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Original article

A 10-year survey on asthma exacerbations: Relationships among emergency medicine calls, pollens, weather, and air pollution

Suivi pendant dix ans des exacerbations d'asthme : relations entre les appels en service d'urgence, les pollens, la météorologie et la pollution atmosphérique

S. Ruffoni^a, G. Passalacqua^b, F. Ricciardolo^c, A. Furgani^a, A. Corrado Negrini^a,
M. De Amici^d, G. Ciprandi^{b,*}

^aEmergency department, IRCCS-Azienda Ospedaliera Universitaria San Martino, Genoa, Italy

^bAllergy and respiratory diseases clinic, university of Genoa, IRCCS-Azienda Ospedaliera Universitaria San Martino,
Viale Benedetto XV 6, 16132 Genoa, Italy

^cDepartment of clinical and biological sciences, division of respiratory disease, university of Turin, Turin, Italy

^dFondazione IRCCS-San Matteo, Pavia, Italy

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Abstract

Background. – Asthma exacerbation is an episode of worsening of asthmatic symptoms. Exacerbations may depend on environmental factors. Therefore, this study investigated possible relationship between emergency calls for exacerbation in adult patients with asthma and environmental factors, including pollen count, meteorological parameters, and air pollution in Genoa (Italy) during a 10-year period.

Methods. – Emergency calls for exacerbation were recorded for 10 years (2002–2011) in Genoa. Betulaceae, Urticaceae (including Parietaria), Gramineae, and Oleaceae pollen counts were measured. Meteorological parameters and air pollutants were also measured in the same area and in the same period.

Results. – The number of emergency calls did not modify over the time. There were significant relationships between emergency calls and pollens during the spring ($r = 0.498$), rainfall ($r = 0.818$), wind speed ($r = 0.727$), and air pollutants ($r = 0.622$ for SO_2 ; $r = 0.699$ for NO ; $r = 0.58$ for NO_2).

Conclusions. – This 10-year survey demonstrates that i) asthma exacerbations did not diminish over the time, ii) there were seasonal peaks (fall and spring), iii) pollens (mainly Parietaria), wind speed and rainfall, SO_2 , NO , and NO_2 were strongly associated with asthma exacerbations in patients with asthma in this area. Therefore, asthma exacerbations may depend on environmental changes.

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Keywords: Asthma; Exacerbation; Emergency call; Pollens; Weather; Air pollution

Résumé

Objectifs. – L'exacerbation de l'asthme est un épisode d'aggravation des symptômes de la maladie. Les exacerbations peuvent être liées à des facteurs environnementaux. Cette étude a pour objectif d'évaluer la possibilité de liens entre les appels téléphoniques en service d'urgence pour exacerbation d'adultes asthmatiques avec des facteurs environnementaux comportant les comptes polliniques, les paramètres météorologiques et la pollution atmosphérique dans la ville de Gênes (Italie), sur une période de dix ans.

Méthodes. – Les appels téléphoniques au centre 118 de Gênes pour exacerbation d'asthme ont été relevés sur une période de dix ans (2002–2011). Les comptes polliniques ont concerné les bétulacées, les urticacées, les graminées et les oléacées. Les paramètres météorologiques et les polluants atmosphériques ont été relevés sur le même site durant la même période.

Résultats. – Le nombre d'appels en urgence ne se modifie pas sur une échelle temporelle. Il existe une relation significative entre les appels et la pollinisation au printemps ($r = 0,498$), la pluviosité ($r = 0,818$), la vitesse du vent ($r = 0,727$) et les polluants atmosphériques ($r = 0,622$ pour le SO_2 ; $r = 0,699$ pour le NO ; $r = 0,58$ pour le NO_2).

* Corresponding author.

E-mail addresses: gio.cip@libero.it, giocip@unige.it (G. Ciprandi).

Conclusions. – Cette étude de suivi pendant dix ans montre que i) le nombre d'exacerbations de l'asthme ne diminue pas avec le temps, ii) il existe des pics saisonniers (automne et printemps), iii) les pollens (essentiellement les pariétaires), la vitesse du vent et la pluviosité, des taux atmosphériques élevés de polluants SO₂, NO et NO₂ sont fortement associés avec les exacerbations de l'asthme dans la même zone géographique. En conséquence, les exacerbations de l'asthme peuvent dépendre de modifications environnementales.

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Mots clés : Asthme ; Exacerbation ; Urgence ; Pollens ; Météorologie ; Pollution atmosphérique

1. Introduction

Asthma has a relevant epidemiologic impact on general population [1]. Asthma is a public health problem and is under-diagnosed and under-treated. It causes substantial burden to patients with asthma and often restricts work and activities. In addition, having an asthma exacerbation is one of the most distressing events [2]. Asthma exacerbation may be defined as an episode of (sub)acute worsening of asthmatic symptoms [3]. The major exacerbation triggers are: respiratory infections, allergen exposure, weather conditions, and air pollutants [4]. However, an accepted and univocal definition of asthma exacerbation is still debated. The common denominator is a deterioration of symptoms, and three aspects to define an exacerbation can be considered: worsened symptoms, fall in lung function parameters, and healthcare utilization [4,5]. A proposed definition of asthma exacerbation is a worsening of asthma requiring the use of systemic corticosteroids to prevent a serious outcome [6]. Anyway, healthcare utilization surely represents a relevant component in exacerbation outcomes.

Despite advances in asthma management, asthma exacerbations continue to occur and the frequency varies depending on the severity and the degree of control [7]. The most comprehensive data on exacerbation incidence derive from therapeutic clinical trials: asthmatics receiving optimum treatment should only have one exacerbation every 3 years [8]. However, these clinical trials do not reflect the real exacerbation rates, as they are conducted in optimal conditions both for patients' characteristics and methodology. For example, a survey analyzing reports of US emergency departments demonstrated that 73% of patients had at least one visit for asthma exacerbation in the prior year [9]. Recently, a survey has been conducted to evaluate the medical emergency calls requiring attention for asthma exacerbations among the population of the territory of Genoa (Italy) in an 8-year period [10]. This survey reported that the frequency of asthma exacerbations did not diminish over time. More recently, the collection of pollen counts, weather and pollutants records concerning the last 30 years in the same city was analyzed [11]. This study reported that some sensitization significantly increased, pollen counts exerted a higher pressure, climate and pollution changed, and very probably influenced pollen release.

For these reasons, this study aimed at evaluating the trend of medical emergency calls for asthma exacerbations in adult patients, also collecting pollen count, weather and air pollutants records during the period of 2002 to 2011 in Genoa area. The purpose was to detect a possible relationship among the clinical

phenomena, such as asthma exacerbations, pollen count, meteorological data, and air pollution.

2. Materials and methods

The territory of Genoa has a population of about 1 million of inhabitants. Genoa is a port city situated on the Mediterranean Sea (20 m above sea level, latitude 44°25' N and longitude 8°56' E), is in the North West of Italy, and has a temperate climate.

2.1. Clinical data

The clinical data were provided by the records of the 118 Medical Emergency Control Center of Genoa, in its capacity of a body officially coordinating all medical emergencies by telephone. The medical staff codes all incoming calls as per the International Classification of Diseases, 9th Revision (ICD-9). The study was observational; all the procedures were part of the standard clinical practice in the emergency community medicine setting. Therefore, the study was simply notified to the Ethical Committees of the IRCCS-San Martino Hospital, according to the Italian law. The data were analyzed both considering the years and months of incidence in adults (aging 18–55 years) and were regularly recorded between January 1, 2002 and December 31, 2011.

2.2. Aerobiological data

It was assessed aerobiological data regarding pollination period, and pollen concentrations recorded in the same period. The monitoring of pollens was performed at the survey center of San Martino Hospital concerning the first two decades, then data were collected by Agenzia Regionale per la Protezione dell'Ambiente Ligure (ARPAL), according to standard methods of the Italian Aerobiology Association (AIA), now also recognised as: UNI 11108. Airborne pollens were collected using a Burkard 7-day-recording volumetric spore trap, standard equipment used for aerobiological sampling worldwide. This spore trap was placed 20 m above ground level and away from sources of pollution. The choice of pollen species was based upon two criteria:

- they had to be the most important pollen types causing sensitizations and allergic symptoms in the people living in this geographic area and;
- they had to be present in the atmosphere, every year, in relatively high or significant concentrations.

For these reasons, four pollen species were measured: Gramineae, Betulaceae, Urticaceae, and Oleaceae.

Gramineae included *Phleum pratense*, *Dactylis glomerata*, *Poa annua*, *Lolium perenne*, and *Festuca elatior*. Betulaceae included *Betula alba*, *Alnus*, and it has been added Corylaceae (such as *Corylus avellana* and *Ostrya carpinifolia*). Urticaceae included *Parietaria judaica* and *Parietaria officinalis*. Oleaceae included olive tree.

For each taxon, 52 mean weekly pollen concentration values and peaks (grains/m³ air) were recorded and the sum of 52 weekly pollen concentration values gave an estimate of the annual amount of each pollen species. These four major allergenic species (Betulaceae, Gramineae, Oleaceae and Urticaceae) were regularly recorded between January 1, 2002 and December 31, 2011.

2.3. Meteorologic data

Meteorologic data included the yearly average values for temperature (°C), rainfall (mm), relative humidity (%), dew point (°C), visibility distance (km) and wind speed (km/h). All the data were collected and managed by “Il Meteo srl” (provided by Air Force Observatory of Genova Sestri Ponente). The data were regularly recorded between January 1, 2002 and December 31, 2011.

2.4. Air pollution data

Air pollution data included the yearly (1993–2010) average values for carbon monoxide CO (µg/m³), sulfur dioxide SO₂ (µg/m³), nitrogen oxide NO (µg/m³), nitrogen dioxide NO₂ (µg/m³), ozone O₃ (µg/m³), and PM₁₀ (µg/m³). All the data were collected and managed by the Environment and Territory Department of the “Provincia di Genova” (Observatory of Genova Quarto). The data were regularly recorded between January 1, 2002, and December 31, 2011.

2.5. Statistical analysis

Correlation between quantitative variables was evaluated by means of the Spearman's correlation coefficient (rho). Regression was used to describe trend of variables during the years. The association between total pollen count and pollen season, meteorological and air pollution data was also estimated by multiple regression analysis in order to find multiple independent predictors of the count. All tests were two sided and a *P*-value less than 0.05 was considered statistically significant. The software Medcalc 9 (Frank Schoonjans, BE) was used for all analyses.

3. Results

3.1. Clinical data

Firstly, there was no statistically significant change of emergency calls over the time (Fig. 1A). The analysis of data concerning the gender of patients shows that there was no

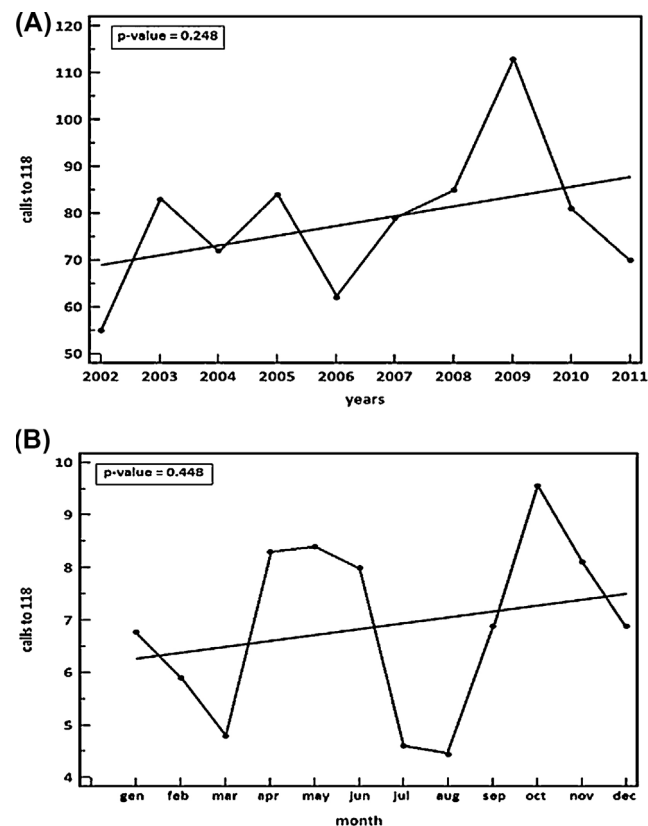


Fig. 1. Total number of emergency calls for asthma exacerbations (calls to 118) distributed per single year (A). Number of emergency calls distributed per month (B), calculated as averages of 10 years.

statistically significant difference between males and females. Secondly, the analysis of the emergency calls per month shows that there were two peaks (with a significant periodic temporal trend; *P* < 0.0001): the main in the fall and the second during the spring, without difference between genders (Fig. 1B).

3.2. Pollen count

Pollen counts tended to increase across the years for Oleaceae, Gramineae and Urticaceae, even if not significantly, instead Betulaceae pollens tended to decrease across the years, even if not significantly (data not shown). Moreover, we observed a linear trend over months for Betulaceae pollen count (*P*-value = 0.05) and a parabolic trend over months for Gramineae (*P*-value = 0.232), Oleaceae (*P*-value = 0.25) and Urticaceae (*P*-value = 0.039) pollen counts (Fig. 2). More interestingly, there was a significant and positive correlation (*P*-value = 0.0006, rho = 0.498) between calls to 118 emergency calls and total pollen count, considering months from April to August.

3.3. Meteorological data

Across the years, wind speed significantly decreased (*P*-value = 0.033). No significant temporal trends were observed for the other meteorological data. There was a positive and strong correlation between wind speed and calls to 118 (*P*-value = 0.0159, rho = 0.727), and a positive and very strong

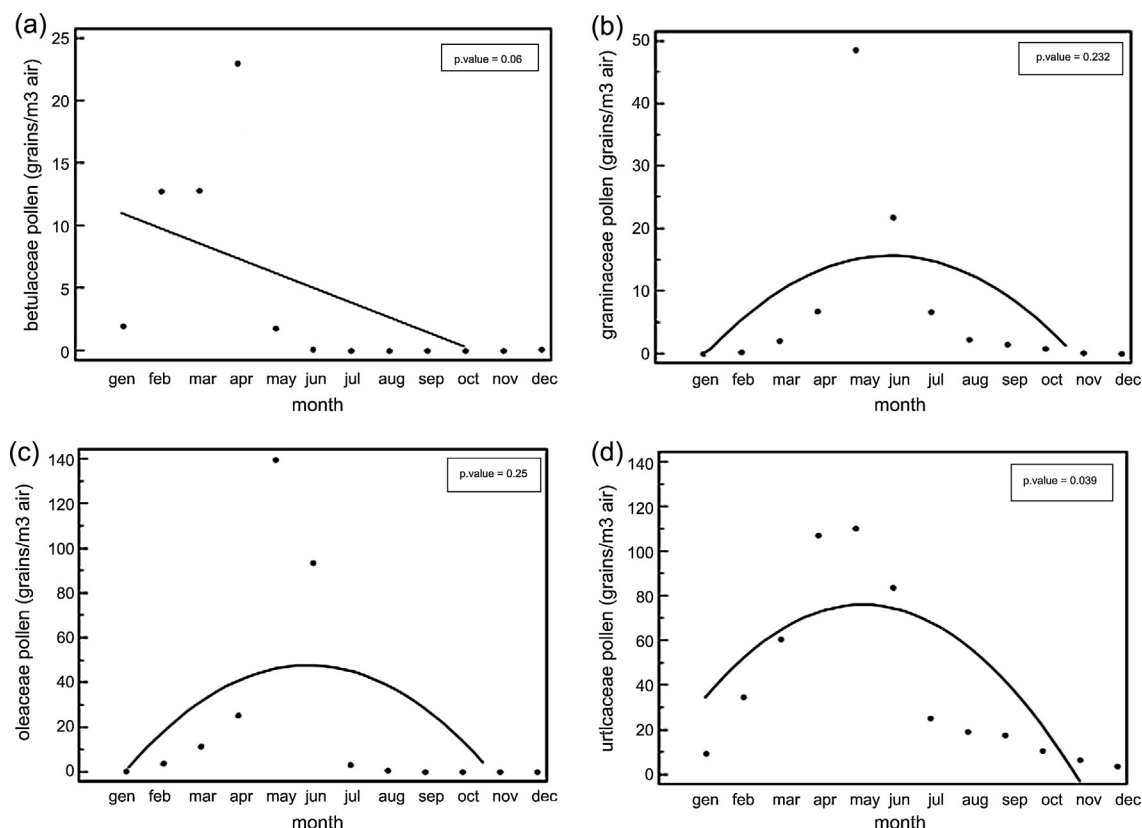


Fig. 2. Trends, during the year, of pollen counts for Betulaceae (a), Graminaceae (b), Oleaceae (c) and Urticaceae (d), expressed with P -value.

correlation between rainfall and calls to 118 (P -value = 0.0067, $\rho = 0.818$).

3.4. Air pollution data

Across the years, CO levels ($P = 0.001$, Fig. 3a), PM₁₀ levels ($P = 0.01$, Fig. 3b) and SO₂ levels ($P < 0.001$, Fig. 3c) significantly decreased, whereas NO levels significantly increased ($P = 0.003$, Fig. 3d).

There were positive and strong correlations between SO₂ and calls to 118 (P -value = 0.039, $\rho = -0.622$) and between NO and calls to 118 (P -value = 0.0204, $\rho = 0.699$); there was a positive and moderate relationship between NO₂ and calls to 118 (P -value = 0.05, $\rho = 0.58$). Calls to 118 were plotted against air pollution data (Fig. 4).

3.5. Multiple regression analysis

Number of calls per month was significantly correlated with dew point, temperature and pollen count for Urticaceae (the peak is at May), CO, NO, O₃, and the best ($P = 0.0007$) multivariate model combined these variables (Table 1).

4. Discussion

Asthma guidelines have been widely spread to both specialists and general practitioners, but it is clear that the number of asthma exacerbations did not diminish during the

years considered. This issue is of great clinical relevance, as asthma exacerbations really represent an emergency and they frequently depend on inadequate treatment. Thus, a great effort should be employed to improve the management of patients with asthma.

Epidemiology of asthma exacerbation depends on individual factors, mainly concerning respiratory infections, and environmental factors, including allergens, meteorological and pollutant factors [12].

The present study investigated the possible relationships between these environmental agents and asthma exacerbations assessed by emergency calls in a 10-year period.

The number of emergency calls does not diminish over the 10-year period. This finding must induce a serious remark on the global management in patients with asthma.

Analyzing the year distribution, two main peaks are evident: the most relevant during the fall and the second during the spring. The fall peak may be most likely due to two main causes: respiratory infections and house dust mites exposure. Both factors are more prevalent during the fall. However, this study did not assess these two issues.

About the pollen count, there was a trend of variation over the study period, but it was not significant. On the other hand, it is more relevant to consider the pollen season. Typically, all pollen species peaked during the spring, with an overlapping among species between April and May, mainly concerning Parietaria. Interestingly, there was a significant and direct relationship between the global quantity of all pollens and

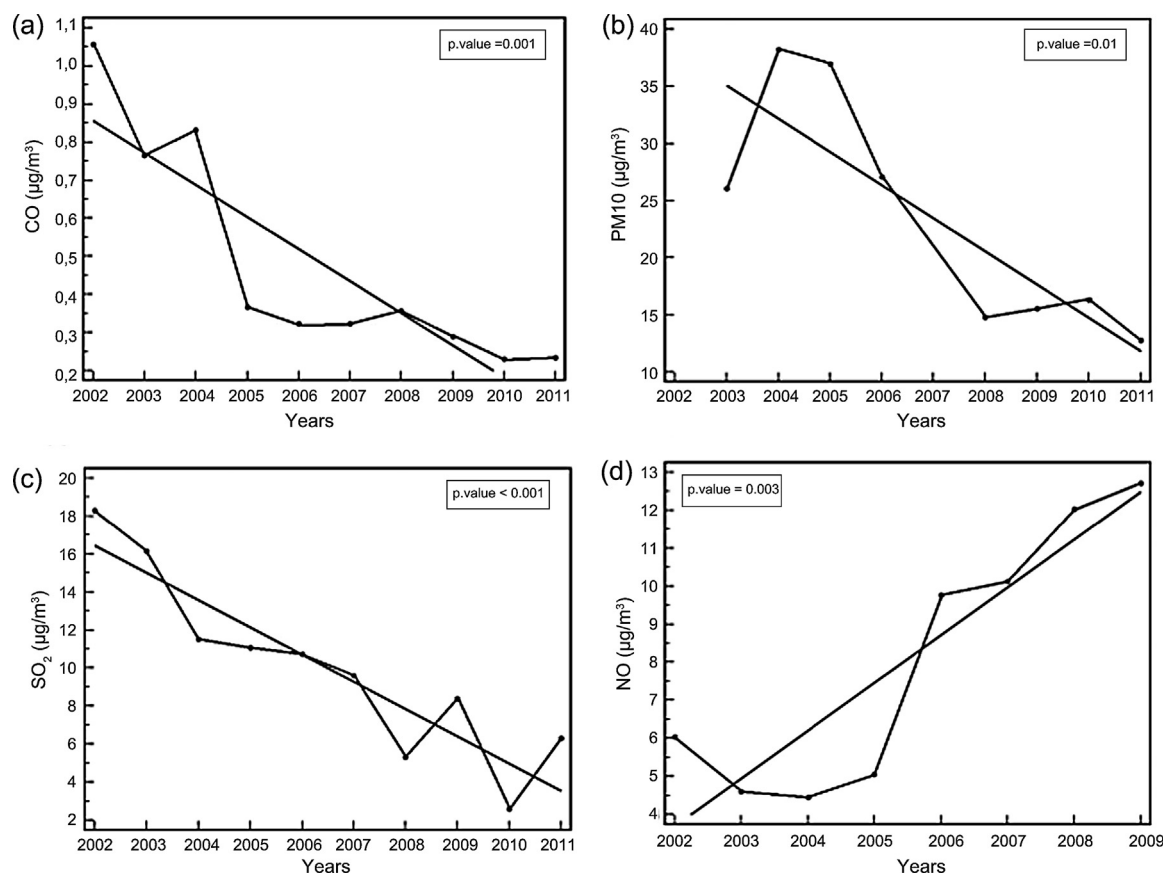


Fig. 3. Trends, during the years, of carbon monoxide (a), PM₁₀ (b), sulfur dioxide (c) and nitric oxide (d), expressed with *P*-value.

emergency calls during the warm months. This finding underlines and confirms the causal role of allergen exposure in inducing asthma exacerbations. In this regard, it is noteworthy to underline that we decided to consider only these four species as they are the most clinically relevant in Genoa, such as able of causing pollen allergy (and not simple sensitization) in more than 10% of our outpatient population. Conflicting results were reported by two studies of Ariano et al. that reported the relevance for cypress allergy in Bordighera [13,14]. Our experience in Genoa is different: patient with cypress allergy are less than 5% in our outpatient setting. The

possible explanation may be that there are substantial geographical, climatic, and environmental (mainly concerning the air pollution) differences between the two evaluated areas. Bordighera is a tourist coastal village, characterized by very few industry and intensive flower growing and olive growing, overlooking the Ligurian sea and about 150 km from Genoa [11]. Therefore, we limited our investigation to four pollen species alone, as clinically relevant.

About meteorological parameters, the unique significant variation over the study period was the wind speed that diminished. This finding might exert a pathogenic role as the wind constitutes a relevant factor able of affecting the presence of air pollutants. On the other hand, there were significant seasonal variations concerning the meteorological variables: typically there were the peaks of humidity and temperature

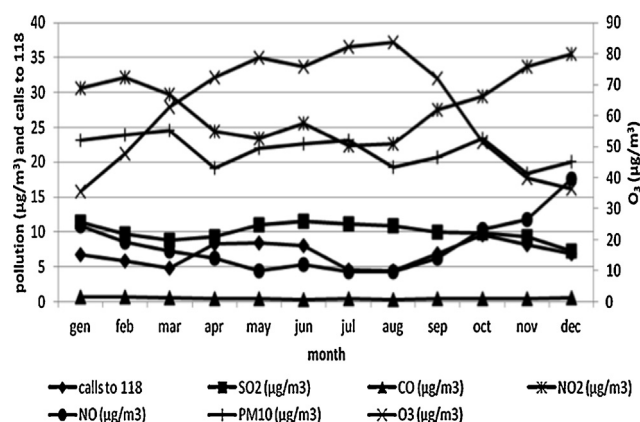


Fig. 4. Calls to 118 were plotted against air pollution data.

Table 1

Multivariate analyses of factors associated with number of calls for month.

Variable	<i>t</i>	<i>P</i> -value
Carbon monoxide	−5.01	0.0041
Nitric oxide	−5.06	0.0039
Ozone	−6.83	0.0010
Temperature	5.63	0.0024
Dew point	−6.67	0.0011
Pollen count for Urticaceae	3.56	0.0163
Model adjustment R ²		0.9252

during the summer associated with a nadir for the wind speed. From a clinical point of view, some seasonal variations correlated with emergency calls. Particularly, the wind speed was strongly and positively related with emergency calls. In other words, the more intense the wind, the more numerous were the emergency calls and the stronger was the relationship between rainfall quantity and emergency calls. These data might represent a practical application: when strong rains and wind blows intensively, it is reasonable to wait for several emergency calls for asthma exacerbations.

About air pollution data, most of the pollutants significantly diminished over time, except NO. This finding may partially depend on rigorous restrictions on pollutant emission. However, NO levels remained high, as NO is a marker for traffic congestion. Anyway, significant seasonal variations were evident during the year: all but ozone pollutants peaked during the cool seasons, mainly depending on home heating and congested traffic. The impact of pollution variations on emergency calls was particularly evident. In fact, SO₂, and NO were significantly and directly associated with emergency calls. This finding confirms and highlights the relevant role exerted by air pollution on respiratory symptoms in childhood, mainly concerning asthma exacerbations.

Finally, the regression model showed that there was a significant correlation among several environmental factors. Parietaria pollens were the most relevant as well as humidity, temperature, and air pollution. Combining relationship outcomes with regression model, it appears evident that several environmental factors contribute to asthma exacerbation occurrence.

Therefore, this study provided demonstration that asthma exacerbations may be significantly dependant on environment, even though probably there is globally not a single factor sufficient.

The topic concerning the causal factors of asthma exacerbations is still debated, but it is the object of several studies. In this regard, a recent review pointed out that although considerable progress has been made, much remains to be done [15]. Current evidence clearly provides suggestion that every effort has to be made to obtain optimal treatment to achieve adequate control of asthma. This goal means to significantly affect the risk of severe asthma exacerbations. In fact, poor control can lead to asthma exacerbation [16]. Other risk factors for asthma exacerbations are:

- viral infections;
- allergen exposure;
- season;
- environmental tobacco smoke exposure and;
- outdoor air pollution [17–19].

Considering all these aspects, the present study confirms the relevance of allergens, weather, and air pollution as factors associated with asthma exacerbations.

However, this study has the limitation that house dust mite levels were not measured as well as viral respiratory infections were not considered, and overall there were no data on single patients about sensitization and lung function. In addition,

another limitation was the analysis of the parameters evaluated yearly or monthly and not daily or weekly, because of the complexity of managing data. On the other hand, the relevant points of this study are a long-term observation, and the contemporary evaluation of pollens, meteorological parameters, and air pollution.

In conclusion, this 10-year survey demonstrates that:

- asthma exacerbations did not diminish over time;
- there were seasonal peaks (fall and spring);
- pollens (mainly Parietaria), wind speed and rainfall, SO₂, NO, and NO₂ were strongly associated with asthma exacerbations.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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