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Running title: Air pollution and asthma

Allergic and non-allergic asthma phenotypes and exposure to air pollution

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Abstract

Objective: Although harmful effects of air pollution on airway diseases are well-established, its effect on allergy still remains unclear. The aim of this study was to examine changes on asthma clinic and oxidant homeostasis due to air pollution between allergic asthma (AA) and non-allergic asthma (NA) phenotypes.

Methods: This prospective, case-control study included patients with well-controlled asthma under regular treatment ($n = 57$) and healthy individuals ($n = 51$). Of asthma patients, 22 had AA and 35 had NA phenotypes. Respiratory symptoms, pulmonary function tests, serum total antioxidant status (TAS) and total oxidant status (TOS), and thiol/disulfide levels were compared between the most (V_1) and least (V_2) air-polluted times.

Results: High air pollution exposure resulted to an increase in the frequency of respiratory symptoms and serum inflammation markers in both asthmatic and healthy individuals. Frequency of dyspnea and cough in AA and rhinitis in NA decreased from V_1 to V_2 . Hospitalization due to asthma exacerbation, systemic corticosteroid use, and eosinophil counts were more frequent in NA group than AA in V_1 . An increase of blood eosinophil counts was observed in AA group at the same visit. Mean TAS and TOS levels were higher in asthma group than control group, and the decline in TAS and TOS levels from V_1 to V_2 was seen only in NA. All thiols decreased and SH/total SH ratios significantly increased from V_1 to V_2 in all groups.

Conclusion: This study demonstrates that air pollution affects both asthma patients and healthy individuals. Through oxidant-antioxidant and thiol pathways, however, it adversely affects respiratory system of asthma patients, at a greater extent, than healthy individuals.

Keywords Allergy; Asthma; Air pollution; Environmental exposure; Non-allergic

Introduction

Asthma is a chronic airway inflammation characterized by reversible respiratory symptoms which may be triggered by several factors such as allergens or air pollution (1). Ambient air pollution is defined as the poor quality of outdoor air composed of high concentrations of pollutants (2). A growing number of evidence suggests that air pollution is one of the leading causes of worsening of existing asthma, with a contributory role to new-onset asthma (1, 3). Short-term exposure to air pollution has been associated with asthma exacerbations, increased use of healthcare resources, and asthma mortality (4, 5), whereas long-term exposure has been shown to increase the risk of incidental self-reported wheezing, and physician-diagnosed asthma in women without baseline symptoms (6).

Although harmful effects of air pollution on asthma have been well established, it is still unclear which asthma phenotype, *i.e.* allergic versus non-allergic, is more affected. Air pollution has been shown to increase allergen susceptibility by increasing the allergen transport, allergen-specific immunoglobulin (Ig) E levels, Th₂ cytokines, remodeling, inflammation, and respiratory symptoms (7, 8). In allergic asthma patients, simultaneous exposure to allergens and diesel exhaust particles had the ability to lead to a more severe inflammation (9). Fang et al. (10) showed that traffic-related air pollution exposure induced cough hypersensitivity and non-allergic eosinophilic inflammation of the airways in guinea pigs. The prevalence of non-allergic respiratory illness such as bronchitis, otitis media, tonsillitis, frequent colds, and cough was associated with sulfur dioxide (SO₂) and total suspended particulate matters (PM) in children (11). In a small-scale study, non-allergic patients with rhinitis were found to live in areas with a higher PM_{2.5} than allergic patients, and the authors concluded that small inhalant pollutants could contribute to non-allergic rhinitis symptoms (12).

One of the mechanisms of air pollution in asthma is based on oxidative stress, and there is a limited number of conclusive data regarding asthma and thiols that are one of the oxidant/antioxidant metabolomics of cells. Total thiol levels were found to be lower in newly diagnosed children with asthma compared to healthy individuals (13). In a study including adult patients, low plasma thiol levels were associated with the increased risk of asthma, but not with the forced expiratory volume in 1 s (FEV₁) (14). Plasma thiol levels were also decreased by forming reversible disulfide bonds under oxidative stress (13). On the other hand, the levels of thiol/disulfide were found to be comparable between patients with asthma and chronic obstructive airway disease, regardless of the smoking status (15).

To the best of our knowledge, there is no study regarding the relation of air pollution with the allergic status of asthma patients and antioxidant homeostasis. We, therefore, hypothesized that air pollution could affect asthma clinic differently according to the allergic status of the patient. In the present study, we aimed to assess the effects of air pollution on allergic and non-allergic phenotypes of asthma and to investigate the role of thiol/disulfide homeostasis, as well as oxidant/antioxidant metabolomics.

Patients and Methods

Study design and ethics approval

This single-center, observational, prospective, case-control study was conducted at Department of Pulmonary Diseases outpatient clinic of a tertiary care center between December 2017 and June 2018. Prior to study, all participants were informed about the nature of the study and a written informed consent was obtained. The study protocol was approved by the Kirikkale University Clinical Researches Ethics Committee (17.10.2017/18–01) and support of University Scientific Project (BAP no: 2018/026). The study was conducted in accordance with the principles of the Declaration of Helsinki.

At the inclusion visit (Vi), the participants were recruited from the outpatient pulmonary clinic by randomly selecting from accommodation addresses located in different areas of the central city. They were scanned for health symptoms and underwent physical examination, pulmonary function tests (PFT)s, and venous blood samples at visit 1 (V₁) and 2 (V₂).

City profile and air pollution

The study was conducted in Kirikkale as an urban city with 300 000 population located in the Central Anatolia with an altitude of 2,420 ft. The city's main and busy high way that is a gate to the eastern provinces, is surrounded with an oil refinery and a machinery chemical industry that are one

of the largest factories of the country, besides many small iron and steel factories, all in a close distance to the city center. One-third of the city population still use solid fuel to warm up, besides natural gas heating. The city center's air quality measurements were collected from website of meteorology for city province (www.havaizleme.gov.tr). January (V_1) was the time with the highest air pollution, and June (V_2) was the lowest polluted times of the previous year. The Mean SO_2 and PM_{10} levels ($340 \mu g/m^3$ and $220 \mu g/m^3$) of the city were found to be higher than standard ambient air quality limits due of the World Health Organization ($125 \mu g/m^3$ and $50 \mu g/m^3$). Air quality and air conditions of the study city (Kirikkale) from National Air Monitoring System are given in Table 1.

Inclusion and exclusion criteria

At V_i , a detailed medical history including chest x-ray and physical examination findings were obtained to identify the eligible cases. Inclusion criteria were as follows: being female or male, being a never-smoker, aged between 18 and 60 years, and living in the city center for at least one year. Exclusion criteria were as follows: being pregnant, having abnormal radiology results, being ever-smoker, receiving treatment with biological agents or systemic corticosteroids (CS)s, and having systemic diseases.

Asthma was diagnosed according to the Global Initiative for Asthma (GINA) guidelines (1). Asthma patients required to have well-controlled asthma at the V_i with no exacerbations for the previous four weeks, and to use step 4 GINA treatment as medium doses of inhaled corticosteroid (ICS) (equivalence of dry powder budesonide: 400 to 800 $\mu g/day$), and long acting β_2 agonist as maintenance and rescue medicine or with as needed short acting β_2 agonist at least for three months. The patients were divided into two groups as allergic (AA) and non-allergic (NA). The former one (AA) was accepted as the presence of respiratory symptoms that were clinically relevant with the positive allergens (pollens, $n = 6$; house dust mites, $n = 8$; blatella, $n = 3$; and mix, $n = 5$ for a total of 22 asthma patients) in allergy test. The latter group (NA) was composed of patients with non-allergic triggers and negative allergy tests. The control group was composed of 51 healthy volunteers with no history of lung diseases or rhinosinusitis, and negative skin prick test (SPT) results.

Data collection

In all visits, patient-reported symptoms (dyspnea, cough, sputum, rhinitis, and sinusitis), history of flu rate, antibiotic use, emergency department admission, hospitalization due to asthma exacerbation, ICS and systemic CS use were collected. Physical examination of airways and measurement of arterial oxygen saturation (SaO_2) by pulse oximetry were performed in all participants by a single pulmonary physician. A reading of $\leq 94\%$ indicated $SaO_2\%$ desaturation. ICS and systemic CS drug use and doses for asthma were also questioned. The patients fulfilled Asthma Control Test (ACT) at each visit which was previously validated in Turkish population (16). An ACT score of ≥ 20 indicated well-controlled asthma, while a score of < 20 indicated uncontrolled asthma.

Clinical tests

The SPTs were done with a battery of common inhalant allergens (ALK, Madrid-Spain) to all participants at V_i . The PFTs (Quark; Cosmed, Rome, Italy) were performed at each visit according to the American Thoracic Society (ATS) and European Respiratory Society (ERS) standards (17). A positive bronchodilator reversibility was considered with an increase in FEV_1 of $> 12\%$ and > 200 ml from baseline after 400 μg salbutamol. A posteroanterior chest x-ray was performed at each visit to all participants with the participant in the normal standing position with deep inspiration breath-hold.

Analyses of serum C-reactive protein (CRP; 0–5 mg/L) using a nephelometer, total IgE (0–100 IU/mL) using a commercial enzyme immunoassay (ECLIA; Roche Diagnostics GmbH, Mannheim, Germany), and eosinophil count (absolute count calculated as the percentage to white blood cell) were performed at the Biochemistry Laboratory of the hospital. The TOS and TAS levels and thiol/disulfide homeostasis were analyzed by Erel method with spectrophotometry (18).

Statistical analysis

The target population size was the number of asthmatic patients who were admitted to the asthma outpatient clinic of our hospital during one-year period. The sample size was calculated as 50 by using the *Raosoft* calculator software (www.raosoft.com/samplesize.html) with the target population size ($n = 2,500$), an acceptable margin of error as 10%, confidence level as 90%, and response distribution 30%. Statistical analysis was performed using the SPSS version 20 (IBM Corp., Armonk, NY, USA) program. Descriptive data were expressed in mean $\pm$ standard deviation (SD) or mean $\pm$ standard error (SE) for continuous variables and in number and frequency for categorical variables, where applicable. Asthma and control groups or allergic asthma (AA) and non-allergic asthma (NA) patients were compared using the chi-square test, while the Student's *t*-test or Mann-Whitney U test was used according to the data distribution. Binary data were compared using the paired samples *t*-test for normally distributed variables and using the Wilcoxon test for non-normally distributed variables. Correlation analysis was performed using the Pearson correlation test. A *p* values of <0.05 was considered statistically significant.

Results

Of the participants included in the study, 64.8% ($n = 36$) were female with an overall mean age of 43.49 ± 11.67 years. There was no significant difference in the age and sex between the patients with asthma and control group. The mean asthma duration was 11.15 ± 7.18 years. The most common comorbidities in asthma patients were obesity ($>24\text{kg/m}^2$) in 21.1% ($n = 12$), chronic rhinosinusitis in 52.6% ($n = 30$), and drug allergy in 5.3% ($n = 3$). Mean body mass index (BMI) of asthma patients were higher than control group. Obesity frequency was 34% of NA group, with none in AA group.

Symptoms and physical findings

The asthma group had significantly higher ratios of dyspnea, cough, sputum, sinusitis, abnormal lung sounds, and $\text{O}_2\%$ desaturation than the control group in both V_1 and V_2 , except for rhinitis which was similar in both groups (Table 2). None of the participants in the control group developed abnormal lung sounds and O_2 desaturation during the study. The frequency of all respiratory symptoms and physical findings were similar between the AA and NA patients in both time points, although the NA group had higher rates of dyspnea than AA in V_2 .

The frequency of dyspnea, rhinitis, abnormal lung sounds, and $\text{O}_2\%$ desaturation significantly decreased in V_2 than V_1 in the asthma group, while the frequency of cough significantly decreased in V_2 in the control group. Similarly, dyspnea and cough significantly decreased among the AA patients, while rhinitis significantly decreased among NA patients in V_2 . Abnormal lung sounds and $\text{O}_2\%$ desaturation were more frequent in V_1 than V_2 in both asthma groups.

Hospital admission, flu, and antibiotic rate

The frequency of having flu, antibiotic use, and hospitalization due to asthma exacerbation was significantly higher in the asthma group than the control group in V_1 (Table 3). Compared to V_1 ,

the rate of flu, antibiotic use, emergency admission, and hospitalization due to exacerbation was significantly lower in the asthma group, while the rate of flu and emergency admission was significantly lower in the control group in V_2 .

The rate of flu, antibiotic use, emergency admission, and hospitalization due to asthma decreased in V_2 than V_1 in both AA and NA groups. Although the rate of flu and antibiotic use was similar between the asthma groups, the decrease in the rate of antibiotic use, emergency admission, and hospitalization due to asthma exacerbation were higher in the NA group than the AA group in V_2 compared to V_1 .

Asthma control and CS use

The mean ACT scores were higher in V_2 than V_1 in all asthma patients (Table 4). The patients with well-controlled asthma had significantly ACT scores in V_2 , whereas the patients with uncontrolled asthma had higher ACT scores in V_1 in both asthma groups. The rate of the patients in whom the ICS dose was increased was higher in V_1 and the rate of those in whom the ICS dose was reduced was higher in V_2 with similar rates among the asthma groups. The rate of short-term systemic CS use was higher in V_1 than V_2 in all asthma patients, particularly in NA patients.

PFT, radiology, and laboratory results

The PFT results were higher in the asthma group than the control group in both time points, but similar between the AA and NA groups, except for FEV_1 (L), which was higher in AA than NA group in both time points (Table 5). All PFT values increased in V_2 than V_1 in both asthma groups with a more significant difference in favor of the NA group.

The rate of abnormal chest X-ray findings decreased in V_2 than V_1 in the overall and each asthma group. Compared to baseline (V_1), common changes on chest X-ray were bilateral pulmonary hyperinflation, bronchial wall thickening, and reticulonodular infiltrates. None of the control subjects had abnormal radiographic findings, while the NA asthma group had slightly higher rates of abnormal chest X-ray findings than the AA group in both time points.

The mean eosinophil counts ($/mm^3$) were higher in asthma patients than the control group, but were similar between the AA and NA asthma groups and significantly decreased in V_2 than V_1 only in the NA group. Serum CRP levels were significantly higher in the asthma group than the control group, as well as in the NA than AA, and significantly decreased in V_2 than V_1 in asthma and control groups. Serum total IgE levels were also higher in the asthma group than the control group, as well as in the AA than the NA group in both time points, although there was no significant change between V_1 and V_2 .

TAS, TOS, and thiol/disulfide levels

The mean TAS and TOS levels were higher in the asthma group than the control group in both time points, except for TAS which was similar in V_2 . Both levels decreased, as the air pollution decreased, except for TAS in the control group (Table 6). The decline in the TAS and TOS levels due to air pollution was seen only in the NA patients.

The mean native thiol and total thiol levels were lower in the asthma group than the control group, as well as in NA than AA groups in V_2 , and other thiol levels were similar between the patients and controls, as well as AA and NA. The native thiols, total thiols, disulfide and disulfide/total thiol (%) were higher in V_1 than V_2 , and native thiol/total thiol% levels were higher in V_2 than V_1 between the asthma and control groups and between the AA and NA groups.

According to the correlation analysis, there was a moderate to strong correlation between native/total thiol levels and TAS, TOS levels, and BMI, but not with the ACT scores, FEV₁ (L), and blood eosinophil counts (Table 7). The increased serum CRP and decreased thiol levels were the only parameters related to air pollution.

Discussion

In the present study, we examined the effects of air pollution on allergic and non-allergic phenotypes of asthma compared to healthy individuals. Our study results showed that dyspnea and cough in AA were the prominent symptoms and improved during the clean air time. In addition, as the air pollution increased, the NA group experienced more severe rhinitis symptoms, impaired PFT values with higher rates of antibiotic and systemic CS use, emergency admissions, hospitalization, serum CRP levels, blood eosinophils, and TAS and TOS levels. However, there was no significant difference in the thiol levels.

In this study, the increased air pollution seemed to affect NA patients with higher rates of exacerbation-related factors, while there were temporary and mild effects in AA patients. The effects of air pollution on asthma patients were also related to non-allergic eosinophilic airway inflammation with an infectious component on NA. We suggest that the reason for why AA patients were less affected from air pollution might be the lack or a lower amount of allergens in the environment in that period, since co-exposure to allergens and diesel exhaust particles had the ability to lead to a more severe inflammation in AA patients (9). The reason why NA patients were more affected from air pollution could be that air pollution caused mainly non-allergic airway inflammation, and it was a main pathology of NA. Likewise, in our NA group, serum CRP and blood eosinophil levels as indirect markers of non-allergic eosinophilic airway inflammation showed significant changes due to air pollution. In pediatric asthma patients, air pollution exposure was associated with a higher prevalence of non-allergic respiratory illness (11). To the best of our knowledge, there is no comprehensive study including both asthma phenotypes and, based on our results, we suggest that air pollution usually causes non-allergic symptoms and patients with NA phenotype seem to be more affected than those with AA.

In this study, exacerbations were higher in V₁ as the time with higher air pollution than V₂. Pollination timing in the study city usually starts in March and lasts until September (Table 1). However, there were no mite fauna counting rates in Kirikkale. The closest city's mite levels were the highest in August to October, and lowest in winter (19). As a result, this study's highest air pollution time as in winter was out of allergen seasons including house dust mite and pollens, suggesting that allergens did not have a role in asthma attacks, when the city had a high level of air pollution. Although the exacerbation rates were similar between AA and NA groups, patients with NA were more vulnerable to air pollution in terms of rhinitis symptoms, impaired PFT values with higher rates of antibiotic and systemic CS use, emergency admissions, hospitalization, serum CRP levels, blood eosinophils, and TAS and TOS levels. It is difficult to exclude the effect of cold weather than air pollution. However, cold weather frequently results in air pollution. When the weather is cold, air becomes heavier and sinks and, thus, exhaust is more visible. Although the industrial emissions remain mostly constant throughout the year, house warming tools such as wood and coal contribute to high pollutants during the cold winter months. The air condition reports of the city served as an explanation to air pollution, as the high pressure and low windy conditions could create stagnant air such as vehicle and factory exhaust concentrate over an area. In the study city, humidity and air pressure were higher at the time of high air pollution, whereas the wind speed and temperature were lower.

Air pollution was also reported to be associated with total IgE. There were associations of proximity to highway and percentage commercial building area with total IgE in childhood (20). In

our study, the total IgE levels were similar between high and low air polluted times, as higher in AR than NAR, as expected. The NA group had slightly elevated levels of serum total IgE than threshold with no significant difference in two time points which were performed with a six-month interval. We suggest that air pollution affects total IgE levels in the long-term and mostly in childhood, since total IgE is considered a blood marker for long exposure to PM_{2.5}. However, the influence of air pollution was found to be smaller than the influence of family history on the mean values of serum IgE (21).

In the current study, the main symptoms which were related to air pollution were cough in asthma and healthy individuals, and dyspnea and rhinitis in asthma patients accompanied by abnormal physical examination findings. These results are consistent with the literature, since air pollution at high concentrations may cause respiratory symptoms primarily in those with lung diseases, and even in healthy subjects (22). In previous studies, the most common respiratory tract symptoms after exposure to air pollution were rhinitis and cough (23). In another study including 504 women, Smith-Sivertsen et al. (24) found that wheezing was seen only in those exposed to air pollution, while cough was the main symptom regressed with decreased air pollution during an 18-month follow-up.

In a meta-analysis, almost all pollutants showed a significant association with moderate-to-severe asthma exacerbations, as well as the increased numbers of hospital admissions and emergency room visits (25). Similarly, in our study, the frequency of patients with uncontrolled ACT scores, the increase in ICS dose, and short-term oral CS use were higher during the ambient air-polluted time with no significant difference between the AA and NA patients. Supporting this result, a study of 32 adult asthma patients revealed that 10 mg/m³ increase in PM₁₀ exposure was associated with decreased ACT scores (26).

Furthermore, all PFT values increased, and radiographic abnormalities improved significantly, as the air pollution decreased in asthma patients in our study. Although PFTs vary depending on age, sex, ethnicity and patient cooperation, they are widely used to define the adverse events of air pollution. In a study of 1,963 residents living in an environment of industrial complexes, the FEV₁ and forced vital capacity (FVC) levels significantly declined, as SO₂, carbon monoxide, and ozone levels increased (27). The increase in the PFT values was greater in the NA group which might be related to more severe airway inflammation due to infection and air pollution. In addition, the number of patients with obesity was higher in NA group and obesity is likely to have a larger effect on NA by reducing lung volumes, and inducing non-Th₂ inflammation (28). A previous study showed that mean daily residential exposure to ECAT, a marker of diesel exhaust exposure, obesity and non-atopic status was significantly associated with poorer asthma control among asthmatic patients (29).

Previous studies have suggested that air pollution may contribute to exacerbations of asthma through oxidative injury to the airways (30, 31). In our study, we found higher TAS and TOS levels in the asthma group than healthy controls, which all decreased during the clean air time, indicating the well-established interaction between air pollution and asthma, which is an oxidative stress-related disease (8). In a 12-year follow-up of a cohort with 1,571 adults, oxidative stress biomarkers increased with PM₁₀ and ozone, and the authors showed that air pollution might not only induce asthma inflammation, but also it was a risk factor for asthma persistency (32). Furthermore, between high and low air pollution visits, there was a decline in elevated TAS and TOS levels in the NA group, whereas they remained unchanged in the AA group in our study. These results suggest that the oxidative stress effect of air pollution is more pronounced in NA patients and that there are some factors such as allergens inducing oxidative stress other than air pollution for patients with AA. Moreover, oxidative stress is one of the biological mechanisms proposed to partly explain the association between outdoor air pollution and asthma. The explanation of significant oxidant level and PFT change in NA patients in relation with air pollution is suggested to be directly by the

production of free reactive oxygen species (ROS) and diffusion from the airway surface or indirectly by inducing inflammation. Neutrophils attracted into the airways after exposure to certain pollutions produce ROS that induce epithelial cell inflammation, airway hyperreactivity, and lung injury. Ozone exposure causes ROS production and changes in the expression of claudins, the major components of tight junctions, thus leading to tight junction barrier permeability and airway hyperreactivity (33).

Thiols are less studied metabolomics in patients with airway diseases and ambient air pollution. Although plasma thiol levels decrease by forming reversible disulfide bonds under oxidative stress (14), we found that all thiols decreased and SH/total SH ratios increased significantly from high to low air pollution time among AA, NA, and healthy controls. The difference during the clean air time, as evidenced by low thiol-disulfide and high TAS/TOS levels in asthma group than healthy controls, is consistent with the previous results showing low thiol-disulfide levels and high oxidant markers in patients with obstructive lung diseases (15). In a study, total thiol levels were found to be lower in newly diagnosed children with asthma, compared to healthy individuals (13). The fact that plasma thiol levels decrease under oxidative stress suggests us that asthma patients might have altered thiol homeostasis under air pollution. On the contrary, the levels of thiol/disulfide were found to be similar among patients with asthma and chronic obstructive airway disease, regardless of the smoking status (15). In our study, we observed no significant difference in thiol levels between AA and NA patients, indicating that thiol/disulfide status as a biomarker of oxidant/antioxidant was affected from air pollution, irrespective of the nature of airway inflammation. Also, we found a significant correlation between thiol levels and TAS/TOS levels, irrespective of air pollution. On the other hand, the disassociation of thiols and asthma-related parameters (*i.e.* ACT scores, FEV₁ (L), and blood eosinophil count) in this study indicate that thiol-disulfide levels may not be directly related to airway inflammation. According to these results, we can speculate that thiol/disulfide and oxidant/antioxidant hemostasis can be disrupted in asthma patients, although further studies are warranted to elucidate its relationship with asthma control and air pollution.

The interaction between obesity and asthma is complex, and there are several potential mechanisms that mediate the recognized clinical phenotype. Air pollution may result to asthma development and exacerbations by increasing oxidative stress, and obesity by reducing physical activity, increasing fat intake, and oxidative stress, and so adipose tissue and airway inflammation. Obesity may result to asthma development and exacerbations by reducing lung volumes, and inducing non-Th2 inflammation. Corticosteroid use in asthma exacerbations, and protection from outside air pollution inducing to reduced physical activity may result to obesity (Figure 1). In this study, mean BMI of asthma patients were higher than the control group which supports the previous reports that obesity increases the risk for developing asthma, unresponsiveness to asthma treatments, and having severe asthma attacks (34). In this study, oxidant levels in asthma group were higher than healthy subjects, and there was a strong correlation of thiol oxidants with BMI, both in high and low air pollution times. The relationship that existed independently of air pollution might have supported a possible relation between BMI and oxidants in asthmatics. On the other hand, air pollution may result in obesity by reducing physical activity such as the probability of walking, and increases fat intake. Moreover, air pollution increases oxidative stress and, thus, adipose tissue and airway inflammation, which is closely linked to obesity and asthma. In a study, 1.54% increase in average PM_{2.5} concentrations in the past 12 months was reported to increase BMI by 0.27% (35). In the light of these findings, air pollution is associated with poor asthma control not only through oxidant pathways, but also by increasing BMI. However, we were unable to collect BMI changes during the study period. Also, the impact of air pollution was reported to be significant after almost one year, in contrast to six-month period of this study. Nonetheless, the higher oxidant levels in high than low air polluted times in asthma patients confirm that both air pollution and possibly obesity adversely affect oxidant dynamics in the body, which is a mechanism that plays a role in the development and progression of asthma, and is likely to be associated with poor asthma control.

The main strength of the present study is that it shows a significant improvement from high to low air-polluted times in the long-term, which is quite rare, as the majority of large-scale studies in the literature have addressed to the short-term effects of air pollution. To the best of our knowledge, this is the first study with a considerably number of parameters to investigate whether air pollution could affect the risk of asthma morbidity. The study population also included well-controlled asthma patients under regular ICS treatment, as well as healthy individuals, yielding sufficient information about respiratory symptoms, physical examination, and PFTs. More importantly, we were able to assess response to oxidative stress, not only by clinical and laboratory findings, but also by oxidant-antioxidant and thiol-disulfide homeostasis.

Nonetheless, there are some limitations to be noted. First, data regarding the level of exposure to indoor air pollution of the participants are lacking. However, participants were non-smokers and living in apartments with no consumption of biofuel. Second, the sample size of the study groups and subgroups is relatively small, despite the presence of a control group. Finally, the effect of the temperature change during the study visits was unable to be examined. Further large-scale, well-designed, prospective studies are needed to gain a better understanding of the effects of air pollution on AA and NA phenotypes and to shed light into the role of thiol/disulfide homeostasis and oxidant/antioxidant metabolomics in asthma patients.

Conclusions

In conclusion, our study results demonstrate that air pollution affects not only asthma patients, both also healthy individuals. The impairment in asthma control, PFTs, chest radiology, and eosinophil counts due to ambient air pollution is more prominent in asthma patients, particularly in NA phenotype. Through oxidant-antioxidant and thiol pathways, however, ambient air pollution adversely affects respiratory system of asthma patients, at a greater extent, than healthy individuals.

Conflict of interests

The authors declare they have no potential conflict of interest regarding the investigation, authorship, and/or publication of this article.

Contribution statement

A.B. designed this study; B.P. collected and processed data; A.B. interpreted the study results; B.P. wrote the study as thesis; A.B. and B.P. contributed to preparing the first draft of the manuscript; And A.F.K. contributed to preparing the revised manuscript. All authors read and approved the final manuscript.

Ethical Approval

This study was approved by the Kirikkale University, Faculty of Medicine, Ethics Committee with the Approval No. 17.10.2017/18–01.

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References

1. The Global Initiative for Asthma. GINA Report, Global strategy for asthma management and prevention (update 2021). www.ginasthma.org/local/uploads/files/GINA_Report_2021.pdf.
2. World Health Organization. Ambient (outdoor) air quality and health. Available at: [http://www.who.int/news-room/fact-sheets/detail/ambient-\(outdoor\)-air-quality-and-health](http://www.who.int/news-room/fact-sheets/detail/ambient-(outdoor)-air-quality-and-health). Last accessed: 18 Jan 2020.
3. Turkish National Society of Allergy and Clinical Immunology and Turkish Thoracic Society. Asthma Diagnosis and Treatment Guideline 2020 Update. December 2020. Ed. Celik G.
4. Orellano P, Quaranta N, Reynoso J, Balbi B, Vasquez, J. Effect of outdoor air pollution on asthma exacerbations in children and adults: Systematic review and multilevel meta-analysis. PLoS ONE 2017; 12: e0174050.
5. Liu Y, Pan J, Zhang H, Shi C, Li G, Peng Z, Ma J, Zhou Y, Zhang L. Short-Term Exposure to ambient air pollution and asthma mortality. Am J Respir Crit Care Med 2019; 200(1): 24-32.
6. Young MT, Sandler DP, DeRoo LA, Vedal S, Kaufman JD, London SJ. Ambient air pollution exposure and incident adult asthma in a nationwide cohort of U.S. Am J Respir Crit Care Med 2014; 190(8): 914-921.
7. Poynter ME, Persinger RL, Irvin CG, et al. Nitrogen dioxide enhances allergic airway inflammation and hyperresponsiveness in the mouse. Am J Physiol Lung Cell Mol Physiol 2006; 290: 144-52.
8. Neophytou AM, Hart JE, Cavallari JM, et al. Traffic-related exposures and biomarkers of systemic inflammation, endothelial activation and oxidative stress: a panel study in the US trucking industry. Environ Health 2013; 12: 105.
9. Guarnieri M, Balmes JR. Outdoor air pollution and asthma. Lancet 2014; 3; 383(9928): 1581-1592.
10. Fang Z, Huang C, Zhang JJ, Xie J, Dai S, Ge E, Xiang J, Yao H, Huang R, Bi X, Wang B, Zhong N, Lai K. Traffic-related air pollution induces non-allergic eosinophilic airway inflammation and cough hypersensitivity in guinea-pigs. Clin Exp Allergy 2019; 49(3): 366-377.
11. Heinrich J. Nonallergic respiratory morbidity improved along with a decline of traditional air pollution levels: a review. Eur Respir J 2003; 21: 64-69.
12. Mady LJ, Schwarzbach HL, Moore JA, Boudreau RM, Kaffenberger TM, Willson TJ, Lee SE. The association of air pollutants and allergic and nonallergic rhinitis in chronic rhinosinusitis. Int Forum Allergy Rhinol 2018; 8(3): 369-376.
13. Dilek F, Ozkaya E, Kocyigit A, Yazici M, Guler EM, Dundaroz MR. Plasma total thiol pool in children with asthma: Modulation during montelukast monotherapy. Inter J Immuno Pharmacol 2016; 29: 84-89.

14. Zinellu A, Fois AG, Sotgia S, Zinellu E, Bifulco F, Pintus G, Mangoni AA, Carru C, Pirina P. Plasma protein thiols: an early marker of oxidative stress in asthma and chronic obstructive pulmonary disease. Eur J Clin Invest 2016;46(2):181-8.
15. Babaoglu E, Kilic H, Hezer H, Dag O, Parlak O, Senturk A, et al. Comparison of thiol/disulphide homeostasis parameters in patients with COPD, asthma and ACOS. Eur Review Med Pharmacol Sciences. 2016; 20: 1537-1543.
16. Uysal, Mehmet Atilla et al. The validation of the Turkish version of Asthma Control Test. Q Life Research 2013; 22: 1773-9.
17. Graham BL, Steenbruggen I, Miller MR, et al. Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. Am J Respir Crit Care Med 2019; 200(8): e70-e88.
18. Eroglu O, Dindar Badem N, Baççioğlu A, Cömertpay E, Neşelioğlu S, Erel Ö. Significance of thiol/disulphide homeostasis and ischemia modified albumin levels in chronic obstructive pulmonary disease. Eur Res J 2019; 5(2): 250-257.
19. Aykut M, Erman Ö, Doğan S, Ayyıldız N. House dust mites of Bitlis and Muş provinces. Turkish Bulletin of Entomology; 2013, 3 (3): 169-177
20. Patel MM, Quinn JW, Jung KH, et al. Traffic density and stationary sources of air pollution associated with wheeze, asthma, and immunoglobulin E from birth to age 5 years among New York City children. Environ Res. 2011;111(8):1222-1229
21. Berciano FA, Crespo M, Bao CG, Alvarez FV. Serum levels of total IgE in non-allergic children. Influence of genetic and environmental factors. Allergy. 1987 May;42(4):276-83
22. Mannucci PM, et al. Effects on health of air pollution: a narrative review. Intern Emerg Med 2015; 10: 657–62.
23. Shusterman D. The effects of air pollutants and irritants on the upper airway. Proc Am Thorac Soc 2011; 8: 101–5.
24. Smith-Sivertsen T, Díaz E, Pope D, Lie RT, Díaz A, McCracken J, Bakke P, Arana B, Smith KR, Bruce N. Effect of reducing indoor air pollution on women's respiratory symptoms and lung function: the RESPIRE Randomized Trial, Guatemala. Am J Epidemiol 2009; 170(2): 211-20.
25. D'Amato G, et al. Urban air pollution and climate change as environmental risk factors of respiratory allergy: an update. J Investig Allergol Clin Immunol 2010; 20: 95–102.
26. Maestrelli P, Canova C, Scapellato ML, Visentin A, Tessari R, Bartolucci GB, Simonato L, Lotti M. Personal exposure to particulate matter is associated with worse health perception in adult asthma. J Investig Allergol Clin Immunol 2011; 21(2):120-8.

27. Hong E, Lee S, Kim GB, Kim TJ, Kim HW, Lee K, Son BS. Effects of environmental air pollution on pulmonary function level of residents in Korean industrial complexes. *Int J Environ Res Public Health* 2018; 15(5): 834.
28. Dixon AE, Peters U, Walsh R, et al. Physiological signature of late-onset nonallergic asthma of obesity. *ERJ Open Res.* 2020;6(3):00049-2020.
29. Epstein et al. *Ann Allergy Asthma Immunol.* 2012; 108(6): 423–428
30. Liu L, Poon R, Chen L, et al. Acute effects of air pollution on pulmonary function, airway inflammation, and oxidative stress in asthmatic children. *Environ Health Perspect.* 2009; 117:668–74.
31. Nel AE, Diaz-Sanchez D, Ng D, Hiura T, Saxon A. Enhancement of allergic inflammation by the interaction between diesel exhaust particles and the immune system. *J Allergy Clin Immunol.* 1998; 102:539–54.
32. Havet A, Li Z, Zerimech F, Sanchez M, Siroux V, Le Moual N, Brunekreef B, Künzli N, Jacquemin B, Varraso R, Matran R, Nadif R. Does the oxidative stress play a role in the associations between outdoor air pollution and persistent asthma in adults? Findings from the EGEA study. *Environ Health.* 2019; 18(1): 90.
33. Kim, B.-G.; Lee, P.-H.; Lee, S.-H.; Park, C.-S.; Jang, A.-S. Impact of ozone on claudins and tight junctions in the lungs. *Environ. Toxicol.* 2018, 33, 798–806.
34. S. Limaye, S. Salvi. Obesity and asthma: the role of environmental pollutants. *Immunology and allergy clinics of North America.* 2014, 34, 739-862.
35. Ramdhan DH, Rizky ZP, Atmajaya H. HbA1c, total IgE, and TNF α as blood markers for long exposure of traffic-related fine particles: a study on mechanics at vehicle test stations. *KnE Life Sciences* 2018;4(4): 428–433

Table 1. Air quality follow up of study city (Kırıkkale) from National Monitoring System for 2016 year (average values).

2016	Pollen/m ³			PM10 (µg/m ³)	SO ₂ (µg/m ³)	Temperatu re (°C)	Wind directio n (Degree)	Win d Spee d (m/s)	Relative Humidit y (%)	Air Pressur e (mbar)
	Betulace ae	Poacea e	Ambros ia							
January	0	0	0	27	18	2	143	2	72	930
February	17	0	0	30	13	9	175	2	65	932
March	12	0	0	26	19	10	169	2	57	926
April	177	71	0	25	11	17	189	2	46	927
May	26	111	0	17	6	19	174	2	59	925
June	0	137	0	18	3	26	201	3	48	926
July	0	29	0	28	2	28	220	3	39	925
August	0	1	17	26	2	29	223	3	45	926
Septemb er	0	0	4	22	5	22	211	2	46	929
October	0	0	0	33	17	16	209	2	51	931
Novembe r	0	0	0	26	48	8	200	2	55	933
Decembe r	0	0	0	41	56	1	173	2	70	933

Table 2. Comparison of symptoms, physical findings asthma and control groups and asthma subgroups at high (V₁) and low polluted (V₂) times.

% (n)	Asthma Group (n = 57)	Control Group (n = 51)	P	AA Group (n = 22)	NA Group (n = 35)	P
Dyspnea						
V ₁	78.9 (45)	3.9 (2)	< 0.001	68.2 (15)	85.7 (30)	0.10
V ₂	70.2 (40)	2 (1)	< 0.001	50 (11)	82.9 (29)	0.01
P	0.01	-		0.04	0.57	
Cough						
V ₁	86 (49)	43.1 (22)	< 0.001	95.5 (21)	80 (28)	0.11
V ₂	75.4 (43)	29.4 (15)	< 0.001	63.6 (14)	82.9 (29)	0.09
P	0.07	0.04		0.01	0.71	
Sputum						
V ₁	63.2 (36)	41.2 (21)	0.02	63.6 (14)	62.9 (22)	0.59
V ₂	57.9 (33)	33.3 (17)	0.01	59.1 (13)	57.1 (20)	0.55
P	0.62	0.21		0.71	0.53	
Rhinitis symptoms (Rhinorrhea, nasal obstruction and itching, sneeze)						
V ₁	61.4 (35)	49 (25)	0.13	63.6 (14)	60 (21)	0.50
V ₂	35.1 (20)	45.1 (23)	0.19	45.5 (10)	28.6 (10)	0.15
P	0.001	0.68		0.10	0.003	
Sinusitis (Headache or postnasal drainage)						
V ₁	70.2 (40)	51 (26)	0.03	59.1 (13)	77.1 (27)	0.19
V ₂	80.7 (46)	60 (30)	0.02	72.7 (16)	85.7 (30)	0.45
P	0.07	0.18		0.18	0.08	
Abnormal lung sounds						
V ₁	43.9 (25)	(-)	< 0.001	36.4 (8)	48.6 (17)	0.26
V ₂	14 (8)	(-)	0.01	9.1 (2)	17.1 (6)	0.33
P	< 0.001	-		-	-	
Subjects with SaO₂ <94 %						
V ₁	8.8 (5)	(-)	0.001	4.5 (1)	11.5 (4)	-
V ₂	1.8 (1)	(-)	0.03	0	2.9 (1)	-
P	-	-		-	-	

Data are given in percentage and number, unless otherwise stated. SaO₂: arterial oxygen saturation; AA: allergic asthma; NA: non-allergic asthma.

Table 3. Clinical parameters between high (Visit: V₁) and low polluted times (Visit 2: V₂).

% (n)	Asthma Group (n = 57)	Control Group (n = 51)	<i>P</i>	AA Group (n = 22)	NA Group (n = 35)	<i>P</i>
Flu rate						
V ₁	66.7 (38)	43.1 (22)	0.03	59.1 (13)	71.4 (25)	0.41
V ₂	26.3 (15)	35.3 (18)	0.24	27.3 (6)	25.7 (9)	0.89
P	< 0.001	< 0.001		< 0.001	< 0.001	
Antibiotic use						
V ₁	66.7 (38)	27.5 (14)	0.001	54.4 (12)	74.4 (26)	0.40
V ₂	29.8 (17)	29.4 (15)	0.98	31.8 (7)	28.6 (10)	0.51
P	< 0.001	0.61		0.03	< 0.001	
Emergency department visit						
V ₁	21.1 (12)	11.8 (6)	0.18	9 (2)	48.9 (12)	-
V ₂	7 (4)	5.9 (3)	-	0	11.4 (4)	-
P	-	-		-	-	
Hospitalization due to asthma						
V ₁	21.1 (12)	(-)	-	9 (2)	28.6 (10)	-
V ₂	1.8 (1)	(-)	-	0	2.9 (1)	-
P	-	-		-	-	

Data are given in percentage and number, unless otherwise stated. AA: allergic asthma; NA: non-allergic asthma.

Table 4. Asthma Control Test results and corticosteroid use in allergic asthma and non-allergic asthma group between high (V_1) and low polluted times (V_2).

% (n)	Visit 1 - V_1	Visit 2 - V_2	<i>P</i>
Overall ACT	17.68 ± 5.45	21.21 ± 3.77	< 0.001
AA	18.18 ± 4.57	21.95 ± 3.69	< 0.001
NA	17.37 ± 5.98	20.74 ± 3.79	< 0.001
<i>P</i>	0.56	0.24	
a. Well-controlled	45.6 (26)	80.7 (46)	< 0.001
AA	50 (11)	90.9 (20)	0.001
NA	42.9 (15)	74.3 (26)	0.003
<i>P</i>	0.39	0.11	
b. Uncontrolled	54.4 (31)	19.3 (11)	0.01
AA	50 (11)	9.1 (2)	
NA	57.1 (20)	25.7 (9)	
<i>P</i>	0.39	0.11	
Decrease in inhaled CS dose	14.3 (1)	62.5 (5)	-
AA	0	13.6 (3)	
NA	2.9 (1)	5.7 (2)	
Increase in inhaled CS dose	85.7 (6)	37.5 (3)	-
AA	9.1 (2)	4.5 (1)	
NA	11.4 (4)	5.7 (2)	
Short-term systemic CS use	19.3 (11)	3.5 (2)	-
AA	13.6 (3)	0	
NA	22.9 (8)	5.7 (2)	

Data are given in percentage and number or mean ± standard deviation, unless otherwise stated. ACT: Asthma Control Test; AA: allergic asthma; NA: non-allergic asthma; CS: corticosteroid.

Table 5. Pulmonary function test, radiology, and laboratory results between patients and healthy individuals.

% (n)	Asthma Group (n = 57)	Control Group (n = 51)	<i>P</i>	AA Group (n = 22)	NA Group (n = 35)	<i>P</i>
Pulmonary function tests						
FEV ₁ (%)						
V ₁	77.05 ± 17.72	93.97 ± 15.91	< 0.001	82.70 ± 17.46	73.50 ± 17.19	0.07
V ₂	84.64 ± 14.76	96.56 ± 9.98	< 0.001	88.81 ± 10.97	82.02 ± 16.31	0.09
<i>P</i>	0.001	0.18		0.07	0.001	
FEV ₁ (L)						
V ₁	2.22 ± 22.95	3.4 ± 0.76	< 0.001	2.61 ± 0.99	1.97 ± 0.63	0.01
V ₂	2.48 ± 0.76	5.19 ± 0.35	< 0.001	2.94 ± 1.15	2.19 ± 0.66	0.01
<i>P</i>	0.001	0.32		0.03	0.005	
FEV ₁ / FVC (%)						
V ₁	84.71 ± 10.02	88.54 ± 5.93	< 0.001	85.80 ± 9.70	84.02 ± 10.29	0.51
V ₂	87.58 ± 7.15	89.93 ± 5.51	0.24	87.86 ± 7.75	87.40 ± 6.86	0.81
<i>P</i>	0.005	0.10		0.19	0.13	
FEF ₂₅₋₇₅ %						
V ₁	67.43 ± 22.95	90.84 ± 18.11	< 0.001	73.77 ± 24.23	63.45 ± 21.51	0.05
V ₂	76.56 ± 21.42	93.60 ± 17.02	< 0.001	81.90 ± 20.85	73.20 ± 21.38	0.05
<i>P</i>	<0.001	0.10		0.04	< 0.001	
Change on chest X-ray						
V ₁	42.1 (24)	(-)	< 0.005	27.3 (6)	51.4 (18)	-
V ₂	31.6 (18)	(-)	< 0.001	18.2 (4)	40 (14)	-
<i>P</i>	0.03			-	-	
Blood eosinophile count (/mm ³)						

V ₁	0.35 ± 0.05	0.15 ± 0.01	0.001	0.31 ± 0.09	0.37 ± 0.03	0.15
V ₂	0.28 ± 0.03	0.21 ± 0.05	0.01	0.27 ± 0.05	0.28 ± 0.06	0.53
P	0.11	0.17		0.72	0.02	
Serum CRP level						
V ₁	4.82 ± 0.75	2.13 ± 0.62	< 0.001	2.71 ± 0.57	6.14 ± 1.12	0.03
V ₂	3.61 ± 0.42	1.44 ± 0.41	< 0.001	2.45 ± 0.44	4.33 ± 0.61	0.01
P	0.04	0.01		0.38	0.06	
Serum total IgE level (kU/L)						
V ₁	257.24 ± 5.92	63.89 ± 1.22	0.001	373.42 ± 123.82	184.20 ± 55.24	0.01
V ₂	254.78 ± 5.65	64.66 ± 1.24	< 0.001	366.84 ± 119.44	184.33 ± 51.66	0.02
P	0.20	0.31		0.77	0.63	

Data are given in percentage and number or mean ± standard deviation, unless otherwise stated.

AA: allergic asthma; NA: non-allergic asthma; FEV₁: forced expiratory volume in one second; FVC: forced vital capacity; FEF: forced expiratory flow; CRP: C-reactive protein; IgE: immunoglobulin E.

Table 6. Total oxidant and anti-oxidant status and thiol/disulfide levels.

	Overall Asthma Group (n = 57)	Control Group (n = 51)	P	AA Group (n = 22)	NA Group (n = 35)	P
TAS						
V ₁	1.77 ± 0.05	1.54 ± 0.04	< 0.001	1.71 ± 0.07	1.81 ± 0.06	0.25
V ₂	1.55 ± 0.24	1.50 ± 0.02	0.06	2.20 ± 0.64	1.58 ± 0.03	0.83
P	0.01	0.81		0.46	0.002	
TOS						
V ₁	21.35 ± 2.23	12.13 ± 1.01	<0.001	19.12 ± 3.59	22.75 ± 2.86	0.34
V ₂	11.76 ± 5.45	5.09 ± 3.83	0.03	19.16 ± 13.86	6.96 ± 0.80	0.04
P	< 0.001	< 0.001		0.99	< 0.001	
Native thiol (-SH) (μmol/L)						
V ₁	295.46 ± 16.23	280.41 ± 9.25	0.96	323.58 ± 26.42	277.78 ± 20.30	0.11
V ₂	249.63 ± 5.80	273.54 ± 5.28	0.01	264.69 ± 8.48	240.16 ± 7.46	0.04
P	0.04	0.73		0.03	0.08	
Total thiol (total -SH) (μmol/L)						
V ₁	346.89 ± 18.05	325.64 ± 9.79	0.89	374.78 ± 28.71	329.35 ± 23.03	0.11
V ₂	272.92 ± 7.20	302.21 ± 5.60	0.002	275.41 ± 14.47	271.35 ± 7.60	0.27
P	0.001	0.05		0.003	0.02	
Disulphid (-SS) (μmol/L)						
V ₁	25.71 ± 1.39	22.67 ± 1.11	0.25	25.60 ± 1.93	25.78 ± 1.94	0.81
V ₂	14.67 ± 1.10	14.33 ± 0.64	0.54	13.21 ± 1.07	15.59 ± 1.66	0.32
P	< 0.001	< 0.001		< 0.001	< 0.001	
-SS/total -SH (%)						
V ₁	8.01 ± 0.52	7.12 ± 0.34	0.26	7.22 ± 0.53	8.51 ± 0.77	0.19
V ₂	4.75 ± 0.20	4.75 ± 0.21	0.27	4.83 ± 0.36	5.76 ± 0.55	0.28
P	< 0.001	< 0.001		0.01	0.01	
-SH/total -SH (%)						
V ₁	83.96 ± 7.87	85.61 ± 0.69	0.31	85.55 ± 1.07	82.96 ± 1.54	0.19
V ₂	87.98 ± 1.48	90.49 ± 0.41	0.26	87.18 ± 3.47	88.47 ± 1.10	0.67
P	< 0.001	< 0.001		0.01	0.01	

Data are given in percentage and number or mean ± standard deviation, unless otherwise stated.

AA: allergic asthma; NA: non-allergic asthma; TAS: total antioxidant status; TOS: total oxidant status.

Table 7. Pearson *rho* correlation coefficients between thiol-dhisulphid parameters and total oxidant/anti-oxidant status in all participants at Visit 2.

Parameters	Native thiol (SH)		Total thiol (total SH)	
	V ₁	V ₂	V ₁	V ₂
TAS	0.515 ^b strong	0.235 ^a moderate	0.591 ^b strong	-0.464 ^b strong
TOS	0.233 ^a moderate	-0.204 ^a moderate	0.269 ^b strong	-0.534 ^b strong
ACT	0.180 weak	0.179 weak	0.170 weak	0.029 weak
FEV ₁	0.122 weak	-0.086 weak	0.110 weak	-0.065 weak
Age	-0.255 ^b strong	-0.308 ^b strong	-0.235 ^b strong	-0.247 ^b strong
BMI	-0.247 ^b strong	-0.356 ^b strong	-0.204 ^b strong	-0.255 ^b strong
CRP	-0.167 weak	-0.301 ^b strong	-0.149 weak	-0.277 ^b strong
Eosinophil counts (/mm ³)	-0.154 weak	-0.118 weak	-0.140 weak	-0.117 weak

^aCorrelation (two-tailed) is significant at .05 level, and ^bat the 0.01 level.

(A value of *r* greater than 0.4 is considered a strong correlation, between 0.2 and 0.4 is a moderate correlation, and less than 0.2 is considered a weak or no correlation). TAS: total antioxidant status; TOS: total oxidant status; ACT: Asthma Control Test; FEV₁: forced expiratory volume in one second; BMI: body mass index; CRP: C-reactive protein.



Figure 1. Relationship between asthma, obesity and air pollution.