

# Total airway mechanics and fractional exhaled nitric oxide levels of children living in *banjihas* (semi-basements)

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# Abstract

**Background:** The ISAAC phase III study in Korea found a higher incidence of wheezing illnesses among residents in basements or semi-basements.

**Objectives:** This study investigates the link between living in *banjihas* (semi-basements) and airway resistance and Th2 airway inflammation in Korean children, compared to those on higher floors

**Methods:** We assessed 575 fifth- and sixth-grade students (aged 10–12) in an inner-city area of South Korea. The study utilized impulse oscillometry to measure small and total airway resistance (Rrs20–5 and Rrs0, respectively) and Fractional Exhaled Nitric Oxide (FeNO) measurements to evaluate airway inflammation. We also considered a range of biological and environmental factors, including allergen sensitization, serum 25-hydroxyvitamin D levels, and urinary metabolites like VOCs, bisphenol, and triclosan. Participants were categorized by living floors: *banjihas*, first-fifth floors, and sixth floors or higher.

**Results:** Twenty-five children (4.3%) lived in *banjihas*, 311 (54.1%) on the first to fifth floor, and 239 (41.6%) on the sixth floor or above. Despite similar levels of allergen sensitization and urinary pollutant metabolite levels across all groups, *banjiha* dwellers showed significantly higher total airway resistance (adjusted  $\beta$ 1: 0.633, 95%CI: 0.156, 1.109; P = 0.009) and a greater prevalence of elevated FeNO levels (> 35 ppb) (P = 0.033). These findings persisted after adjusting for critical factors like height, gender, BMI z-score, and birth conditions.

**Conclusion:** Children in *banjihas* exhibit elevated airway resistance and FeNO levels independently of allergen sensitization or pollution exposure, underscoring the necessity for enhanced focus on their respiratory health in such living conditions.

Key words: Fractional exhaled nitric oxide (FeNO), airway resistance, semi-basements, allergen sensitization or pollution exposure, children

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Abbreviations:

FeNO	factional exhaled nitric oxide
SDOH	social determinants of health
SES	Socioeconomic Status
ISAAC	International Study of Asthma and Allergies in Childhood
IOS	impulse oscillometry
Rrs	respiratory system resistance
VOCs	volatile organic compounds

#### Introduction

The concept of social determinants of health (SDOH) plays a pivotal role in understanding the myriad sociological and economic factors influencing health outcomes. These determinants, encompassing environmental exposures and social conditions, are crucial in assessing the prevalence of of allergic disease,<sup>1-4</sup> lung function, and the risk of pulmonary diseases.<sup>5,6</sup> In recent years, Korea, along with other nations, has increasingly focused on addressing health care disparities rooted in race, ethnicity, and economic status.<sup>7-9</sup>

In the 1970s, South Korea's revised building codes allowed for basements in new houses, originally intended as emergency shelters. The 1980s saw a significant population surge in Seoul and its metropolitan areas, leading to the legalization of residence in *banjihas* (semi-basements) due to housing shortages. Over time, *banjihas* have become a common residence for the economically and socially marginalized. However, the health implications of living in such spaces, particularly for children, who are more susceptible to adverse residential environments, remain under-researched.

The International Study of Asthma and Allergies in Childhood (ISAAC) phase III study in Korea<sup>10</sup> highlighted that residents in basements or semi-basements faced increased exposure to dampness and mold, correlating with a higher incidence of wheezing illnesses. Furthermore, mold or dampness in homes is linked to amplified risk and severity of childhood wheezing.<sup>11,12</sup> The typical conditions of semi-basement residences, such as poor ventilation, limited sunlight, and higher radon levels, are conducive to Th2 inflammation and increased airway resistance.<sup>13-17</sup>

This study aims to investigate whether residing in a *banjiha* impacts airway resistance and Th2 airway inflammation in Korean children. By comparing children living in *banjihas* to those in upper floors, we assessed clinical indicators of airway inflammation, lung resistance, urinary pollutant metabolite levels, serum 25-hydroxyvitamin D concentration, and sensitization to inhaled allergens. Our study seeks to contribute to a deeper understanding of the health impacts of residential environments on children's respiratory health.

# Methods

#### Subjects and protocols for data collection

A total of 576 fifth- and sixth-grade elementary school students (10–12 years old) who participated in the Seongnam Atopy Project (SAP) 2017 cohort study were enrolled. This study was supported by the Seongnam City Government in an effort to prevent and provide education about allergic diseases in Korean children, and was conducted from January 2017 to October 2017.<sup>18</sup>

Data regarding residence (housing type and floor number), baseline characteristics of children (age, sex, height, weight, gestational age, and birth weight), and passive smoking by the parents were recorded. All allergy-related symptoms during the previous 12 months (wheezing, nasal symptoms, and eczema) were recorded using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire.<sup>19</sup> Urine samples were collected in sterile cups and stored at  $-70^{\circ}$ C for up to 3 months before analysis. Blood samples were collected stored at -70°C until analysis of allergen-specific immunoglobulin (Ig) E and serum 25[OH]D. The fractional exhaled nitric oxide (FeNO) level and impulse oscillometry (IOS) data were recorded by a trained technician. The study protocol was approved by the appropriate Institutional Review Board of CHA University (2017-04-049). Written informed consent was obtained from the parents or guardians of all participating children.

#### Housing type and floor of residence

The floor of each child's residence was determined using the following question from the survey instrument: "What floor do you live on?" The possible answers were: "semi-basement", "first floor", "second to fifth floor", or "sixth floor or higher". For analysis, these answers were recategorized as "semi-basement", "first floor to fifth floor", and "sixth floor or higher". The "first floor" was considered the floor at ground level. The type of housing was determined by asking the question: "What is the type of the dwelling?" The possible answers were: "detached house", "townhouse", or "apartment".

#### FeNO

The FeNO concentration in parts per billion (ppb) was measured using a portable nitric oxide analyzer (NIOX MINO<sup>°</sup>; Aerocrine, Solna, Sweden) according to the American Thoracic Society (ATS) guidelines.<sup>20</sup> Measurements were conducted twice for each participant to minimize variability, with an applied exhalation time set at 10 seconds. This methodology ensures the reliability and consistency of our FeNO measurements.

#### Airway mechanics

Oscillometric tests were performed using a Jaeger MasterScreen device (Jaeger Co., Wurzburg, Germany), and quality control measures were used to inspect the IOS system according to the manufacturer's guidelines. IOS measurements were conducted with considerations for seasonal variations and recent infections. Children who had experienced recent infections were excluded from the study to ensure the accuracy of the IOS results. A minimum of three technically acceptable measurements were recorded for each participant, and mean values were reported. The signals were recorded for 30 s at each frequency. Airway resistance was also measured at 1, 2, 3, 5, 10, 15, and 20 Hz, and the difference of the respiratory system resistance (Rrs) at 5 Hz and 20 Hz (Rrs5-20) was recorded as a function of frequency. Rrs0 was calculated by extrapolation in a plot of resistance vs. the exponential of frequency.

In our study, Rrs0, representing extrapolated respiratory system resistance at zero frequency, was utilized to measure total airway resistance in IOS. Our use of Rrs0 is based on studies by Oostveen E et al.<sup>21</sup> and Bickel S et al.<sup>22</sup>

#### Measurement of serum biomarkers

Serum total and specific IgE antibodies for common inhaled allergens (*Dermatophagoides farinae*, cat dander, dog dander, birch, *Alternaria alternata*, and *Humulus japonicus*) were measured using the ImmunoCAP system (Phadia, Uppsala, Sweden). Atopy was defined by positive specific IgE antibodies to at least one of these allergens. Serum 25-hydroxyvitamin D3 [25-(OH)D3] level was determined using an enzyme-linked immunoassay (ELISA) kit (Immunodiagnostic Systems, COBAS 6000 Roche, Manheim Germany).The serum (25[OH]D) levels were measured by a chemiluminescence immunoassay Liaison (DiaSorin, Stillwater, Minnesota) with sensitivity of 4 ng/mL, linearity 150 ng/mL, and intra-assay coefficient of variation  $\pm$  10%.

#### Measurement of urinary metabolites of pollutants

Urinary levels of cotinine (nicotine metabolite) and urinary metabolites of phthalates, bisphenol, triclosan, paraben, and volatile organic compounds (VOCs) were measured. The phthalate metabolites included mono-(isobutyl) phthalate (MiBP), mono-n-butyl phthalate (MnBP), mono-benzyl phthalate (MBzP), mono-(3-carboxypropyl) phthalate (MCPP), mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP). The urinary metabolites of VOCs were benzene, toluene, xylene, styrene, and formaldehyde.23-25 To reduce bias caused by daily and seasonal variations, the levels of these metabolites were measured using single spot urine samples that were collected from 9:00 AM to 11:00 AM on 27 June to 21 July 2017, and were immediately stored at -70°C. These metabolites were analyzed by liquid chromatography-tandem mass spectrometry and were expressed relative to the urinary creatinine level (µg metabolite/g UCr) to control for urine dilution.

#### Statistical analysis

The data were analyzed using SPSS version 21.0 (SPSS, Chicago, IL), with emphasis on addressing approximately 20% missing data to ensure robustness of our statistical analysis. Continuous data were expressed as medians with interquartile ranges (IQRs). Differences of categorical variables in the three groups (semi-basement residents, first floor to fifth floor residents, sixth floor or above residents) were evaluated using the Kruskal-Wallis test. The relationships of residence location with FeNO, Rrs0, and Rrs5–20 were analyzed using generalized linear regression analysis with an identity function and adjustment for different confounders using two models. Model 1 adjusted for height,



gender, BMI z-score, prematurity/low birth weight (no or yes). Model 2 adjusted for all Model 1 variables as well as asthma during the previous 12 months (no or yes), secondary smoking (no or yes), vitamin D level (continuous level), residency area (new city or old city), housing type (single house, town house, or apartment), and aeroallergen sensitization (no or yes). The estimates were presented as regression slopes for the different groups, with beta ( $\beta$ ) and a 95% confidence interval (CI). Because FeNO values had a log-normal distribution, they were analyzed as continuous variables after log-transformation. A two-sided *P* value of 0.05 or less indicated statistical significance.

#### Results

#### Characteristics of study subjects

We examined 575 fifth- and sixth-grade students and classified them into three groups according to the floor of residence: *banjihas* (n = 25, 4.3%), first floor to fifth floor (n = 311, 54.1%), and sixth floor or above (n = 239, 41.6%). These three groups had no significant differences in age, sex distribution, body mass index (BMI), or prematurity/low birth weight (Table 1). However, relative to children living in banjihas, passive smoke exposure was lower for children living on the first floor to fifth floor and on the sixth floor or above (P = 0.002). The three groups also differed in the type of building where they lived (P < 0.001). In particular, most children living on the first floor to fifth floor lived in townhouses (n = 154, 49.5%) or apartments (n = 122, 39.2%), most children living on the sixth floor or above lived in apartments (n = 238, 99.6%), and most children living in *banjihas* lived in townhouses (n = 22, 88.0%).

# Allergic disease, airway mechanics, biomarkers, and pollutant metabolites

The prevalence of allergic rhinitis was significantly higher for children living on the sixth floor or above and in *banjihas* than for children living on the first floor to fifth floor (P = 0.014; **Table 2**). The vitamin D level was significantly higher for children living in *banjihas* (23.6 IU/mL [21.6, 29.3]) than for those living on the first floor to fifth floor (21.0 IU/mL [17.5, 25.2]) and the sixth floor or above (20.6 IU/mL [16.5, 25.3]) (P = 0.023). The three groups had no statistically significant differences in the prevalence of asthma, atopic dermatitis, overall sensitization to inhaled allergens, or total eosinophil count (TEC). However, children living in *banjihas* had greater sensitization to cat allergen (P = 0.003; **Table 3**).

Analysis of the urinary levels of metabolites of different pollutants indicated the three groups had no significant differences in cotinine, metabolites of most VOCs, or bisphenol (**Supplementary Table E1**). However, the urinary level of triclosan and two VOC metabolites (2-phenylethanol and poly [2-hydroxyethyl methacrylate]) were significantly higher for children living on the sixth floor or above compared to the other two groups (all P < 0.05).



Table 1.	Demographic and	clinical character	eristics of study	subjects in the	three groups $(N = 575)$ .

Variable	<i>Banjiha</i> (n = 25, 4.3%)	Floor 1–5 (n = 311, 54.1%)	Floor 6 or higher (n = 239, 41.6%)	P value
Age, years, median [IQR]	11.0 [10.0 to 11.5]	11.0 [10.0 to 12.0]	11.0 [11.0 to 12.0]	0.294
Sex, male, n (%)	15 (60.0)	151 (48.6)	125 (52.3)	0.416
BMI z score, mean (SD)	-0.15 (1.13)	0.06 (1.03)	-0.14 (0.98)	0.068
Prematurity or low birth weight*, n (%)	2 (8.0)	37 (12.1)	27 (11.4)	0.822
Passive smoking exposure, n (%)	13 (52.0)a	156 (50.2)	83 (35.0)	0.002
Building type, n (%)				
Detached House	3 (12.0)	35 (11.3)	0 (0.0)	< 0.001
Townhouse	22 (88.0)	154 (49.5)	1 (0.4)	
Apartment	0 (0.0)	122 (39.2)	238 (99.6)	

SD, standard deviation; BMI, body mass index; \*Prematurity: birth before 35 weeks; low birth weight: less than 2.5 kg. Comparisons of numerical variables in the three groups were evaluated using the Kruskal-Wallis test. *Post hoc* pairwise comparisons were performed with the Bonferroni correction to determine differences between groups. Comparisons of categorical variables were evaluated by a  $\chi^2$  test. Missing data: prematurity/low birth weight, n = 8; passive smoking, n = 2. <sup>a</sup>P < 0.05 vs. first floor to fifth floor.

#### Table 2. Allergic diseases, total airway mechanics, and biomarkers of study subjects in the three groups (N = 575).

Variable	<i>Banjiha</i> (n = 25, 4.3%)	Floor 1–5 (n = 311, 54.1%)	Floor 6 or higher (n = 239, 41.6%)	P value
Allergic diseases				
Asthma, n (%)	1 (4.0)	8 (2.6)	6 (2.5)	0.905
Allergic rhinitis, n (%)	14 (56.0) <sup>a</sup>	158 (51.1)	152 (63.6) <sup>a</sup>	0.014
Atopic dermatitis, n (%)	4 (16.0)	43 (14.0)	44 (18.5)	0.385
Total airway mechanics				
Rrs0, hPa/L/sec, median [IQR]	8.8 [7.5 to 9.7] <sup>a</sup>	7.7 [6.9 to 8.7]	7.6 [6.9 to 8.5]	0.010
Rrs20–5, hPa/L/sec, median [IQR]	2.0 [1.7 to 2.4]	1.7 [1.3 to 2.3]	1.8 [1.4 to 2.3]	0.182
Biomarkers				
TEC count, > 4%, n (%)	6 (35.3)	76 (30.0)	54 (28.1)	0.785
Inhaled allergen sensitization <sup>9</sup> , n (%)	11 (64.7)	168 (65.1)	134 (66.7)	0.937
FeNO, > 35 ppb, n (%)	5 (20.0)ª	22 (7.1)	14 (5.9)ª	0.033
25[OH]D, IU/mL, median [IQR]	23.6 [21.6 to 29.3] <sup>a</sup>	21.0 [17.5 to 25.2]	20.6 [16.5 to 25.3]	0.023

IQR, interquartile range; FeNO, fractional exhaled nitric oxide; ppb, parts per billion; TEC, total eosinophil count.

<sup>3</sup>Inhaled allergen-specific IgE > 0.35 kU/L for at least 1 of 6 allergens (*Alternaria*, birch, cat dander, dog dander, *Dermatophagoides farina*, and Japanese hop). Comparisons of numerical variables were evaluated by the Kruskal-Wallis test. *Post hoc* pairwise comparisons were performed with the Bonferroni correction to determine differences between groups. Comparisons of categorical variables were evaluated by a  $\chi^2$  test.

Missing data: asthma, n = 2; allergic rhinitis, n = 2; atopic dermatitis, n = 4; TEC, n = 13; aeroallergen sensitization, n = 99; FeNO, n = 1; Vitamin D, n = 99.  ${}^{a}P < 0.05$  versus 1-5th floor.



		Banjiha		Floor 1–5	Floor 6 or higher	
		aβ (95% CI)	P value	P value	aβ (95% CI)	P value
Log FeNO	Crude	0.104 (-0.011 to 0.218)	0.075	1 (Ref.)	-0.044 (-0.088 to -0.001)	0.047
	Adj.1	0.100 (0.006 to 0.194)	0.038	1 (Ref.)	-0.040 (-0.080 to -0.001)	0.044
	Adj. <sup>2</sup>	0.130 (0.020 to 0.240)	0.020	1 (Ref.)	-0.052 (-0.105 to 0.001)	0.056
IOS Rrs0	Crude	0.867 (0.174 to 1.560)	0.014	1 (Ref.)	-0.059 (-0.326 to 0.207)	0.663
	Adj.1	0.633 (0.156 to 1.109)	0.009	1 (Ref.)	-0.063 (-0.260 to 0.134)	0.531
	Adj. <sup>2</sup>	0.647 (0.082 to 1.213)	0.025	1 (Ref.)	-0.089 (-0.364 to 0.185)	0.523
Rrs5-20	Crude	0.242 (-0.123 to 0.608)	0.194	1 (Ref.)	-0.022 (-0.164 to 0.119)	0.764
	Adj.1	0.076 (-0.198 to 0.350)	0.583	1 (Ref.)	-0.032 (-0.145 to 0.082)	0.583
	Adj. <sup>2</sup>	0.112 (-0.212 to 0.437)	0.497	1 (Ref.)	-0.081 (-0.239 to 0.076)	0.312

Table 3. Generalized linear regression analysis of the association of FeNO level and airway mechanics values with floor of residence.

<sup>1</sup>Model 1: *P* values calculated by a generalized linear regression analysis with identity function for IOS level, after adjustment for height, gender, BMI z score, prematurity/low birth weight (no or yes).

<sup>2</sup>Model 2: *P* values calculated by a generalized linear regression analysis with identity function for IOS levels, after adjustment for height, gender, BMI z score, asthma in the previous 12 months (no or yes), prematurity/low birth weight (no or yes), secondary smoking (no or yes), vitamin D level (continuous level), residency area (new city or old city), type of residence (single house, town house, or apartment), and aeroallergen sensitization (no or yes).



**Figure 1.** Total airway resistance of study subjects in the three groups. Logistic regression analysis indicated significant associations of airway resistance with residency floor in Model 1 (adjusted  $\beta$ 1: 0.100 [95%CI: 0.006, 0.194], *P* = 0.038) and Model 2 (adjusted  $\beta$ 2: 0.130 [95%CI: 0.020, 0.240], *P* = 0.020).



		Banjiha	Floor 1-5	Floor 6 or higher	P value	
There a last with	No	6 (35.3)	104 (40.3)	89 (44.5)	0.540	
House dust mite	Yes	11 (64.7)	154 (59.7)	111 (55.5)	0.569	
Cat	No	9 (52.9)	217 (84.1)	169 (84.5)	0.002	
Cat	Yes	8 (47.1)	41 (15.9)	31 (15.5)	0.003	
Dec	No	13 (76.5)	222 (86.0)	170 (85.0)	0.554	
Dog	Yes	4 (23.5)	36 (14.0)	30 (6.3)	0.554	
Dinal	No	13 (76.5)	205 (79.5)	147 (73.5)	0.325	
Birch	Yes	4 (23.5)	53 (20.5)	53 (26.5)		
There	No	15 (88.2)	236 (91.5)	178 (89.0)	0.646	
) nop	Yes	2 (11.8)	22 (8.5)	22 (11.0)		
Altannania	No	16 (84.1)	242 (93.8)	179 (89.5)	0.220	
Alternaria	Yes	1 (5.9)	16 (6.2)	21 (10.5)	0.230	
A ny allargan	No	6 (35.3)	90 (34.9)	67 (33.5)	0.050	
Any anergen	Yes	11 (64.7)	168 (65.1)	133 (66.5)	0.950	

Table 4. Sensitization to specific inhaled allergens of study subjects in the three groups.

Missing aeroallergen data: n = 99.

#### Airway lung function

Analysis of airway mechanics indicated the Rrs0 was significantly higher for children living in banjihas (8.8 hPa/L/s [7.5, 9.7]) than for children living on the first floor to fifth floor (7.7 hPa/L/s [6.9, 8.7]) and the sixth floor or higher (7.6 hPa/L/s [6.9, 8.5] hPa/L/sec) (P = 0.010; Table 2). We also performed regression analysis to determine the relationship of residential floor with log(FeNO), Rrs0, and Rrs5-20 (Table 3). The unadjusted analysis (P = 0.014) and adjusted analyses from Model 1 (P = 0.009) and Model 2 (P = 0.025) showed there were significant associations between Rrs0 and residence in a banjiha (Table 3). However, there was no relationship of Rrs5-20 with residence floor. Detailed analysis at discrete frequencies of 1, 2, 3, 5, 10, 15, and 20 Hz revealed that airway resistance was notably higher at the 1, 2, and 3 Hz frequencies in children from banjihas, pointing to increased central airway obstruction in these environments. Conversely, at the higher frequencies of 5, 10, 15, and 20 Hz, the differences in airway resistance among the groups were less pronounced, particularly at 15 and 20 Hz, where the resistance measurements converged, suggesting similar peripheral airway resistance across the different residential settings. These observations are detailed in Figure 1.

#### FeNO level

There is a statistically significant difference in FeNO levels among the three groups. Notably, the proportion of children living in semi-basements (*banjihas*) with FeNO levels of 35 ppb or greater was 20.0%, which is significantly higher compared to children living on the first to fifth floors (7.1%) and those living on the sixth floor or above (5.9%)

(P = 0.033, Table 2). Adjusted regression analysis from Model 1 (P = 0.038) and Model 2 (P = 0.020) indicated significant associations of FeNO with residence in a *banjiha* (Table 3). These results were consistent in a more detailed analysis of the effect of residential floor on total airway resistance (Figure 1).

#### Discussion

Our major finding is that children residing in banjihas exhibited higher FeNO levels and greater airway resistance compared to children on the first floor or above. This aligns with the 2014 ISAAC study,10 which associated living in basements or semi-basements with increased wheezing illnesses. Despite expectations of lower vitamin D levels due to reduced sunlight exposure in semi-basements, we found unexpectedly higher serum 25[OH]D levels in banjiha residents. The unexpectedly higher vitamin D levels observed in children residing in banjihas may be explained by several factors. Firstly, these children might engage in more outdoor activities than their counterparts on higher floors, resulting in greater sunlight exposure despite their semi-basement living conditions. Secondly, dietary variations could contribute, as families in different residential environments might have different access to or preferences for vitamin D-rich or fortified foods. Finally, inherent biological or genetic factors might influence how these children metabolize and synthesize vitamin D, possibly making them more efficient at vitamin D synthesis from limited sunlight. Each of these hypotheses suggests avenues for further research to explore the underlying mechanisms that influence vitamin D levels across different residential settings.



The impact of Socioeconomic Status (SES) within the framework of Social Determinants of Health (SDOH) is significant, particularly in how it affects asthma prevalence, allergic rhinitis, food allergies, and atopic dermatitis. There is a growing body of evidence indicating that underserved populations face significant healthcare disparities linked to SDOH.<sup>26,27</sup> This observation is consistent with previous findings<sup>5,6</sup> that lower SES is associated with increased exposure to adverse environmental conditions like air pollution and indoor allergens,1-4 which aggravate respiratory conditions. Moreover, despite higher reported smoke exposure in banjiha residents, cotinine levels were similar across all groups, suggesting that factors such as intermittent exposure, metabolic variations, or reporting inaccuracies might influence these measurements.

We also found that children in *banjihas* demonstrated significantly greater airway resistance, an impact of their residential environment on pediatric respiratory health, assessed using the Impulse Oscillation System (IOS). This system is advantageous as it is less reliant on patient cooperation than spirometry and sensitive to small changes in lung function.<sup>28</sup> The differences in lung function we observed align with research by Moshammer et al.,<sup>29</sup> and are further emphasized by findings from Keidel et al.,<sup>30</sup> which highlight the role of socioeconomic factors in shaping respiratory outcomes linked to ambient  $NO_2$  exposure. Extensive research<sup>5,6,31</sup> confirms that SES significantly correlates with lung function, indicating that social and economic conditions are vital in shaping respiratory health disparities in various environments.

Children in semi-basements showed significantly higher airway resistance and FeNO levels, irrespective of similar allergen and pollutant exposure levels. Several factors may explain the elevated FeNO levels in children living in banjihas despite comparable allergen and pollutant exposures. Firstly, the poorer air exchange rates in banjihas can lead to an accumulation of airborne irritants and gases like radon and carbon monoxide, which are not fully reflected by urinary metabolite measurements. These environmental conditions may enhance airway inflammation and hyperresponsiveness, as indicated by the elevated FeNO levels. Studies like those by Turner, M.C. et al.,<sup>32</sup> suggest that conditions such as long-term radon exposure prevalent in semi-basements can intensify pulmonary diseases through inflammatory mechanisms. Additionally, the lower perceived living standards and natural light in semi-basements might elevate psychological stress levels, contributing to increased airway inflammation.<sup>33-35</sup> To further understand these dynamics, comprehensive studies comparing environmental and psychosocial factors in semi-basements versus above-ground residences are necessary.

Addressing the concerns raised, we acknowledge several notable limitations. Firstly, as a cross-sectional study, it cannot establish cause-and-effect relationships. We could not conduct a randomized longitudinal study in the context of children living in *banjihas* due to ethical challenges.

Secondly, our research did not employ a randomization method, focusing instead on a general population study involving elementary school students in a specific region. Thirdly, we used Impulse Oscillometry (IOS) rather than spirometry for evaluating small airway function, noting the differences in lung function assessment. Additionally, we did not explore educational opportunities or stress responses among the different groups of children, nor did we measure several potentially relevant variables such as temperature, humidity, radon exposure, and household characteristics like mold or mildew presence, water leaks, and infestations. Furthermore, we did not include measurements of traffic-related air pollution, such as PM2.5, which could significantly influence the respiratory health outcomes observed in the different residential settings. This omission is an important limitation and a valuable area for future research to understand environmental impacts on respiratory health better.

As far as we are aware, this is the first study to investigate Th2 airway inflammation in children living in *banjihas*, contrasting it with those residing on upper floors. Our research extends previous findings<sup>5,6</sup> by establishing a direct link between SES-related factors and measurable physiological outcomes in pediatric populations. We demonstrate that the distinctive environment of *banjihas*, compounded by socioeconomic limitations, independently contributes to poorer asthma-related health outcomes. This conclusion is supported by the observed increases in airway resistance and elevated FeNO levels, which occur regardless of other allergen exposures or pollution levels.

In conclusion, our findings indicate that children living in *banjihas* face a significantly higher risk for elevated FeNO levels and increased airway resistance, independent of allergic sensitization or pollutant exposure.

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# **Conflict of Interest**

There are no financial or other issues that might lead to conflicts of interest.

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Metabolite or precursor	Banjiha	Floor 1–5	Floor 6 or higher	
Cotinine, µg/L	11.7 [8.2 to 18.3]	8.9 [5.1 to 14.6]	8.9 [4.7 to 14.3]	0.154
Bisphenol, μg/L	3.2 [2.0 to 5.8]	2.8 [1.5 to 5.3]	2.6 [1.3 to 8.4]	0.576
Triclosan, μg/L	0.4 [0.1 to 0.9]	0.4 [0.2 to 0.9]	0.6 [0.3 to 1.2]	0.043
Phthalate				
High MWP	82.9 [42.5 to 106.5]	51.7 [32.2 to 80.1]	52.9 [32.6 to 79.7]	0.166
Low MWP	108.2 [61.9 to 166.9]	90.5 [55.9 to 143.1]	86.7 [54.5 to 131.5]	0.820
Paraben				
Methyl-	5.4 [1.7 to 39.3]	14.9 [2.7 to 60.9]	12.8 [3.3 to 60.8]	0.825
Propyl-	1.9 [0.5 to 9.8]	2.8 [0.5 to 7.8]	3.3 [0.8 to 9.5]	0.111
Ethyl-	7.8 [2.2 to 172.7]	23.5 [3.8 to 112.5]	13.5 [2.1 to 68.8]	0.437
Butyl-	1.1 [0.1 to 3.1]	0.9 [0.2 to 2.3]	0.8 [0.0 to 2.0]	0.298
VOC				
TZCA	127.0 [68.7 to 220.7]	141.1 [77.6 to 248.4]	133.9 [65.3 to 236.5]	0.629
s-phenylmercapturic acid	0.56 [0.33 to 0.80]	0.45 [0.26 to 0.72]	0.45 [0.17 to 0.74]	0.689
o-cresol	0.61 [0.37 to 0.90]	0.75 [0.48 to 1.16]	0.72 [0.52 to 1.35]	0.329
Benzylmercapturic acid	0.90 [0.69 to 2.72]	1.68 [0.88 to 2.99]	1.86 [0.94 to 3.44]	0.175
1-phenylethanol	1.29 [0.44 to 1.52]	0.94 [0.58 to 1.58]	0.84 [0.43 to 1.34]	0.059
2-phenylethanol	0.63 [0.21 to 1.28]	0.68[0.35 to 1.71]	0.96 [0.43 to 2.73]	0.023
2-methylbenzyl alcohol	0.57 [0.11 to 0.95]	0.44 [0.07 to 0.98]	0.28 [0.00 to 0.83]	0.140
3,4-methylbenzyl alcohol	0.28 [0.13 to 0.63]	0.23 [0.05 to 0.52]	0.22 [0.04 to 0.52]	0.607
РНЕМА	0.00 [0.00 to 0.60]	0.00 [0.00 to 0.86]	0.47 [0.00 to 1.49]	0.007

# Supplementary Table E1. Urinary metabolites of environmental pollutants (µg/g UCr).

Phthalate metabolites were grouped by molecular weight and reported as the sum of 4 major high-molecular weight phthalate (MWP) metabolites (MEHP, MEOHP, MEOPP, and MCPP), or the sum of the 3 major low-molecular weight phthalate (MWP) metabolites (MiBP, MnBP, and MBzP); PHEMA, poly(2-hydroxyethyl methacrylate); VOC, volatile organic compounds; TZCA, thiazolidine-4-carboxylate.