demographic factors. The socioeconomic status (SES) was assessed based on the Modified Kuppuswamy socioeconomic scale.[25] The third section collected information on the child's current life factors, such as housing type, source of drinking water, dietary preferences, exposure to pets, smoke, etc. The fourth section collected information about the pre-, peri-, and postnatal factors, such as maternal smoking during pregnancy, birth type and weight, duration of breast feeding, solid food introduction patterns, etc. The fifth section collected data on family history of allergies. The sixth section was aimed at collecting information about the child's current health conditions. The final section of the questionnaire collected data on food allergens, signs, and symptoms of a food-allergic reaction.

Data collection occurred via a web-based data capture system (REDCap), which allowed for seamless data collection. The data were collected either through a paper-based approach or a computer-assisted personal interviewing approach. For the paper-based approach, spot-checks were performed when the collected data was entered into REDCap to ensure accurate data entry. No patient identifiers were collected to ensure privacy and anonymity.

Statistical analysis

Data obtained through REDCap was exported to Microsoft Excel. Univariate statistics were used to describe frequencies, percentages, and 95% confidence intervals for survey items. Chi-square tests assessed differences among variables for urban and rural school participants, with p-values indicating the significance of urban-rural distinctions. All statistical analyses were performed with SPSS v28.0. Two-sided $P \leq 0.05$ was taken as statistically significant.

RESULTS

As shown in Table 1, the demographic characteristics of a total of 1072 participants, comprising 717 children from urban areas (66.9%) and 355 from rural areas (33.1%) were examined. Overall, majority of the study participants were female (69.3%, 95% CI: 66.5–72.0), in the 14–16 years of age group (43.4%, 95% CI: 40.4–46.4), and underweight (65.8%, 95% CI: 62.9–68.6). With regard to SES, most participants indicated that they belonged to the middle class (41.4%, 95% CI: 38.5–44.4). The findings showed statistically significant differences among children going to urban and rural schools for various demographic variables, for example, sex, age, religion, family type, SES, and body mass index (Table 1).

Data on differences in the exposure to environmental factors among urban and rural school children have been detailed in Table 2. Nearly all urban children consumed semi-purified water (97.4%, 95% CI: 96.0–98.3) and used non-biomass fuels for cooking or heating (87.2%, 95% CI: 84.6–89.5), while nearly half of the rural children consumed natural or non-purified water (53.2%, 95% CI: 48.0–58.4) and used biomass fuels for cooking and heating (cow dung: 55.8%, wood: 52.4%). Statistically significant differences were seen for source of water, fuel used for cooking, indoor smoke, smoking inside the home, pest, and pets in the house.

Table 3 describes the early life factors, grouped into three categories (prenatal, perinatal, and postnatal) among children. The majority of children were breastfed within 6 h of birth (93.6%, 95% CI: 92.0–94.9). Solid food was introduced earlier to the diet of rural children (<6 months-rural: 29.9%, 95% CI: 25.3–34.8 vs urban: 5.4%, 95% CI: 4.0–7.3), although a majority reported delayed top milk (milk other than breast milk)/milk products introduction (>12 months-rural: 69.3%, 95% CI: 64.4–73.9 vs urban: 5%, 95% CI: 3.6–6.8). Statistical significance was seen based on school settings for several prenatal, perinatal, and postnatal variables examined in the study.

The parent-reported and physician diagnosed FA among the total of 1072 participants showed that parent-reported FA was 0.8% (95% CI: 0.4–1.5), with 0.4% (95% CI: 0.1–1.1) in urban areas and 1.7% (95% CI: 0.7–3.5) in rural areas (Table 4). Fruits such as mango (0.3%, 95% CI: 0.1–0.9), strawberry (0.1%, 95% CI: 0.0–0.7), orange (0.1%, 95% CI: 0.0–0.7), and custard apple (0.1%, 95% CI: 0.0–0.7) were reported by the urban subgroup, while yogurt (0.6%, 95% CI: 0.1–1.8) and wheat (0.3%, 95% CI: 0.0–1.3) were reported by the rural subgroup. Symptoms commonly reported by those with FA (N = 9) included rash/itchy skin (66.7%, 95% CI: 34.8–89.6), diarrhea and/or vomiting (100%, 95% CI: 76.2–100), and abdominal pain (88.9%, 95% CI: 58.6–98.8). Among those with parent reported FA, 66.7% (95% CI: 34.8–89.6) of FAs were diagnosed by a physician, of which 33.3% were diagnosed via history alone (95% CI:7.7–71.4) and 66.7% (95% CI: 28.6–92.3) were confirmed via SPT and/or specific IgE testing.

DISCUSSION

Food allergy prevalence and characteristics

The estimated prevalence of parent-reported FA in this retrospective study cohort was very low (0.8%), urban vs rural (0.4% vs. 1.7%). To our knowledge, the present study is the first to establish the prevalence of parent-reported FA among children aged 6–14 years, living in Delhi and Khekra, and to comprehensively compare environmental and early life factors among urban and rural children from this region.

An important theme that emerged from our study was the overall low prevalence of FA in Delhi, which is in concordance with the limited data on FA among children available from Karnataka, southern Indian state, that showed an overall prevalence of self-reported adverse reactions to foods to be 1.8%.[10] Despite the presence of common risk factors, this low burden may be due to a lack of disease awareness among the general public, poor recognition and reporting, or due to possible protective effect of the Indian environment, including environmental microbes that are prominent in traditional farming environments, helminth infection, and high fiber diet, that may result in lower prevalence despite the presence of common risk factors.[26,27] While multicenter studies are warranted to understand the population level burden of FA in children and adults, public education about FA should

Variable	Total (*n* = 1072)			Urban (*n* = 717-66.9%			Rural (*n* = 355-33.1%			*p*-value
	n	%	95% CI	*n*	%	95% CI	*n*	%	95% CI	
Birth order										
First	548	51.1	48.1-54.1	369	51.5	47.8-55.1	179	50.4	45.2-55.6	0.795
Second +	524	48.9	45.9-51.9	348	48.5	44.9-52.2	176	49.6	44.4-54.8	
Sex										
Male	329	30.7	28.0-33.5	151	21.1	18.2-24.2	178	50.1	45.0-55.3	<0.0001[a]
Female	743	69.3	66.5-72.0	566	78.9	75.8-81.8	177	49.9	44.7-55.0	
Age (in years)										
6 to 10	235	21.9	19.5-24.5	70	9.8	7.8-12.1	165	46.5	41.3-51.7	<0.0001[a]
11 to 13	372	34.7	31.9-37.6	242	33.8	30.4-37.3	130	36.6	31.7-41.7	0.376
14 to 16	465	43.4	40.4-46.4	405	56.5	52.8-60.1	60	16.9	13.3-21.1	<0.0001[a]
Religion[b]										
Hindu	940	87.7	85.6-89.6	677	94.4	92.6-95.9	263	74.1	69.3-78.4	<0.0001[a]
Muslim	131	12.2	10.4-14.3	39	5.4	4.0-7.3	92	25.9	21.6-30.7	<0.0001[a]
Type of family[c]										
Nuclear	650	60.6	57.7-63.5	489	68.2	64.7-71.5	161	45.4	40.2-50.6	0.000[a]
Joint	422	39.4	36.5-42.3	228	31.8	28.5-35.3	194	54.6	49.4-59.8	
Socioeconomic status (SES)[d]										
Upper (16-29)	309	28.8	26.2-31.6	229	31.9	28.6-35.4	80	22.5	18.4-27.1	0.001[a]
Middle (11-15)	444	41.4	38.5-44.4	318	44.4	40.7-48.0	126	35.5	30.6-40.6	0.006[a]
Lower (03-10)	319	29.8	27.1-32.5	170	23.7	20.7-26.9	149	42.0	36.9-47.2	<0.0001[a]
Body Mass Index (BMI)[e]										
Underweight (<18.5)	705	65.8	62.9-68.6	446	62.2	58.6-65.7	259	73.0	68.2-77.4	0.000[a]
Normal (18.5-22.9)	320	29.9	27.2-32.6	235	32.8	29.4-36.3	85	23.9	19.7-28.6	0.003[a]
Overweight (23-24.9)	47	4.4	3.3-5.7	36	5.0	3.6-6.8	11	3.1	1.7-5.3	0.158
Obese (≥25)	0	0.0	0.0-0.2	0	0.0	0.0-0.3	0	0.0	0.0-0.7	1.00

Table 1. Demographic characteristics of study participants (N = 1072). [a]*p < 0.05, CI: Confidence interval.* [b]*The percentage does not add up to 100% to protect the identity of religion of one participant.* [c]*Nuclear family: Single married couple with/without their unmarried children. Joint family: Two or more married couples of a single generation (horizontal level) or three or more couples if multiple generations (vertical levels).* [d]*SES scores were calculated based on the Modified Kuppuswamy socioeconomic scale. It is a well-validated scale, particularly ideal for assessing SES in the Indian context. This scale includes three parameters-occupational status of the head of the family, educational status of the head of the family, and overall aggregate income of the whole family, pooled from all sources. Each of these parameters is divided into subgroups and scores have been allotted to each subgroup. The total score of Kuppuswamy socioeconomic scale ranges from 3 to 29.* [e]*BMI is calculated as weight in kilograms divided by height in meters squared (kg/m²) based on Asia-Pacific guidelines*

not be ignored. Families should be educated on FA in terms of its natural history (which is related to the type of food allergen involved), prevention of accidental exposure, and management in the event of an adverse reaction.

A particularly notable observation in our study was the slightly higher prevalence of FA among rural children when compared to urban children. It is possible that this difference may be multifactorial, attributed to prenatal factors such as positive family history of atopic disorders that was reported more frequently by children from rural sites, compared to urban sites; greater exposure to passive smoking during pregnancy among rural mothers or environmental factors such as, exposure to indoor smoke.[19,28] In the present study, exposure to passive smoking, a practice commonly witnessed in rural Indian households,[29] was over three times higher among rural children, compared to their urban counterparts. In a recent systematic review

Variable	Total (n = 1072)			Urban (n = 717-66.9%			Rural (n = 355-33.1%			*p*-value
	n	%	95% CI	*n*	%	95% CI	*n*	%	95% CI	
Primary source of water										
Natural/non purified (ex-Handpump or tube well)	205	19.1	16.9-21.6	16	2.2	1.3-3.5	189	53.2	48.0-58.4	<0.0001[a]
Semi-purified (ex-Municipal corporation supply)	852	79.5	77.0-81.8	698	97.4	96.0-98.3	154	43.4	38.3-48.6	<0.0001[a]
Purified water (ex-bottled water)	15	1.4	0.8-2.2	3	0.4	0.1-1.1	12	3.4	1.9-5.7	0.0002[a]
Fuel use for cooking/heating[b]										
Biomass	291	27.1	24.5-29.9	92	12.8	10.5-15.4	199	56.1	50.9-61.2	<0.0001[a]
Cow dung	264	24.6	22.1-27.3	66	9.2	7.3-11.5	198	55.8	50.6-60.9	<0.0001[a]
Wood	255	23.8	21.3-26.4	69	9.6	7.6-11.9	186	52.4	47.2-57.6	<0.0001[a]
Non-biomass (ex-LPG, induction)	781	72.9	70.1-75.5	625	87.2	84.6-89.5	156	43.9	38.8-49.1	<0.0001[a]
Indoor smoke										
Aagarbatti/ dhoopbatti/ mosquito coil	973	90.8	88.9-92.4	677	94.4	92.6-95.9	296	83.4	79.2-87.0	<0.0001[a]
Smoking inside the home[b]	199	18.6	16.3-21.0	70	9.8	7.8-12.1	129	36.3	31.5-41.4	<0.0001[a]
		***n* = 199**			***n* = 70**			***n* = 129**		
Cigarette	25	12.6	8.5-17.7	24	34.3	24.0-45.9	1	0.8	0.1-3.6	<0.0001[a]
Bidi	139	69.8	63.2-75.9	41	58.6	46.9-69.6	98	76	68.1-82.7	0.014[a]
Hukkah	34	17.1	12.3-22.8	5	7.1	2.8-14.9	29	22.5	15.9-30.2	0.005[a]
Cigar	1	0.5	0.1-2.3	0	0	0.0-3.5	1	0.8	0.1-3.6	1.00
Pest at home (*n* = 1072)	894	83.4	81.1-85.5	573	79.9	76.9-82.7	321	90.4	87.0-93.2	<0.0001[a]
		***n* = 894**			***n* = 573**			***n* = 321**		
Lizard	703	78.6	75.9-81.2	443	77.3	73.8-80.6	260	81.0	76.4-85.0	<0.0002[a]
Cockroach	408	45.6	42.4-48.9	380	66.3	62.4-70.1	28	8.7	6.0-12.2	<0.0001[a]
Rat	576	64.4	61.2-67.5	298	52.0	47.9-56.1	278	86.6	82.6-90.0	<0.0001[a]
Pets in the house (*n* = 1072)[b]	143	13.3	11.4-15.5	30	4.2	2.9-5.8	113	31.8	27.1-36.8	<0.0001[a]
		***n* = 143**			***n* = 30**			***n* = 113**		
Dog	56	39.2	31.4-47.3	18	60	42.2-76.0	38	33.6	25.4-42.7	0.011[a]
Cat	9	6.3	3.2-11.2	3	10	2.9-24.3	6	5.3	2.2-10.6	0.397
Cow	45	31.5	24.3-39.4	6	20	8.8-36.7	39	34.5	26.2-43.6	<0.0001[a]
Goat	5	3.5	1.3-7.5	0	0	0.0-8.0	5	4.4	1.7-9.4	0.584
Hen	2	1.4	0.3-4.4	0	0	0.0-8.0	2	1.8	0.4-5.6	1.000
Buffalo	25	17.5	11.9-24.3	2	6.7	1.4-19.7	23	20.4	13.7-28.5	0.105
Parrot	2	1.4	0.3-4.4	1	3.3	0.4-14.5	1	0.9	0.1-4.1	0.377
Rabbit	3	2.1	0.6-5.5	2	6.7	1.4-19.7	1	0.9	0.1-4.1	1.000

Table 2. Environmental factors impacting childhood development ($N = 1072$). [a]$p < 0.05$, *CI: Confidence interval.* [b]*Categories are not mutually exclusive*

Variable	Total (*n* = 1072)			Urban (*n* = 717-66.9%			Rural (*n* = 355-33.1%			*p*-value
	n	%	95% CI	*n*	%	95% CI	*n*	%	95% CI	
PRENATAL FACTORS										
Maternal smoking during pregnancy										
Active smoking	13	1.2	0.7-2.0	5	0.7	0.3-1.5	8	2.3	1.1-4.2	0.038[a]
Passive smoking	264	24.6	22.1-27.3	70	9.8	7.8-12.1	194	54.6	49.4-59.8	<0.0001[a]
FH of any atopic disease	86	8.0	6.5-9.8	47	6.6	4.9-8.5	39	11.0	8.1-14.6	0.016[a]
PERI NATAL FACTORS										
Mode of birth										
Natural	821	76.6	74-79	519	72.4	69.0-75.6	197	55.5	50.3-60.6	<0.0001[a]
C-section	251	23.4	21.0-26.0	198	27.6	24.4-31.0	158	44.5	39.4-49.7	
Birth weight (kg) (mean ± SD)	2.8 ± 0.6		N/A	2.6 ± 0.6		N/A	2.6 ± 0.6		N/A	1.000
Period of gestation										
Pre-term	27	2.5	1.7-3.6	10	1.4	0.7-2.5	17	4.8	2.9-7.4	0.002[a]
Full term	1045	97.5	96.4-98.3	707	98.6	97.5-99.3	338	95.2	92.6-97.1	
Breast fed within 6 h of birth	1003	93.6	92.0-94.9	682	95.1	93.4-96.5	321	90.4	87.0-93.2	0.005[a]
POST NATAL/INFANCY										
Duration of breast feeding										
<6 months	140	13.1	11.1-15.2	73	10.2	8.1-12.6	67	18.9	15.1-23.2	0.0001[a]
6-12 months	298	27.8	25.2-30.5	238	33.2	29.8-36.7	60	16.9	13.3-21.1	<0.0001[a]
>12 months	634	59.1	56.2-62.1	406	56.6	53.0-60.2	228	64.2	59.1-69.1	0.018
Top milk/milk products (ex-yoghurt) introduction age[b]										
<3 months	120	11.2	9.4-13.2	113	15.8	13.2-18.6	7	2.0	0.9-3.8	<0.0001[a]
3-6 months	215	20.1	17.7-22.5	209	29.1	25.9-32.6	6	1.7	0.7-3.5	<0.0001[a]
6-12 months	282	26.3	23.7-29.0	359	50.1	46.4-53.7	96	27.0	22.6-31.8	<0.0001[a]
>12 months	455	42.4		36	5.0	3.6-6.8	246	69.3		<0.0001[a]

(continued)

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Variable	Total (*n* = 1072)			Urban (*n* = 717-66.9%			Rural (*n* = 355-33.1%			*p*-value
	n	%	95% CI	*n*	%	95% CI	*n*	%	95% CI	
			39.5–45.4						64.4–73.9	
Age of introduction of solid food										
<6 months	145	13.5	11.6–15.7	39	5.4	4.0-7.3	106	29.9	25.3–34.8	<0.0001[a]
6-9 months	462	43.1	40.2–46.1	360	50.2	46.6–53.9	102	28.7	24.2–33.6	<0.0001[a]
>9 months	302	28.2	25.5–30.9	266	37.1	33.6–40.7	36	10.1	7.3-13.6	<0.0001[a]
Introduction of peanut	40	3.7	2.7-5.0	36	5.0	3.6-6.8	4	1.1	0.4–2.7	0.0009[a]
	***n* = 40**			***n* = 36**			***n* = 4**			
Boiled	7	17.5	8.2-31.3	6	16.7	7.3-31.2	1	25	2.8-71.6	0.552
Roasted	26	65	49.6–78.3	24	66.7	50.5–80.3	2	50	12.3–87.7	0.602
Other (ex-peanut butter, oil etc.)	7	17.5	8.2-31.3	6	16.7	7.3-31.2	1	25	2.8-71.6	0.552
Current dietary preferences of child										
Vegetarian	533	49.7	46.7–52.7	315	43.9	40.3–47.6	218	61.4	56.3–66.4	<0.0001[a]
Non-vegetarian	539	50.3	47.3–53.3	402	56.1	52.4–59.9	137	38.6	33.6–43.7	
Medications and immunization										
Antibiotics intake during first year of life	288	26.9	24.3–29.6	185	25.8	22.7–29.1	103	29.0	24.5–33.9	0.273
Anti-helminthic medications	852	79.5	77.0–81.8	590	82.3	79.4–84.9	262	73.8	69.0–78.2	0.001[a]
Completed immunization schedule	1043	97.3	96.2–98.1	703	98.0	96.8–98.9	340	95.8	93.3–97.5	0.044[a]

Table 3. Early life exposures: factors impacting childhood development (*N* = 1072). [a]*p* < 0.05, *CI: Confidence interval.* [b]*Top milk in India refers to milk other than the breast milk*

Variable	Total ($n = 1072$)			Urban ($n = 717$)			Rural ($n = 355$)		
	n (%)	%	95% CI	*n* (%)	%	95% CI	*n* (%)	%	95% CI
Parent reported food allergy	9	0.8	0.4-1.5	3	0.4	0.1-1.1	6	1.7	0.7-3.5
Vegetarians	4	0.4	0.1-1.0	2	0.3	0.03-1.0	2	0.6	0.07-2.0
Non-vegetarians	5	0.5	0.2-1.2	1	0.1	0.0-0.7	4	1.1	0.3-2.8
Parent reported food trigger									
Brinjal (Eggplant)	2	0.2	0.0-0.6	1	0.1	0.0-0.7	1	0.3	0.0-1.3
Banana	2	0.2	0.0-0.6	1	0.1	0.0-0.7	1	0.3	0.0-1.3
Mango	2	0.2	0.0-0.6	2	0.3	0.1-0.9	0	0	0.0-0.7
Strawberry	1	0.1	0.0-0.4	1	0.1	0.0-0.7	0	0	0.0-0.7
Orange	1	0.1	0.0-0.4	1	0.1	0.0-0.7	0	0	0.0-0.7
Custard apple	1	0.1	0.0-0.4	1	0.1	0.0-0.7	0	0	0.0-0.7
Wheat	1	0.1	0.0-0.4	0	0	0.0-0.3	1	0.3	0.0-1.3
Yogurt	2	0.2	0.0-0.6	0	0	0.0-0.3	2	0.6	0.1-1.8
Other	1	0.1	0.0-0.4	0	0	0.0-0.3	1	0.3	0.0-1.3
Symptoms reported	***n* = 9**			***n* = 3**			***n* = 6**		
Itchy, tingling/swelling in mouth, lips, throat	0	0	0.0-23.8	0	0	0.0-53.6	0	0	0.0-33.0
Rash/itchy skin	6	66.7	34.8-89.6	2	66.7	17.7-96.1	4	66.7	28.6-92.3
Diarrhea and/or vomiting	9	100	76.2-100	3	100	46.4-100	6	100	67.0-100
Abdominal pain	8	88.9	58.6-98.8	3	100	46.4-100	5	83.3	44.2-98.1
Trouble breathing or wheezing	0	0	0.0-23.8	0	0	0.0-53.6	0	0	0.0-33.0
Trouble swallowing	0	0	0.0-23.8	0	0	0.0-53.6	0	0	0.0-33.0
Fainting and/or dizziness	0	0	0.0-23.8	0	0	0.0-53.6	0	0	0.0-33.0
Other	1	11.1	1.2-41.4	1	33.3	3.9-82.3	0	0	0.0-33.0
Physician diagnosed FA	6	66.7	34.8-89.6	0	0	0.0-53.6	6	100	67.0-100
	***n* = 6**			***n* = 0**			***n* = 6**		
History only	2	33.3	7.7-71.4	0	0	N/A	2	33.3	7.7-71.4
SPT and/or blood test	4	66.7	28.6-92.3	0	0	N/A	4	66.7	28.6-92.3
Oral food challenge	0	0.0	0.0-0.0	0	0	N/A	0	0	0.0-0.0

Table 4. Parent-reported food trigger(s) and physician-diagnosed food allergies ($N = 1072$). *CI: Confidence interval, SPT: Skin prick test.Note: Statistical tests were not conducted due to the limited sample sizes within specific categories*

and meta-analysis, both active and passive exposure to secondhand smoke were associated with a modest increased risk for allergic diseases, and passive smoking was associated with an increased risk for FA, both among children and adolescents.[30] Importantly, this difference in burden may be due to different criteria for determining FA. Patients in rural settings may have been mis-classified as food allergic resulting from an inaccurate interpretation of SPT or serum-specific IgE (sIgE). While we know that these clinical parameters can predict the likelihood of a food-related allergic reaction, they are not sufficient for diagnosis alone. A thorough clinical history is the first-line approach in diagnosing FAs. A study by Hossny et al. noted how physicians may consider any detectable level as diagnostic of FA and put their patients onto unnecessary elimination diets.[31] Moreover, it is common to have access to methods for sIgE measurement to single components in most developed countries; however, this is not the case in many low-income countries.[32,33] Finally, there may be an insufficient number of specialists to perform oral food challenges (OFCs) in India, and they may require specialized training to allow them to do so safely.[34] This is evident from our study findings that suggest that over two-thirds of parent reported FAs in rural Delhi were diagnosed by a physician via SPT and/or sIgE, one-third were diagnosed by history alone, and none by OFCs. Clearly, methods available for diagnosis are limited and sufficient resources should be directed towards training of health care providers dealing with FA.

Food allergens frequently reported in the present study were yogurt (a food produced by bacterial fermentation of milk), wheat, fruits (banana, custard apple, orange, strawberry, mango), and vegetables (brinjal or eggplant); different from the ones commonly reported in the Western countries of United States, United Kingdom, and Australia. This may be attributed to the unique components of the diet (commonly linked to religious beliefs in India), variation in geographic locations, as well as feeding practices.[35,36] Particularly, systematic differences exist in the manner of food preparation between North India and the West (eg, fermented milk products vs homogenized, pasteurized milk). Our study showed that 1 in 3 rural participants with a parent-reported FA suggested "yogurt" as the triggering food. However, it is interesting to note that the predominantly reported clinical manifestation was digestive discomfort consisting of abdominal pain, diarrhea, and vomiting. It is critical to differentiate this clinical presentation from non-immune mediated reactions, such as "lactose intolerance". People who are lactose intolerant are missing the enzyme lactase, that breaks down lactose, a sugar found in milk and dairy products.[37,38] As a result, people with lactose intolerance are unable to digest these foods. This condition can mimic a food allergic reaction,[37] and typically leads to overestimates of prevalence in population-based studies that rely on self-report/parent-report.[39,40] Since the management of these disorders is distinctly different, an inappropriate recognition or management may have significant implications for the patient.

Differences in early life factors among urban and rural children

We specifically examined prenatal (eg, exposure to smoking during pregnancy), perinatal (eg, mode of birth), and postnatal factors (eg, breast-feeding and infant-feeding practices, age of weaning, and age at first introduction of solids) that are known to contribute to variations in FA prevalence around the globe.[19,28,41-43] In our study, cesarean section accounted for higher childbirths in rural areas than urban. Overall, the majority of children were breast fed within 6 h of birth and approximately 3 in 5 children from the rural regions were breastfed for over 1 year. Despite some high-quality research, inconsistencies are evident around the protective role of breastfeeding in relation to many non-communicable diseases, including immunological outcomes.[44] While previous studies have demonstrated that breastfeeding is prophylactic against atopic disorders, including eczema and FA-throughout childhood and adolescence,[45,46] more recent studies investigating the long-term effects of breastfeeding on FA showed no or even an increased risk in children who were breastfed.[47,48] In a prospective twenty-year follow-up study, exclusive breastfeeding for $>$ or $=$ 9 months was associated with atopic dermatitis and symptoms of food hypersensitivity at age 5 years, and with symptoms of food hypersensitivity at age 11 years, in children with a family history of allergy.[48] There is conflicting evidence on the role of dietary proteins in human milk and the risk for FA development. It has been suggested that maternal allergen consumption during pregnancy and breastfeeding can limit allergen sensitization in the offspring.[49] Ohsaki et al and Verhasselt et al showed that the induction of tolerance can be mediated by oral intake of antigenic molecules.[50,51] These findings have led to the hypothesis that specific human milk molecules, such as intact human insulin, gliadin, and other food allergens (ie, peanut proteins, ovalbumin, wheat, β-lactoglobulin, casein, and bovine γ-globulin) may be involved in the prevention of FA.[52]

While there is strong evidence to support the early introduction of allergenic solids to prevent FA, a firm conclusion about the role of these early life factors in preventing or delaying the onset of FAs cannot be drawn from our results. In the present study, solid food was introduced earlier (before 6 months of age) to the diet of rural children, though a majority reported delayed (after 12 months) top milk (milk other than breast milk)/milk products introduction. A recent systematic review suggested that there is insufficient evidence to determine whether never vs ever being fed human milk, or whether the duration of any human milk feeding, are associated with FA development.[53]

Environmental factors

Significant differences were also observed between the urban and rural household environment, such as variation in the quality of water supply and exposure to pets. First, while children in rural households primarily consumed natural/non-purified water, ie, water from handpump or tube wells, nearly all urban children consumed semi-purified water (municipal corporation supply). This may have impacted their exposure to microbiomes and infections in early life. Research suggests that pathogenic microbiomes and allergens can damage the skin, gut, and respiratory epithelial cells, allowing for penetration of environmental insults leading to pathological changes including fibroblast activation, and smooth muscle hyperplasia, resulting in various inflammatory conditions such as atopic dermatitis, FA, and asthma.[27] In contrast, environmental microbes that are prominent in traditional farming environments and helminth infections can protect against allergic diseases via a range of putative immunomodulatory mechanisms (eg, induction of T-regs, modulation of the microbiota).[54]

Similarly, non-biomass fuels (liquified petroleum gas, induction) were commonly used in urban households, while biomass fuels (cow dung, wood) were the main source of cooking/heating in rural households, implying higher indoor pollution in rural households. While disruption of the epithelial barrier with subsequent exposure to external pathogens offers to be a promising mechanism linking air pollution to allergic disease pathways,[55] and underpins the dual allergen exposure hypothesis, studies are needed to examine the association between indoor air pollution and the risk of FA.

Lastly, both urban and rural children were exposed to animals, although the type of animal varied. This may also be a possible explanation for the overall reduced FA burden in our study cohort. Early-life exposure to pets has been suggested to be effective in the prevention of allergic diseases. Results of a recent study suggest that the protective effect of pet exposure is dependent on the specific kind of pet and the extent to which it traverses the indoor and outdoor environments.[56] Particularly, exposure to dogs and cats might be beneficial against the development of certain food allergies. Future research that investigates the relationship between outdoor environment and risk of FA and unravels the complex interplay between numerous environmental factors is also essential to comprehend the reasons for India's low FA burden, despite the presence of factors that are frequently acknowledged as FA triggers in the West.

Limitations

Although this study provides important data on FA prevalence and compares the environmental and early life factors among urban and rural children in Delhi and Khekra, there are several limitations. First, the study is cross-sectional, which does not allow for the temporal analyses and longitudinal assessment of FA symptoms. Second, the data are based on parent response, which is subject to reporter and recall biases. Third, regression analyses could not be performed due to the small sample size and rare events. Fourth, selection bias may also be a study limitation. While all schools were eligible to participate in the study, subjects drawn from select urban and rural schools may not be representative of all schools in Delhi NCR. Lastly, marked regional differences regarding environmental exposures, lifestyle, and dietary habits exist across different regions in India such that results of our study may not reflect all the regional variations within India.

CONCLUSION

The present study demonstrates that the prevalence of FA among urban and rural school children aged 6–14 years in Delhi and Khekra is among the lowest in the world and with its diversity and culture, India is potentially an important source of information on FA. The observed differences in FA burden, household environment, and early life factors among the subgroups in our study are intriguing and deserve further investigation to reveal the true extent of the problem and provide epidemiological clues to prevention.

Abbreviations

FA, Food allergy; IgE, Immunoglobulin E; NCR, National Capital Region; SPT, Skin Prick Test; US, United States

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Availability of data and materials
The data will be made available on reasonable request to the corresponding author and conditional on Institutional Review Board approval.

Author contributions
SS, NG, ShN, RuG, MJV, LB, AS, SN, RG conceived the study, interpreted the results, and prepared the manuscript. PD, KI, and CW contributed to data analysis. All authors critically reviewed the manuscript and approved the final draft for submission to WAOJ.

Ethics approval
This study was approved by the Institutional Review Board (IRB) at Northwestern University (STU00215816), Chicago, United States, and Sigma IRB (10071/IRB/21–22), New Delhi. Informed consent was obtained from the parents prior to commencing the study interview.

Authors' consent for publication
All authors have agreed to the publication of this manuscript.

Declaration of competing interest
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Appendix A. Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.waojou.2024.100916.

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