



The Impact of Air Pollution and Aeroallergens Levels on Upper Airway Acute Diseases at Urban Scale

Giancarlo Ottaviano¹ · Alfonso Luca Pendolino^{2,3} · Gino Marioni¹ · Maria Angiola Crivellaro⁴ · Bruno Scarpa⁵ · Ennio Nardello¹ · Chiara Pavone¹ · Maria Vittoria Trimarchi¹ · Enrico Alexandre¹ · Clervie Genovais⁶ · Angelo Moretto⁴ · Marco Marani⁶ · Peter James Andrews^{2,3} · Rosario Marchese-Ragona¹

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Abstract

Air pollution (AP) represents one of the main environmental threats to public health and exposure to AP has been connected to upper airway (UA) disease. We evaluated the relationships between the ENT urgent referrals recorded at the Hospital of Padua and the daily levels of particulate matter (PM) as well as other environmental factors in a single year. Patients with UA disorders were included in the study group while those referred for facial trauma or foreign body inhalation formed the control group. Daily PM concentrations, meteorological data and the concentrations of the commonest aeroallergens were obtained. 6368 patients formed the study group and 910 the control one. The concentration of compositae allergens showed a positive effect on the total number of admissions ($p=0.001$). PM_{10} did not demonstrate an effect on the total number of admissions or either the study or control groups admissions ($p=0.25$). *Alternaria* positively influenced admissions of patients in the study group ($p=0.005$). Significant relationships were found between the following: PM_{10} measured on the seventh day before A&E admission and rhinosinusitis ($p=0.007$), PM_{10} on the fifth day and laryngitis ($p=0.01$), PM_{10} on the second day and otitis media ($p=0.03$), PM_{10} on the admission day and epistaxis ($p=0.0198$). Our study confirms the causal relationship between aeroallergen concentration and ENT admissions. The levels of PM_{10} at specific days preceding A&E admission correlated with certain UA disorders. This study strongly points towards the harmful effects of pollution and climate change on UA disease.

Article Highlights

- Air pollution represents one of the main environmental threats to public health and exposure to pollutants has been connected to upper airway (UA) diseases.
- The relationships between the ear, nose and throat (ENT) urgent referrals registered in a single year at the Hospital of Padua and the daily levels of particulate matter (PM_{10}) as well as other environmental factors measured in the same period were evaluated.
- Our study confirms the relationship between PM_{10} levels, climate change and pollens levels.

Giancarlo Ottaviano and Alfonso Luca Pendolino share the first authorship.

✉ Alfonso Luca Pendolino
alfonso.pendolino.19@ucl.ac.uk

✉ Angelo Moretto
angelo.moretto@unipd.it

¹ Department of Neurosciences, Section of Otolaryngology, University of Padua, Padua, Italy

² Department of ENT, Royal National ENT and Eastman Dental Hospitals, 47-49 Huntley St, Bloomsbury, London WC1E 6DG, UK

³ Ear Institute, University College London, London, UK

⁴ Department of Cardiac Thoracic Vascular Sciences and Public Health, University of Padova, Padua, Italy

⁵ Department of Statistical Sciences and Department of Mathematics Tullio Levi-Civita, University of Padova, Padua, Italy

⁶ Department of Civil and Environmental Engineering, University of Padova, Padua, Italy

- A significant influence of *Alternaria* on the number of ENT referrals for UA disorders was demonstrated.
- Levels of PM₁₀ at specific days preceding the Accident and Emergency admission were found to correlate with the number of ENT referrals for certain UA disorders.
- Accurate identification of the atmospheric factors and processes responsible for the increased UA morbidity might allow appropriate protocols to be adopted to minimize their impact on health.

Keywords Environment · Pollution · Public health · Climate change · Particulate matter

Introduction

Air pollution (AP) represents one of the main environmental threats to public health (Jo et al. 2017; European Environment Agency 2019). It is a heterogeneous mixture of gases, liquids, and solid particles including particulate matter (PM), nitric oxides (NO_x), sulphur oxides, carbon monoxide (CO), and ozone (O₃) (Jo et al. 2017). Inhalable PM is further classified according to the aerodynamic equivalent diameter of its particles as coarse (2.5–10 µm), fine (0.1–2.5 µm) and ultrafine (<0.1 µm) with fine PM being able to reach the lungs (Michalska et al. 2020). Vehicle traffic and heating systems represent some of the most common urban outdoor emission sources (Hime et al. 2018). Traffic-related AP is a complex mixture of primary gaseous emissions (such as NO_x) which are derived from combustion (including elemental or black carbon) and non-combustion sources (e.g. road dust, tyre wear, and brake wear) (Hime et al. 2018). These primary emissions lead to the generation of secondary pollutants such as O₃, nitrates and organic aerosol. Another important source of atmospheric pollutant is derived from heating systems and are considered as primary emitters of PM and CO (Burns et al. 2020). Industry is also an additional major source of PM release (Burns et al. 2020; Zhang et al. 2020).

As a consequence of growing urbanisation, more than 90% of the population live in places where air quality does not meet World Health Organization (WHO) recommendation. WHO sets daily exposure limits for PM_{2.5} and PM₁₀ at 25 µg/m³ and 50 µg/m³ respectively, with an annual cumulative exposure limit for PM_{2.5} at less than 10 µg/m³ (World Health Organization 2021). In this regard, the European Environment Agency (EEA) reported that most city dwellers have been exposed in the last years to levels higher than those recommended by WHO (74% and 42%, respectively, for PM_{2.5} and PM₁₀) (European Environment Agency 2019). Worldwide EEA estimates that 7 million people yearly die because of AP exposure and in Europe AP remains the single largest environmental health hazard leading to a reduced quality of life caused by AP-related illness (European Environment Agency 2020). The impact on health is due to both short- (over a few hours or days) and long-term (over months or years) AP exposure. Morbidity is mainly linked to respiratory and cardiovascular diseases (Abe and Miraglia 2016; Jo et al. 2017; Lokotola et al. 2020; Sompornrattanaphan et al. 2020) and encompasses acute

illness, chronic disease and long-term disability, ranging from mild symptoms such as coughing to more severe conditions that may require hospitalization (Jo et al. 2017; Lokotola et al. 2020). Due to the fact AP affects the whole population on a daily basis, even the less severe effects might have significant public health implications (European Environment Agency 2019, 2020; World Health Organization 2021). In this regard, AP exposure has also been connected to respiratory allergy. In fact, exposure to AP, and in particular to PM, is considered a main driver of the significant increase in the prevalence of allergic respiratory diseases observed in the past decades (Chung et al. 2011; Zhang et al. 2015a, b; Zheng et al. 2015; Wise et al. 2018) and an important contributor to the development and exacerbation of asthma (Sompornrattanaphan et al. 2020). Moreover, it has been suggested that PM can also interact with airborne allergens, whereas AP acts as adjuvant by altering the immunogenicity of allergenic proteins (Reinmuth-Selzle et al. 2017). As a contributing factor, climate change (in particular temperature, relative humidity and ultraviolet radiations) is known to affect abundance and properties of bioaerosols as carriers of aeroallergens (Reinmuth-Selzle et al. 2017).

Veneto is one of the most industrialized regions in Italy (Masiol et al. 2017; Forlivesi et al. 2018), and the city of Padua, in particular, is one of the most PM-polluted cities in Europe (Tapparo et al. 2020). Due to the high AP levels observed in this area, we had the opportunity to explore and quantify the link between AP and upper airway (UA) morbidity. Therefore, the main aim of the present investigation was to evaluate the relationships between the ear, nose and throat (ENT) urgent referrals registered at the University Hospital of Padua in one year and the daily levels of PMs as well as other environmental factors such as rainfall, air temperature, and humidity measured in the same period. As a secondary endpoint, we investigated the influence of aeroallergens levels on these relationships.

Materials and Methods

This retrospective study was conducted in accordance with the principles of the Helsinki Declaration. Data were examined in agreement with the Italian privacy and sensitive data laws, and the internal regulations of Padua University's Otolaryngology Section.

Population Considered

Azienda Ospedale Università Padova (AOUP) is a Tertiary (teaching) hospital in the Italian region of Veneto covering a population of roughly 210,000 people and recording more than 70,000 referrals to A&E every year.

In this study, only patients admitted to the Accident and emergency (A&E) department and then referred to the ENT urgent clinic during the year 2017 were considered. Patients with UA disorders were included in the study group while those referred for facial trauma or foreign body inhalation formed the control group.

Pollution and Meteorological Data

Daily AP concentrations ($\mu\text{g}/\text{m}^3$), wind speed (km/h), rainfall depth (mm), air temperature ($^{\circ}\text{C}$), minimum and maximum relative humidity (%) and the concentrations of the commonest aeroallergens in the Padua urban area (*Alternaria*, *Betulaceae*, *Compositae*, *Corylaceae*, *Graminae*) (g/m^3) were obtained from fixed-site monitoring stations operated by ARPAV (Regional Agency for Environmental Protection and Prevention of the Veneto Region) and working 24 h a day.

Statistical Analysis

Pollution and meteorological daily mean values were calculated as the average of 24-hourly measurements in the same day. Data on referrals have been aggregated by day and the Bravais-Pearson correlation coefficient has been used to measure the marginal relation between the different indicators. Multiple Poisson count regression was fitted to explain the number of referrals with all daily variables (PM_{10} of the admission day and PM_{10} of the single days of the previous week, weather factors, aeroallergens), by allowing also quadratic effects (Agresti 2013). The joint effect of sex with PM_{10} , obtained by considering the daily access by sex and estimating the interaction between sex and pollutant concentration, was also evaluated. *p* values have been calculated for all tests, and 5% was considered as the critical level of significance. Values in the range of $0.15 > p \text{ value} \geq 0.05$ were assumed to indicate a marginal significance. All analyses were performed using the R: a language and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria).

Results

Population

In total, 7278 patients (3604 males and 3674 females) were referred to the ENT urgent clinic in 2017. Of these, 910

were referred for facial trauma or foreign body inhalation and formed the control group. Table 1 reports patients' demographics, $\text{PM}_{10}/\text{PM}_{2.5}$, weather factors and aeroallergen recorded levels and the characteristics of the ENT referrals in the year 2017.

$\text{PM}_{2.5}/\text{PM}_{10}$ Concentrations

There was a strong positive correlation between PM_{10} and $\text{PM}_{2.5}$ concentrations (Fig. 1a). For simplicity and without loss of generality, we further considered only PM_{10} levels as potential explanatory variable in view of the fact that statistical results and inferences remained unchanged when $\text{PM}_{2.5}$ concentrations were used in the analysis in place of PM_{10} . The 2017 mean PM_{10} level was $38.8 \mu\text{g}/\text{m}^3$ and PM_{10} levels were between $50 \mu\text{g}/\text{m}^3$ and $99 \mu\text{g}/\text{m}^3$ for 76 days and above $100 \mu\text{g}/\text{m}^3$ for 14 days, with the coldest months being the worst in terms of PM_{10} levels (Fig. 1b). Table 1 reports the mean PM_{10} and $\text{PM}_{2.5}$ levels.

PM_{10} Concentration and Weather Factors

Significant correlations were found between PM_{10} levels and the mean air temperature (Fig. 2a; Table 2) and the minimum and the maximum relative humidity level (Fig. 2b, c; Table 2). There was a significant correlation between maximum and minimum relative humidity level.

PM_{10} Concentration and Aeroallergens

Among the aeroallergens considered, only *Betulaceae* and *Corylaceae* showed a significant positive correlation with PM_{10} levels (Fig. 3a, b).

Weather Factors and Aeroallergens

Negative correlations were found between maximum relative humidity level and *Alternaria*, *Gramineae* and *Compositae* allergens, with the latter being a marginal one. (Table 2). Mean air temperature significantly correlated with all the studied allergens, positively with the *Gramineae* and *Alternaria* allergens, while negatively with the others allergens (Table 2). Rainfall depth (mm) significantly correlated only with *Compositae* allergens (Table 2).

Influence of Available Variables on the Number of Admissions During the Year

PM_{10} levels did not show any effect on the admissions when comparing the study group—which includes all the admissions except facial traumas and foreign body inhalations—and the control group. Considering the influence of the other variables (weather factors and common

Table 1 Demographic, weather factors and detailed characteristics of the ENT referrals in the year 2017

	Subjects (<i>n</i> = 7.278)
<i>Demographic</i>	
Age, mean [SD; range], yr	47.6 [23.3; 0–102]
Sex, No (%)	
Female	3674 (50.5%)
Male	3604 (49.5%)
Most frequent comorbidities, No (%)	
Hypertension	1189 (16.3%)
Cardiovascular disease	1003 (13.8%)
Neurologic disease	330 (4.5%)
Cancer	317 (4.4%)
Diabetes	301 (4.1%)
At least one comorbidity	2968 (40.8%)
<i>Weather factors</i>	
PM _{2.5} , mean [SD; range], µg/m ³	32.1 [26.6; 0.0–148]
PM ₁₀ , mean [SD; range], µg/m ³	38.8 [28.7; 2–181]
Aeroallergens level, mean [SD; range], gr (or spore)/m ³	
<i>Betullaceae</i>	4.9 [11.3; 0–49.6]
<i>Corylaceae</i>	4 [10.7; 0–60.4]
<i>Alternaria</i>	62.7 [61.3; 0–222.5]
<i>Gramineae</i>	15.1 [25.1; 0–126.3]
<i>Compositae</i>	0.7 [1.9; 0–11.5]
Air temperature, mean [SD; range], °C	14.5 [8.3; – 2 to 30.8]
Maximum relative humidity, mean [SD; range], %	90.5 [9.8; 57–100]
Minimum relative humidity, mean [SD; range], %	50.2 [16.9; 13–100]
Rainfall, mean [SD; range], mm	0.5 [3.3; 0–47]
<i>Characteristics of ENT referrals</i>	
Study Group, No (%)	<i>n</i> = 6368
Rhinitis/Rhinosinusitis	229 (3.6%)
Acute otitis media	433 (6.8%)
Pharyngitis	210 (3.3%)
Laryngitis	273 (4.3%)
Tracheitis	4 (0.1%)
Tonsillitis	353 (5.5%)
*Other UA disorders	4866 (76.4%)
Control Group, No (%)	<i>n</i> = 910
Facial Trauma	727 (79.9%)
UA foreign bodies	183 (20.1%)

ENT ear, nose and throat; PM particulate matter; SD standard deviation; UA upper airways

*Other UA disorders include: epistaxis, tinnitus, dizziness, sudden hearing loss, acute otitis externa, facial nerve palsy, stomatitis, sialadenitis, lymphadenopathy, lymphadenitis, UA abscess, head and neck tumours, etc

aeroallergens), only *Alternaria* positively influenced admissions of patients in the study group if compared to those in the control group.

In the study group PM₁₀ concentrations did not show an effect on the admission rate, regardless of the sex. At the Multiple Poisson count regression, considering also the influence of weather factors and common aeroallergens, the maximum relative humidity, and *Compositae* allergens showed a positive effect on admissions.

Influence of Air Pollution and Meteorological Conditions on the Admissions for Upper Airway Disorders

Table 1 shows the distribution of the patients in the study group according to the different diagnoses. We did not observe any influence of PM₁₀ on the number of admissions in the sub-cohort of patients affected by disorders possibly related to AP (patients with a diagnosis of rhinitis/

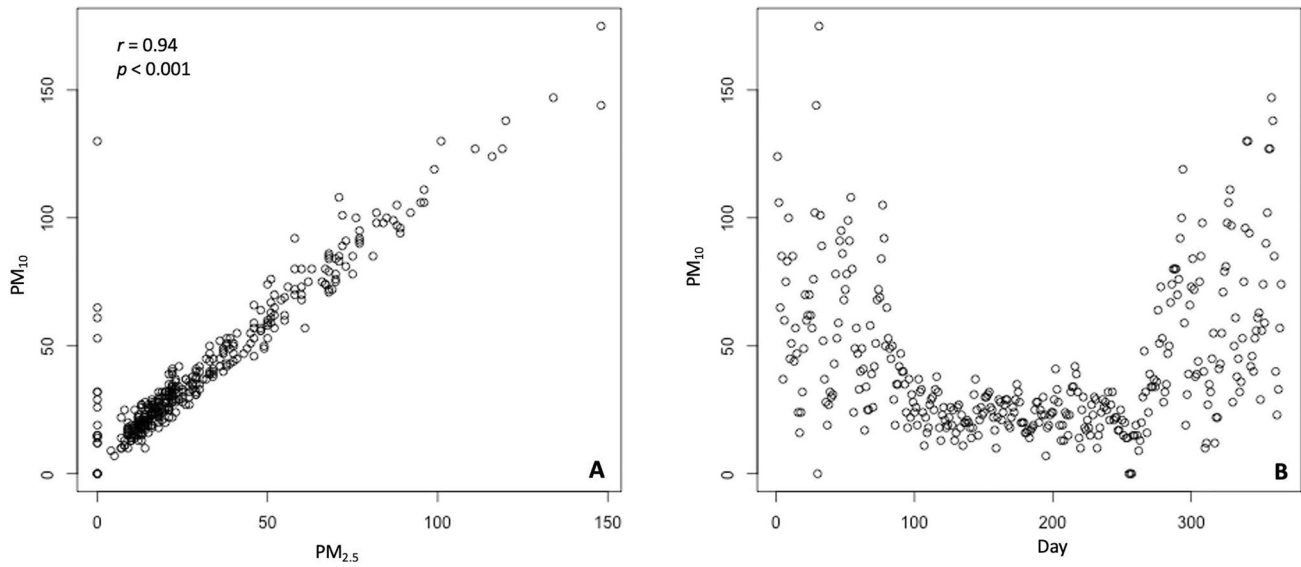


Fig. 1 Strong positive correlation between PM_{10} and $PM_{2.5}$ concentrations (a) and PM_{10} levels throughout the year (b)

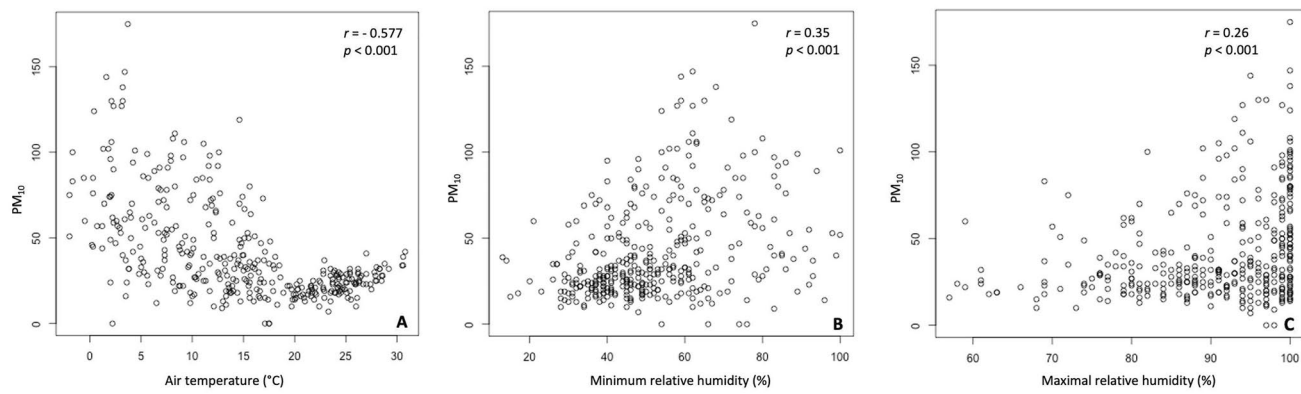


Fig. 2 Correlation between PM_{10} levels and the mean air temperature (a), the minimum relative humidity level (b) and the maximum relative humidity level (c)

Table 2 Correlations (r) between PM_{10} and aeroallergens and weather factors

	Maximum relative humidity	Minimum relative humidity	Air temperature	Rainfall
PM_{10}	0.26 (<0.001)	0.35 (<0.001)	-0.577 (<0.001)	-0.06 (<0.001)
Betulaceae	0.01 (0.815)	-0.106 (0.068)	-0.29 (<0.001)	-0.08 (0.145)
Corylaceae	-0.01 (0.825)	-0.101 (0.083)	-0.30 (<0.001)	-0.09 (0.129)
Gramineae	-0.20 (0.005)	-0.225 (<0.001)	0.15 (<0.001)	0.06 (0.321)
Alternaria	-0.19 (<0.006)	-0.263 (<0.001)	0.74 (<0.001)	-0.0008 (0.980)
Compositae	-0.16 (0.05)	-0.106 (0.067)	-0.29 (<0.001)	0.14 (0.018)

p value in brackets with significant ones marked in bold

rhinosinusitis, acute otitis media, pharyngitis, laryngitis, tracheitis and tonsillitis) ($n = 1502$). The same result was also

found when we considered the effects of the most common aeroallergens and the weather factors.

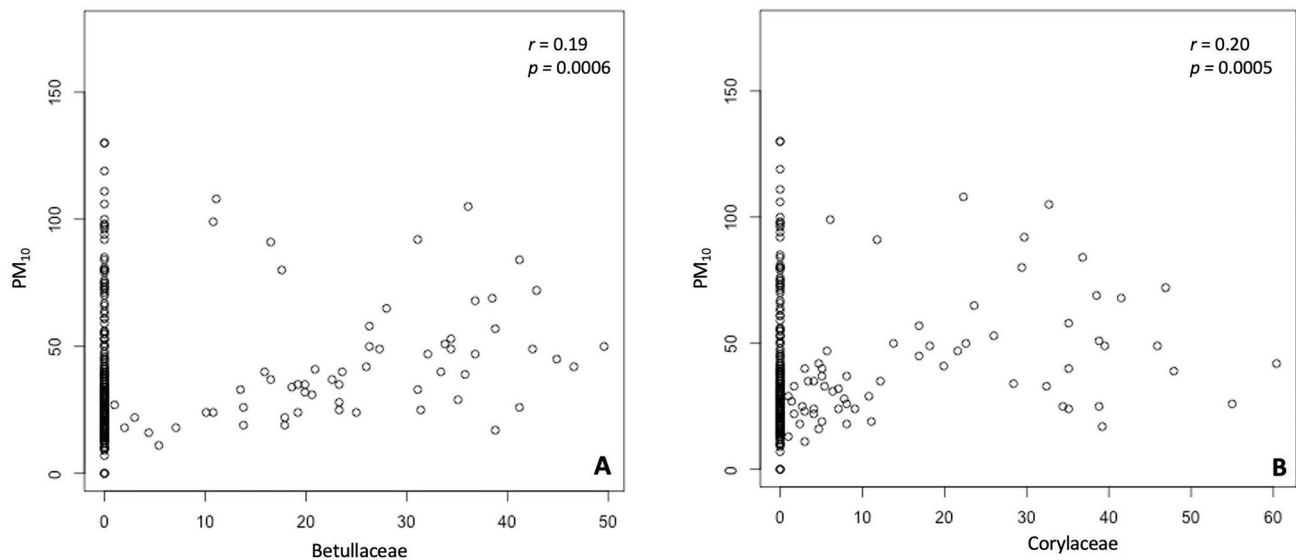


Fig. 3 Correlation between PM₁₀ levels and Betullaceae (a) or Corylaceae (b)

Once we considered each disease separately and the effect of PM₁₀ level on the day of A&E admission, a marginal effect was found only for rhinosinusitis when taking into account the influence of the weather and aeroallergens. This effect became significant when we considered the PM₁₀ level measured on the seventh day before A&E admission when the influence of the aeroallergens was included. Similarly, the PM₁₀ level measured on the second day before admission showed a positive effect on the admissions for otitis media when considering the influence of the weather and aeroallergens, while that registered on the fifth day before admission had a positive effect on the admissions for laryngitis when including the influence of the weather factors. Influence of PM₁₀ levels on upper airway disorders on the day of admission (Day 0) and at different days before it is reported in Table 3.

Influence of Air Pollution and Meteorological Conditions on the Admissions for Upper Airway Disorders

The admissions for other UA disorders were further investigated. When we analysed the PM₁₀ values at the day of the admission in comparison with that of the control group, also considering the effects of the most common aeroallergens and the weather factors, PM₁₀ levels showed a positive effect on the number of admissions only for epistaxis. When we took into account the effects of the most common aeroallergens and the weather factors, the effect did not change.

Considering the PM₁₀ levels of the whole week before A&E admission, the PM₁₀ level measured on the third day

Table 3 Output of the multiple poisson count regression: influence of PM₁₀ levels on upper airway disorders on the day of admission (day 0) and at different days before it, considering also weather and aeroallergens covariates.

	PM ₁₀ day -7	PM ₁₀ day -5	PM ₁₀ day -2	PM ₁₀ day 0
Rhinitis/Rhinosinusitis	0.007	–	–	0.07
Laryngitis	–	0.01	–	–
Acute otitis media	–	–	0.03	–
Epistaxis	–	–	–	0.02

Please note that only diseases in which PM₁₀ values demonstrated a significant influence have been included in the table

before the admission showed a marginally positive effect on the admissions for other UA disorders. This effect became significant when we considered the additional effect of the maximum relative humidity level, while it remains marginally significant when the influence of air temperature was added.

Discussion

Environmental PM is an atmospheric aerosol which is able to reach the nose, pharynx, larynx, trachea, bronchi, and distal lung. This results in the respiratory tract being the most highly exposed system. In particular, coarse PM, with an aerodynamic diameter of 2.5–10 μm, mainly deposits in the nose, pharynx, and large conducting airways. Exposure to PM may increase the risk of infection by altering various defence mechanisms of the respiratory tract and leading to

impaired mucociliary function and decreased phagocytosis by macrophages (Yang et al. 2020). PM often contains various immunogenic substances, such as fungal spores and pollen, which have been independently associated with exacerbation of asthma symptoms. Experimental exposure to PM causes oxidative stress, airway hyper-responsiveness, and airway remodelling, either alone or in combination with allergic sensitization (Qiu et al. 2022). Moreover, the existence of a dose–response relationship between PM and the risk of infection has been reported (Stanek et al. 2011).

In the present study, PM₁₀ levels correlated with weather factors confirming the already known close relationship between PM and meteorological variables (Perez et al. 2020). In particular, a negative correlation was found between PM₁₀ levels and air temperature, while PM₁₀ showed a positive correlation with humidity (both minimum and maximal). The PM₁₀ increase found in cold seasons/days could be caused by an increase in the use of heating systems in that period and possibly to a more intense vehicular traffic (Hime et al. 2018; Burns et al. 2020), but also to the inversion of temperature (Wallace et al. 2010; Cichowicz et al. 2017).

It is now accepted that the prevalence of allergic disease has increased in recent decades throughout the industrialized world (Wise et al. 2018) and our results confirm a significant correlation between Betullaceae, Corylaceae and PM₁₀ levels. AP, in fact, can influence aeroallergens, and in heavily polluted zones pollens can express a larger number of proteins described as being allergenic (Bartra et al. 2007). The constituents of AP can disrupt pollen particles. This leads to the release of pauci-micronic (diameter of 2–5 µm) molecules which increases the penetration into the upper airway (D'Amato 2001). Moreover, climate change has led to temperature variations during the seasons. As a result, plants may vary their pollination calendar and/or prolong their pollination period (Bartra et al. 2007; Cichowicz et al. 2017; Cane 2021), as reported for Betullaceae (Zhang et al. 2014) which in the present study has been found to be associated with PM₁₀ levels. AP may also exert a direct influence on allergen production and concentration of fungal spores such as *Alternaria*. Fungal spores are more influenced by atmospheric variables when compared to pollens (Bartra et al. 2007). Table 2 shows the correlation between the aeroallergens considered and weather factors.

We did not observe effects of PM₁₀ levels on the total number of ENT urgent referrals. However, when we took into account the influence of other variables (weather factors and aeroallergens), maximum relative humidity showed a negative effect on the total number of ENT referrals. This result could be explained by the fact that 1502 admissions occurred for acute inflammatory response of UA epithelium, with 19.9% (299/1.502) of them diagnosed with rhinosinusitis. Moreover, a significant effect of

Compositae allergens on the admissions was also observed regardless of the sex. When comparing the study group of ENT urgent referrals with the control group, the influence of PM₁₀ levels was not observed. However, whilst taking into account the influence of other variables (weather factors and aeroallergens), only *Alternaria* allergens had a significant influence on the number of ENT referrals observed in the study group. *Alternaria* has very small spores (1–20 µm in diameter) (Bartra et al. 2007) which can easily reach the upper and lower airways causing inflammation and asthmatic flare-ups (Williams et al. 2016; Tham et al. 2017). *Alternaria* spores represents one of the main risk factors for fatal asthma (Vianello et al. 2016). Considering the different UA disorders separately, a marginal effect of PM₁₀ levels on rhinosinusitis was demonstrated ($p = 0.07$); this effect became significant ($p = 0.007$) when we considered the levels of PM₁₀ measured 7 days before the admission to the A&E department. The influence of PM₁₀ on rhinosinusitis observed in our study confirms previous results reported on large cross-sectional studies which suggest a relationship between rhinosinusitis and AP (Bhattacharyya 2009; Park et al. 2019). Moreover, the significant effect of PM₁₀ levels on epistaxis ($p = 0.0198$) demonstrated by our data could be a consequence of the nasal mucosal inflammation caused by AP (Bhattacharyya 2009; Park et al. 2019). Additionally, high PM₁₀ levels measured five days before the admission to the emergency department had a significant effect on the incidence of laryngitis ($p = 0.01$), whereas PM₁₀ levels registered 2 days before the admission significantly influenced the occurrence of acute otitis media ($p = 0.03$). A relationship between otitis media and AP had already been reported by Zemek et al. who found an association between A&E access for otitis media and interquartile increase in CO and NO_{x-2} levels, in the warmest months in girls and all patients with regards to CO and NO_{x-2} exposure, and in boys for CO exposure in the 2 days before the A&E access (Zemek et al. 2010). Similarly, Park et al. showed in a population-based study a significant relationship between AP, especially PM₁₀, and the incidence of otitis media in paediatric patients (Park et al. 2018).

The present investigation has its limitations. Although our study was conducted in one of the most polluted urban areas (Padua) both in Italy and in Europe, it remains a single-centre study and a comparison with other urban areas with lower PM levels is warranted for future studies. Second, we analysed only hospital-based ENT referrals for UA disease which required A&E access even though the incidence of UA disease registered at a primary care level might have been different (possibly higher).

Conclusions

Our study confirms the relationship between PM₁₀ levels, climate change and pollen levels (Betullaceae and Corylaceae) highlighting a significant influence of *Alternaria* on the number of ENT referrals for UA disorders. We did not find a clear link between air pollution and the number of ENT referrals, even though the experimental exposure to PM has been reported to cause oxidative stress, airway hyper-responsiveness, and remodelling (Stanek et al. 2011), with previous studies showing an association between AP and the number of ENT referrals (Zhang et al. 2015a, b; Choi et al. 2019; Kim et al. 2020). However, we did show that the levels of PM₁₀ at specific days preceding the A&E admission were found to correlate with the number of referrals for certain UA disorders which may help in predicting and better managing UA disorders. Accurate identification of the atmospheric factors and processes responsible for the increased UA morbidity might allow appropriate protocols to be adopted to minimize their impact on health.

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Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

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