Moazzen *et al.*
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RESEARCH

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The temporal-spatial association of respiratory manifestations and air pollution in children referred to the Emergency Department of Akbar Children's Hospital, Mashhad, Iran

Nasrin Moazzen[1], Amirreza Memari[2] and Nafiseh Todarbary[3*]

Abstract

Background Air pollution causes many respiratory disorders, especially in children and the elderly. These disorders include asthma exacerbations, bronchiolitis, and pneumonia. Research on the association between air pollution and respiratory disorders helps to reevaluate environmental policies in developing countries.

Methods This descriptive cross-sectional study was conducted on 932 children with respiratory manifestations admitted from December 2017 to December 2019 at the Emergency Department of Akbar Children's Hospital of Mashhad University of Medical Sciences, Mashhad, Iran. Air pollution indices such as concentration of sulfur dioxide (SO_2), nitrogen dioxide (NO2), carbon monoxide (CO), and particulate matter (PM) smaller than 2.5 and 10 μm and other parameters, including the air quality index (AQI), air temperature, and humidity level from 2017 to 2019, were retrieved from Mashhad Environmental Pollution Monitoring Center. Demographic and clinical data of patients were collected from patients' hospital documents. We used descriptive analytical methods such as central tendency, variability, and frequency distribution to report and analyze demographic and clinical data through tables and diagrams. The association between air pollution indices and respiratory manifestations was examined by the Spearman correlation test. The correlation between the AQI and total hospital admissions and asthma-related hospital admissions was also evaluated by the Spearman correlation test.

Results Hospital admissions due to respiratory manifestations were not associated with the AQI of each month (p-value = 0.794). The concentration of SO_2 was correlated with respiratory-related hospital admissions (correlation coefficient = 0.487, p-value = 0.016) but not asthma attacks.

Conclusion Generally, our cross-sectional study showed no statistically considerable association between air pollution and hospital admissions due to respiratory manifestations and asthma attacks in children. Of the air pollution indices, only SO_2 concentration was associated with respiratory-related hospital admissions but not asthma attacks.

Keywords Air pollution, Respiratory manifestations, Children, Sulfur dioxide, Nitrogen dioxide, Carbon monoxide, Particulate matter, Air quality index (AQI)

*Correspondence:
Nafiseh Todarbary
Ntoodarbary@yahoo.com; TodarbariN2@mums.ac.ir
Full list of author information is available at the end of the article

Background

The prevalence of respiratory disorders has increased significantly among children over the last few years, highly related to air pollution. Persistent exposure to photochemical and traffic-related pollutants, especially in highly polluted cities of developing countries, can deteriorate lung growth and function. Consequently, the respiratory morbidity and mortality increase among children [1]. Air pollution can affect the respiratory system by stimulating oxidative stress and inflammatory processes, modulating the immune system, and altering genetic and epigenetic mechanisms [2]. Traffic-related air pollution containing gases such as nitrogen dioxide (NO2), nitric oxide (NO), nitrogen oxides (NOX), and ozone (O3), as well as particles less than 2.5 µm and 10 µm in diameter, can contribute to the development and exacerbation of asthma and other allergic diseases [3]. Although the development of asthma was not related to air pollution in previous studies, recent studies have found notable associations [4]. Based on estimations of the United Nations International Children's Emergency Fund (UNICEF), the level of air pollution is sixfold higher than the standards in the living places of almost 300 million children around the world, which accounts for the deaths in 600,000 children under the age of 5 each year [5]. Considering the relative immaturity of respiratory and immune systems and the more outdoor activity children engage in, they are more vulnerable to adverse outcomes of air pollution.

Additionally, the peripheral airways of infants are more prone to inflammatory narrowing than adults because of anatomic differences; therefore, the chance of irritation-induced airway obstruction increases in children [6]. Asthmatic children may also experience more severe symptoms in exposure to air pollution since they do not stop their activity even during asthma exacerbations. The other biological factors involving children's susceptibility to pollution exposure refer to different ways of metabolizing, detoxifying, and excreting environmental stimuli [7]. The acute complications of air pollution consist of lung inflammation, reduction of lung function, increase in episodes of asthma attacks, respiratory and cardiac hospital admissions, and also a higher incidence rate of premature death. Long-term exposure to air pollution can result in respiratory diseases like asthma, bronchitis, and premature death; however, outcomes of chronic exposure are not as complicated as acute ones [8]. This study evaluated the association between air pollution and respiratory manifestations among children referred to the Emergency Department of Akbar Children's Hospital, Mashhad, Iran.

Method

This descriptive cross-sectional study was conducted on 932 children with respiratory manifestations admitted from December 2017 to December 2019 at the Emergency Department of Akbar Children's Hospital of Mashhad University of Medical Sciences, Mashhad, Iran. Patients who were not admitted to the hospital or without their parents' consent were excluded. Demographic and clinical data of patients, including age, sex, living place, past medical history, chief complaint, the duration of hospital admission, the duration of admission at the intensive care unit (ICU), season of hospital admission, mortality rate, and final diagnosis, were collected from hospital documents and recorded into a checklist as well. The air quality index (AQI), air temperature, and humidity level from 2017 to 2019 were retrieved from the Mashhad Environmental Pollution Monitoring Center. Air pollution indices include the concentration of sulfur dioxide (SO_2), carbon monoxide (CO), nitrogen dioxide (NO_2), and particulate matter (PM) smaller than 2.5 and 10 µm. The formula for calculating the AQI is as follows:

$$AQI_p = \frac{(I_{Hi} - I_{Lo})}{(BP_{Hi} - BP_{Lo})} \times (C_p - BP_{Lo}) + I_{Lo}$$

(AQI_p): The air quality index for pollutant (p)

(C_p): The estimated concentration of pollutant (p)

(BP_{Hi}): The breakpoint that is greater than or equal to (C_p)

(BP_{Lo}): The breakpoint that is less than or equal to (C_p)

(I_{Hi}): The AQI value corresponding to (BP_{Hi})

(I_{Lo}): The AQI value corresponding to (BP_{Lo}).

This formula converts pollutant concentrations into an AQI value, which can be used to inform the public about air quality. The breakpoints (BP) and the corresponding AQI values (I) are determined based on health impact categories and are provided in Table 1. The highest AQI value calculated from individual pollutants is reported as the AQI for the location [9].

The review board of Mashhad University of Medical Sciences approved the study, and the children's parents filled out the informed consent form. We used descriptive analytical methods such as central tendency, variability, and frequency distribution to report and analyze demographic and clinical data through tables and diagrams. The association between air pollution indices and the prevalence of asthma attacks and other respiratory signs and symptoms was examined by the Spearman correlation test. The AQI and total hospital admission and asthma-related hospital admission were shown in two diagrams separately, and their correlation was evaluated by the Spearman correlation test as well. Data analysis was performed using the Statistical Package for Social

Table 1 The breakpoints of AQI [9]

Classification	The breakpoints					
	AQI	NO_2 (ppm) 1 h	SO_2 (ppm) 24 h	CO (ppm) 8 h	PM_{10} (µg/m^3) 24 h	$PM_{2.5}$ (µg/m^3) 24 h
Good	0–50	0–0.053	0.00–0.034	0.0–4.4	0–54	0–12
Moderate	51–100	0.054–0.1	0.035–0.144	4.5–9.4	55–154	12–35.4
Unhealthy for sensitive groups	101–150	0.101–0.360	0.145–0.224	9.5–12.4	155–254	35.5–55.4
Unhealthy	151–200	0.361–0.640	0.225–0.304	12.5–15.4	255–354	55.5–150.4
Very unhealthy	201–300	0.65–1.24	0.305–0.604	15.5–30.4	355–424	150.5–250.4
Hazardous	301–400	1.25–1.64	0.605–0.804	30.5–40.4	425–504	250.5–350.4
	401–500	1.65–2.04	0.805–1.004	40.5–50.4	505–604	350.5–500

Science (SPSS) version 25. p-value < 0.05 was considered statistically significant in this study.

Results

Altogether, 932 children with respiratory manifestations enrolled in our study, including 574 boys (61.6%) and 358 girls (38.4%), and their mean age was 34.94 ± 27.77 months. Seven-hundred thirty-six out of 932 patients (79%) resided in Mashhad. A total of 299 patients (32.1%) were admitted to a hospital in the past, but 633 patients (67.9%) had no history of hospital admission. Based on prevalence, signs and symptoms of the patients were cough (14.3%), fever and cough (13.7%), dyspnea (11.8%), respiratory distress (10.1%), cough and wheeze (3.2%), wheeze (2.8%), cough and dyspnea (3.9%), fever (1.7%), and asthma attack (1.4%). Forty-seven out of 932 patients (5%) were admitted to the intensive care unit. The mortality rate was reported at 3.3% (31/932). The demographic and clinical data are summarized in Table 2. The first diagnosis of 262 patients (28.1%) was bronchiolitis, 188 patients (20.2%) had asthma attacks, 85 patients (9.2%) had pneumonia, and the rest were diagnosed with other respiratory disorders. As a final diagnosis, bronchiolitis was more prevalent among patients (36.7%) compared to asthma attacks (25%) and pneumonia (9.8%).

The majority of patients (312 out of 932) were admitted to the hospital during winter, and hospital admission was more prevalent in spring (237/932), autumn (232/932), and summer (151/932), respectively. Figure 1 demonstrates the season of hospital admissions due to respiratory manifestations.

Most patients diagnosed with asthma and bronchiolitis were admitted to the hospital in autumn and winter, respectively. In contrast, the frequency of pneumonia-related hospital admissions was almost the same during different seasons of the year. Figure 2 shows the season of hospital admission with a diagnosis of asthma, bronchiolitis, and pneumonia. Table 3 demonstrates the survival and mortality rate association with age, sex, and final diagnosis. There was a significant correlation between the final diagnosis and mortality of patients (p-value < 0.001). Thirty-one out of 932 patients died, of which 22.6% were diagnosed with pneumonia, and 77.4% had another diagnosis, while none of the patients with asthma or bronchiolitis died.

Table 2 Demographic and clinical data of 932 patients

Variable	Number/mean ± SD	Percentage
Age (month)	**34.94 ± 27.77**	-
Sex		
Male	**574**	**61.6**
Female	**358**	**38.4**
Living place		
Mashhad	**736**	**79**
Other cities	**196**	**21**
History of hospital admission		
Yes	**299**	**32.1**
No	**633**	**67.9**
Sign and symptom		
Cough	**133**	**14.3**
Fever and cough	**128**	**13.7**
Dyspnea	**110**	**11.8**
Respiratory distress	**94**	**10.1**
Cough and wheeze	**30**	**3.2**
Wheeze	**26**	**2.8**
Cough and dyspnea	**36**	**3.9**
Fever	**16**	**1.7**
Asthma attack	**13**	**1.4**
Other	**346**	**37.1**
Duration of hospital admission (day)	**4.10 ± 4.14**	-
Admission at ICU[a]	**47**	**5**
Mortality	**31**	**3.3**

[a] Intensive care unit

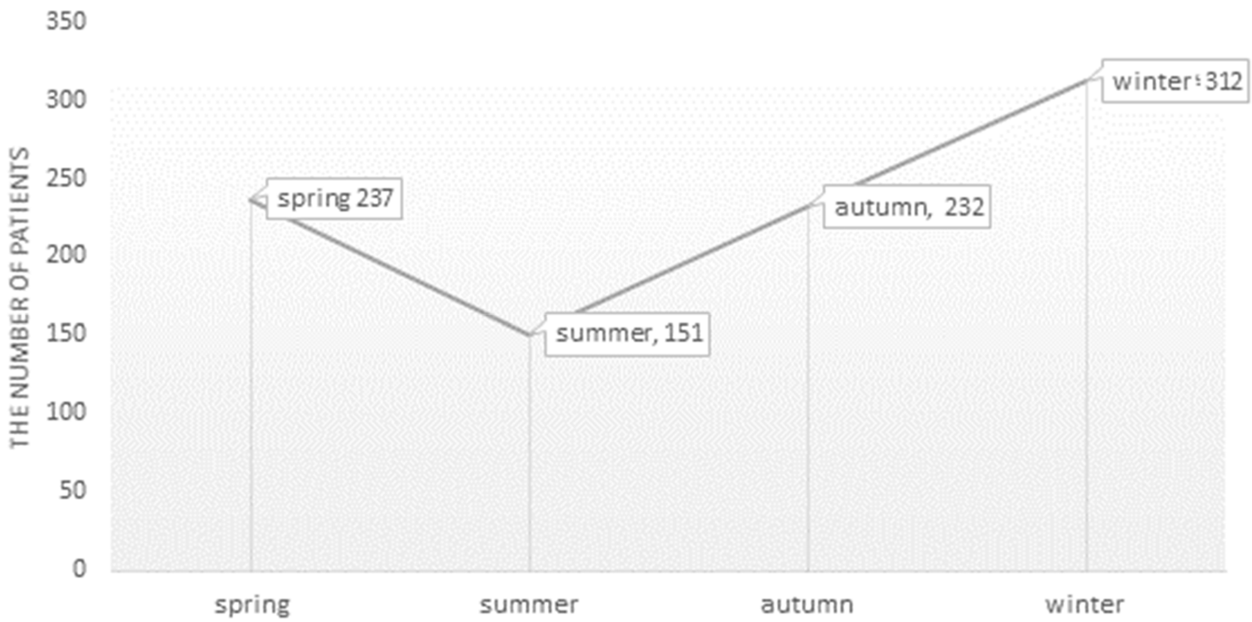

Fig. 1 The season of hospital admission because of respiratory manifestations

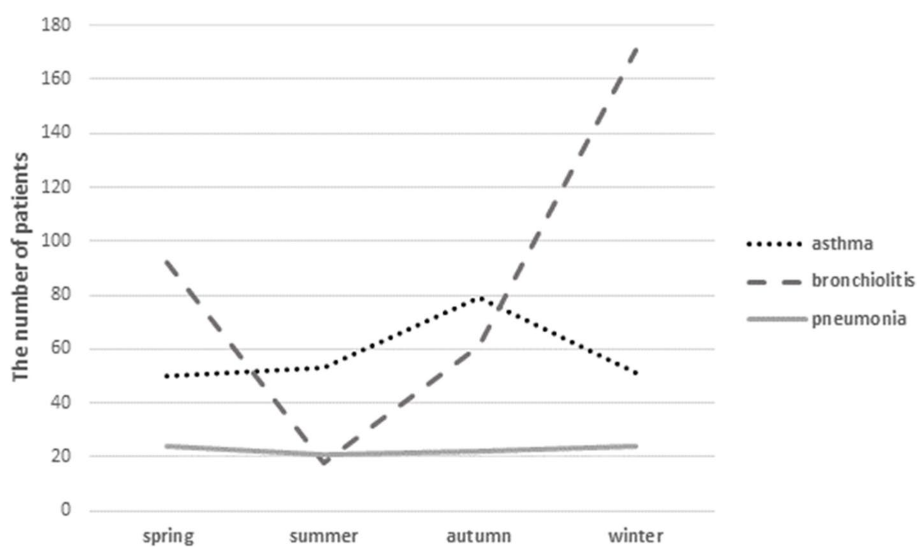

Fig. 2 The season of hospital admission with a diagnosis of asthma, bronchiolitis, and pneumonia

Figure 3 shows the number of hospital admissions due to respiratory manifestations and the AQI of each month from January 2018 to December 2019. Hospital admissions due to respiratory manifestations were not associated with the AQI of each month (p-value = 0.794).

Similarly, asthma attacks were not associated with the AQI of each month (p-value = 0.311). Figure 4 shows asthma attack-related hospital admissions and the AQI of each month from January 2018 to December 2019.

More concentration of sulfur dioxide (SO_2) was remarkably associated with an increase in the total number of hospitalized patients with respiratory manifestations (correlation coefficient = 0.487, p-value = 0.016) but not with an asthma attack (correlation coefficient = 0.382, p-value = 0.066). The total number of hospital admissions due to asthma attacks and other respiratory manifestations was not correlated to the concentrations of carbon monoxide (CO), nitrogen dioxide (NO_2), and also particulate matter (PM) smaller than 2.5 and 10 µm. The results

Table 3 The association of mortality and survival with age, sex, and final diagnosis

Feature	Survival		Mortality		
	Number	Percentage	Number	Percentage	*p*-value
Sex					
Male	**650**	**62.20%**	**14**	**45.20%**	**0.062**
Female	**341**	**37.80%**	**17**	**54.80%**	
Disease					
Asthma	**233**	**25.90%**	**0**	**0**	**< 0.001**
Bronchiolitis	**342**	**38%**	**0**	**0**	
Pneumonia	**84**	**9.30%**	**7**	**22.6%**	
Other	**242**	**26.90%**	**24**	**77.40%**	
Age (month)	**27.65 ± 34.87**		**31.23 ± 37.59**		**0.581**

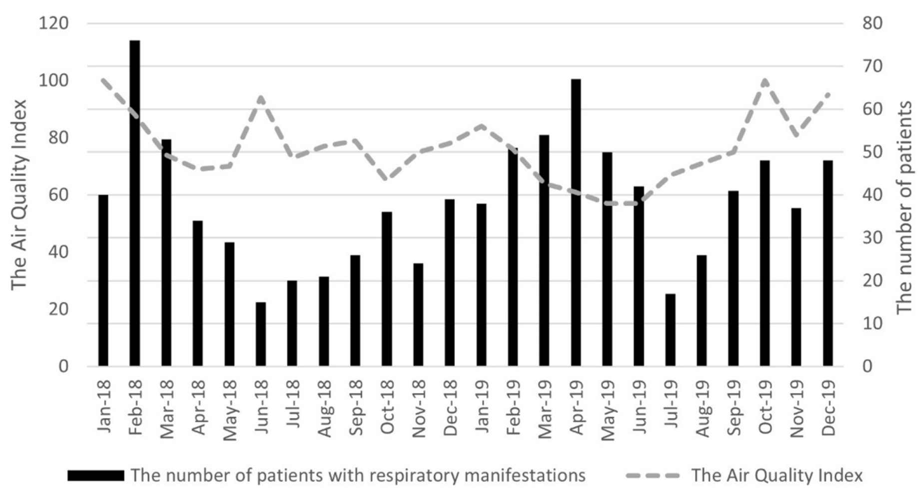

Fig. 3 The number of hospital admissions due to respiratory manifestations and the AQI index of each month from January 2018 to December 2019

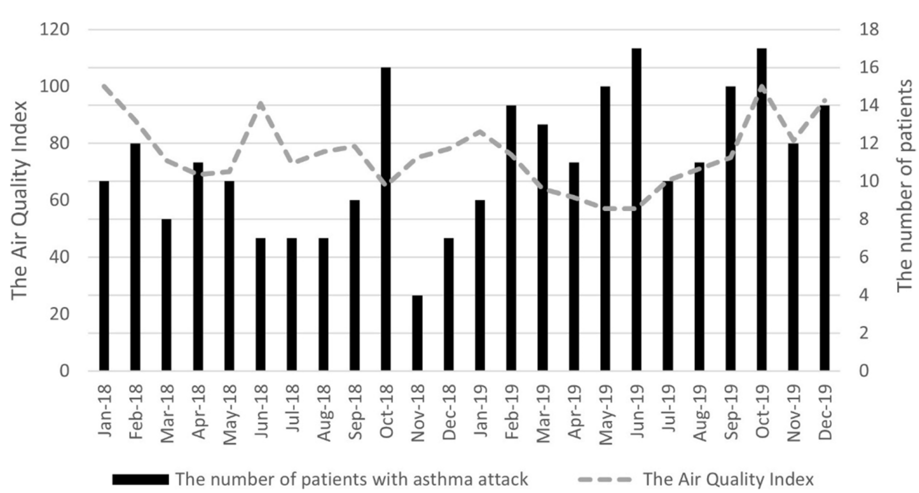

Fig. 4 Asthma attack-related hospital admissions and the AQI of each month from January 2018 to December 2019

of the correlation between the total number of hospital admissions due to respiratory manifestations and asthma attacks and the concentration of air pollution indices of each month are summarized in Table 4.

Discussion

Children are more vulnerable to air pollution-induced respiratory disorders because of immature immune and respiratory systems, more permeability of airway epithelium, higher respiratory and resting metabolic rate due to growing and larger surface area per unit body weight, and smaller airways leading to earlier obstruction [8, 10]. Children have higher air intake because of more outdoor activity than adults, making them more susceptible to air pollution [8]. Air pollution can cause various respiratory disorders, including asthma attacks and respiratory infections such as pneumonia, bronchiolitis, and tuberculosis [2]. In our study, patients' final diagnoses were bronchiolitis, asthma attack, and pneumonia. Of these, the correlation between asthma attacks and the AQI was studied, and no significant correlation was found. In contrast, Evangelisti et al. investigated the association between air pollution and hospital admission due to bronchiolitis. The results revealed that short-term exposure to PM_{10}, $PM_{2.5}$, and NO_2 was significantly correlated to bronchiolitis [11]. Two other studies demonstrated the remarkable relation between severe bronchiolitis and exposure to PM_{10}, $PM_{2.5}$, and NO_2 [12, 13]. Darrow et al. have researched upper respiratory tract infection (URI) and air pollution in 0–4-year-old children and concluded that short-term exposure to NO_2, PM_{10}, and $PM_{2.5}$ can lead to a higher hospital admission rate due to pneumonia [14]. Similarly, Liu et al. showed a statistically significant association between URI and concentration of SO_2, CO, NO_2, PM_{10}, and $PM_{2.5}$ [15]. Bronchiolitis is among the most common causes of children's hospital admission during winter [16]. However, asthma exacerbations occur mostly in the autumn season [17]. Likewise, our results showed that most bronchiolitis and asthmatic patients were admitted to a hospital in winter and spring, respectively. Similarly, Hoeppner et al. found that hospital admission due to bronchiolitis increases during winter [18]. We also investigated the association between asthma attacks and the concentration of air pollution indices (SO_2, CO, NO_2, PM_{10}, and $PM_{2.5}$), and none of them was associated with hospital admission due to asthma attacks. Similarly, using traffic proximity and density as proxies for air pollution exposure, some earlier studies found no remarkable association between asthma development and air pollution [19–21]. In contrast, some other studies showed a notable correlation between the concentration of SO_2, NO_2, and $PM_{2.5}$ and a higher prevalence of asthma attacks [3, 22, 23]. We found that the concentration of air pollution indices (CO, NO2, PM_{10}, and $PM_{2.5}$) did not correlate to hospital admission due to respiratory signs and symptoms such as cough, fever, dyspnea, respiratory distress, and wheezing, but the concentration of SO_2 did. Our results also showed no significant association between the AQI and hospital admission because of asthma attacks and other respiratory signs and symptoms.

Table 4 Correlation between the total number of hospital admissions due to respiratory manifestations and asthma attacks and concentration of air pollution indices of each month

Indices		Correlation with the total number of patients with respiratory manifestations	Correlation with the total number of patients with asthma attack
[a]CO (ppm)	Correlation coefficient	−0.89	−0.213
	P-value	0.679	0.317
[b]NO2 (ppb)	Correlation coefficient	0.164	−0.216
	P-value	0.444	0.311
[c]SO2 (ppb)	Correlation coefficient	0.487	0.382
	P-value	0.016	0.066
[d]PM_{10} (mic-g/m^3)	Correlation coefficient	−0.390	−0.131
	P-value	0.059	0.541
[e]$PM_{2.5}$ (mic-g/m^3)	Correlation coefficient	−0.173	−0.302
	P-value	0.419	0.152

[a] Carbon monoxide

[b] Nitrogen dioxide

[c] Sulfur dioxide

[d] Particulate matters less than 10 µm

[e] Particulate matters less than 2.5 µm

Correspondingly, Nicolai's research demonstrated that nonspecific respiratory symptoms like chronic cough are associated with long-term exposure to SO_2 but not asthma [24]. Similarly, Pan et al. showed that the prevalence of respiratory symptoms such as persistent cough and phlegm has increased in exposure to SO_2 [25]. Another study also showed that short-term exposure to SO_2 is strongly associated with hospital admission due to respiratory diseases, especially among children aged 0–4 [26]. Likewise, Mansourian et al. found a significant association between SO_2 and PM_{10} concentrations and respiratory-related children's hospital admissions in Isfahan, Iran [27]. Similar to our study, Ranzi and his colleagues found that exposure to traffic-related pollution is weakly associated with respiratory issues in children during the first 7 years of their lives [28]. Another study, based on a large Swedish birth cohort, showed that asthma is not significantly associated with exposure to air pollutants [29]. Exposure to NO_2 can trigger asthma attacks by increasing leukotriene production [30]. Unlike our study, several studies demonstrated a remarkable association between the concentration of NO_2 and the development of respiratory symptoms [31, 32]. Clark et al. found that early exposure to air pollutants such as NO_2, carbon monoxide (CO), nitric oxide (NO), PM_{10}, SO_2, and black carbon can contribute to the development of asthma in preschool ages [4]. A similar study showed higher concentrations of NO_2 and $PM_{2.5}$, which resulted in asthma symptoms and boosted its prevalence [33]. Contrary to our study, a higher PM concentration resulted in more respiratory symptoms and asthma exacerbation among 6- to 12-year-old children exposed to petrochemical pollution. Seemingly, more exposure to PM was concomitant with higher rates of hospital admission for respiratory disorders, especially asthma attacks [1]. Another study suggested higher levels of $PM_{2.5}$ can contribute to new-onset wheeze among 5- to 7-year-old children [34]. A meta-analysis comprised of 41 studies also showed a remarkable association between the development of asthma and exposure to NO_2, $PM_{2.5}$, and PM_{10} [35]. This study also found a significant correlation between the final diagnosis and mortality of patients. Thirty-one out of 932 patients died, of which 22.6% were diagnosed with pneumonia and 77.4% had another diagnosis. Pneumonia was reported as the most prevalent cause of death among children aged more than 5 years old suffering from respiratory diseases [36]. In 2019, 740,180 children died from pneumonia, which accounts for 14% of all deaths in children under the age of 5 [37]. From 1968 to 2000, pneumonia, asthma, and cystic fibrosis were responsible for 73% of all respiratory mortality among 1- to 16-year-old patients in England and Wales [38].

Conclusion

The present study investigated the association of air pollution with the respiratory health of children admitted at one of the pediatric hospital centers in Mashhad, Iran. Mashhad is one of the most extensive and most populated cities in Iran. A few similar researches have studied the association between air pollution and the respiratory health of Iranian children. As air pollution is accelerating and its health effects are devastating, more research is necessary to improve environmental health policies in developing countries. Generally, our cross-sectional study showed no statistically significant association between air pollution and hospital admissions due to respiratory manifestations in children; however, achieving comprehensive results requires more investigation into the enormous population exposed to air pollution for a long time.

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Authors' contributions
NM visited the patients and supervised on data gathering, analysis, and writing the manuscript. AM collected and analyzed the data. NT wrote and submitted the article. All authors reviewed and edited the manuscript.

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Availability of data and materials
The date used and/or analyze during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The questionnaire and methodology for this study were approved by the Human Research Ethics Committee of the Mashhad University of Medical Sciences (ethics approval number: IR.MUMS.MEDICAL.REC.1399.494). Written informed consent was obtained from the parents.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
[1] Allergy Research Center, Mashhad University of Medical Sciences, Mashhad, Iran. [2] Student Research Committee, Mashhad University of Medical Sciences, Mashhad, Iran. [3] Medical Genetics Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

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References

1. Wichmann FA, Müller A, Busi LE, Cianni N, Massolo L, Schlink U et al (2009) Increased asthma and respiratory symptoms in children exposed to petrochemical pollution. J Allergy Clin Immunol 123(3):632–638
2. Dondi A, Carbone C, Manieri E, Zama D, Del Bono C, Betti L et al (2023) Outdoor air pollution and childhood respiratory disease: the role of oxidative stress. Int J Mol Sci. 24(5):4345
3. Bowatte G, Lodge C, Lowe AJ, Erbas B, Perret J, Abramson MJ et al (2015) The influence of childhood traffic-related air pollution exposure on asthma, allergy and sensitization: a systematic review and a meta-analysis of birth cohort studies. Allergy 70(3):245–256
4. Clark NA, Demers PA, Karr CJ, Koehoorn M, Lencar C, Tamburic L, Brauer M (2010) Effect of early life exposure to air pollution on development of childhood asthma. Environ Health Perspect 118(2):284–290
5. Clear the air for children. United Nations Children´s Fund (UNICEF) (2016). Available from: https://www.unicef.org/publications/index_92957.html
6. Griscom NT, Wohl ME, Kirkpatrick JA Jr (1978) Lower respiratory infections: how infants differ from adults. Radiol Clin North Am 16(3):367–387
7. Guzelian PS, Henry CJ, Olin SS (1992) Similarities and differences between children and adults: Implications for risk assessment. Washington, D.C.: ILSI Press/International Life Sciences Institute
8. Trasande L, Thurston GD (2005) The role of air pollution in asthma and other pediatric morbidities. J Allergy Clin Immunol 115(4):689–699
9. A guide for calculating, determining, and announcing air quality index. Tehran University of Medical Sciences (TUMS). https://ier.tums.ac.ir/ZYvt. Accessed 17 Nov 2018
10. Salvi S (2007) Health effects of ambient air pollution in children. Paediatr Respir Rev 8(4):275–280
11. Evangelisti M, Cangiano G, Nenna R, Nicolai A, Frassanito A, Papasso S et al (2015) Air pollution and bronchiolitis from 2004 to 2014 in Rome. Eur Respir J 46(suppl 59):PA4505
12. Leung SY, Lau SYF, Kwok KL, Mohammad KN, Chan PKS, Chong KC (2021) Short-term association among meteorological variation, outdoor air pollution and acute bronchiolitis in children in a subtropical setting. Thorax 76(4):360–369
13. Milani GP, Cafora M, Favero C, Luganini A, Carugno M, Lenzi E et al (2022) PM2.5, PM10 and bronchiolitis severity: a cohort study. Pediatr Allergy Immunol 33(10):e13853
14. Darrow LA, Klein M, Flanders WD, Mulholland JA, Tolbert PE, Strickland MJ (2014) Air pollution and acute respiratory infections among children 0–4 years of age: an 18-year time-series study. Am J Epidemiol 180(10):968–977
15. Liu Y, Wang Y, Dong J, Wang J, Bao H, Zhai G (2022) Association between air pollution and emergency department visits for upper respiratory tract infection inLanzhou China. Environ Sci Pollut Res 29(19):28816–28828
16. Erickson EN, Bhakta RT, Mendez MD. Pediatric Bronchiolitis. Updated 26 June 2023. https://www.ncbi.nlm.nih.gov/books/NBK519506/
17. Morita Y, Campos Alberto E, Suzuki S, Sato Y, Hoshioka A, Abe H et al (2017) Pranlukast reduces asthma exacerbations during autumn especially in 1- to 5-year-old boys. Asia Pac Allergy 7(1):10–18
18. Hoeppner T, Borland M, Babl FE, Neutze J, Phillips N, Krieser D et al (2017) Influence of weather on incidence of bronchiolitis in Australia and New Zealand. J Paediatr Child Health 53(10):1000–1006
19. Wjst M, Reitmeir P, Dold S, Wulff A, Nicolai T, von Loeffelholz-Colberg EF, von Mutius E (1993) Road traffic and adverse effects on respiratory health in children. BMJ 307(6904):596–600
20. English P, Neutra R, Scalf R, Sullivan M, Waller L, Zhu L (1999) Examining associations between childhood asthma and traffic flow using a geographic information system. Environ Health Perspect 107(9):761–767
21. Ciccone G, Forastiere F, Agabiti N, Biggeri A, Bisanti L, Chellini E et al (1998) Road traffic and adverse respiratory effects in children SIDRIA Collaborative Group. Occup Environ Med 55(11):771–778
22. Smargiassi A, Kosatsky T, Hicks J, Plante C, Armstrong B, Villeneuve PJ, Goudreau S (2009) Risk of asthmatic episodes in children exposed to sulfur dioxide stack emissions from a refinery point source in Montreal Canada. Environ Health Perspect 117(4):653–659
23. Gaffin JM, Hauptman M, Petty CR, Sheehan WJ, Lai PS, Wolfson JM et al (2018) Nitrogen dioxide exposure in school classrooms of inner-city children with asthma. J Allergy Clin Immunol 141(6):2249–55.e2
24. Nicolai T (1999) Air pollution and respiratory disease in children: what is the clinically relevant impact? Pediatr Pulmonol Suppl 18:9–13
25. Pan G, Zhang S, Feng Y, Takahashi K, Kagawa J, Yu L et al (2010) Air pollution and children's respiratory symptoms in six cities of northern China. Respir Med 104(12):1903–1911
26. Ibrahim MF, Hod R, Ahmad Tajudin MAB, Wan Mahiyuddin WR, Mohammed Nawi A, Sahani M (2022) Children's exposure to air pollution in a natural gas industrial area and their risk of hospital admission for respiratory diseases. Environ Res 210:112966
27. Mansourian M, Javanmard SH, Poursafa P, Kelishadi R (2010) Air pollution and hospitalization for respiratory diseases among children in Isfahan. Iran Ghana Med J 44(4):138–143
28. Ranzi A, Porta D, Badaloni C, Cesaroni G, Lauriola P, Davoli M, Forastiere F (2014) Exposure to air pollution and respiratory symptoms during the first 7 years of life in an Italian birth cohort. Occup Environ Med 71(6):430–436
29. Gruzieva O, Bergström A, Hulchiy O, Kull I, Lind T, Melén E et al (2013) Exposure to air pollution from traffic and childhood asthma until 12 years of age. Epidemiology 24(1):54–61
30. Glencross DA, Ho T-R, Camiña N, Hawrylowicz CM, Pfeffer PE (2020) Air pollution and its effects on the immune system. Free Radical Biol Med 151:56–68
31. Hajat S, Haines A, Goubet SA, Atkinson RW, Anderson HR (1999) Association of air pollution with daily GP consultations for asthma and other lower respiratory conditions in London. Thorax 54(7):597–605
32. Shima M, Adachi M (2000) Effect of outdoor and indoor nitrogen dioxide on respiratory symptoms in schoolchildren. Int J Epidemiol 29(5):862–870
33. Gehring U, Wijga AH, Brauer M, Fischer P, de Jongste JC, Kerkhof M et al (2010) Traffic-related air pollution and the development of asthma and allergies during the first 8 years of life. Am J Respir Crit Care Med 181(6):596–603
34. Jung KH, Hsu S-I, Yan B, Moors K, Chillrud SN, Ross J et al (2012) Childhood exposure to fine particulate matter and black carbon and the development of new wheeze between ages 5 and 7 in an urban prospective cohort. Environ Int 45:44–50
35. Khreis H, Kelly C, Tate J, Parslow R, Lucas K, Nieuwenhuijsen M (2017) Exposure to traffic-related air pollution and risk of development of childhood asthma: a systematic review and meta-analysis. Environ Int 100:1–31
36. Njuguna HN, Zaki SR, Roberts DJ, Rogena EA, Walong E, Fligner CL et al (2021) Postmortem Study of cause of death among children hospitalized with respiratory illness in Kenya. Pediatr Infect Dis J 40(8):715–722
37. (WHO) WHO. Pneumonia in children 2022 [Available from: https://www.who.int/news-room/fact-sheets/detail/pneumonia
38. Panickar JR, Dodd SR, Smyth RL, Couriel JM (2005) Trends in deaths from respiratory illness in children in England and Wales from 1968 to 2000. Thorax 60(12):1035–1038

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