The differential impact of air pollutants on acute urticaria and chronic urticaria: a time series analysis

Xiuping Han (hanxiuping66@126.com)
Shengjing Hospital of China Medical University https://orcid.org/0000-0002-0774-8148
Jiawei Li
Shengjing Hospital of China Medical University
Guoqiang Song
Shenyang No.7 People's Hospital
Zhenzhen Mu
Shengjing Hospital of China Medical University
Xiaoou Lan
Shenyang No.7 People's Hospital
Fan Yang
Shengjing Hospital of China Medical University
Lin Li
Shengjing Hospital of China Medical University

Research Article

Keywords: Air pollutants, Acute urticarial, Chronic urticarial, Time series analysis

Posted Date: March 21st, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1414136/v1

Abstract

Several studies have revealed links between short-term exposure to air pollution and the exacerbation of certain skin conditions. The present study sought to expand on these findings by exploring the potential relationship between exposure to air pollutants including particulate matter, sulfur dioxide, and ozone, and the incidence of acute and chronic urticaria in Shenyang, China, from 2016–2018. Exposure-response relationships between daily mean concentrations of these airborne pollutants and visits to outpatient dermatological clinics for acute urticaria and chronic urticaria were evaluated via a time series analysis approach using a generalized additive model. This analysis revealed that a 10 μg/m^3 increase in daily mean O_3_8h concentrations was associated with a 0.36% (95% CI, 0.31–0.41%), 0.35% (95% CI, 0.30–0.40%), and 0.34% (95% CI, 0.29–0.39%) increase in the number of outpatients for acute urticaria on the (lag0), lagging day 1 (lag1), and lagging day 2 (lag2), respectively. The increment in O^3 levels remained statistically significant associated with outpatient for acute urticaria on cumulative lagging days. The increase in particulate matter levels had a similar cumulative effect on patients with chronic urticaria. In summary, these results indicated that short-term O_3, $PM_{2.5}$, and PM_{10} exposure can increase the risk of acute urticaria and chronic urticaria.

Introduction

Air pollution has been identified as a major cause of adverse health outcomes throughout the world. In an effort to increase public awareness of these risks and to improve health outcomes, regional environmental monitoring departments perform real-time monitoring of airborne pollutants including ozone (monitored over an 8-hour period; O_3_8h), particulate matter ($PM_{2.5}$, PM_{10}), nitric oxide (NO), sulfur dioxide (SO_2), and CO (carbon monoxide), reporting their levels to the public. These airborne pollutants can affect a range of respiratory, circulatory, endocrine, and nervous system disorders in exposed individuals, potentially increasing the incidence or mortality rates associated with particular diseases (Cho et al. 2014, Hansel et al. 2016, Kloog et al. 2014, Levinsson et al. 2014, Miah et al. 2012, Yunquan et al. 2016). The skin is the largest organ in the human body, and serves as a barrier to the entry of potential pathogens and other environmental threats such as air pollution.

The dermatological effects of chronic exposure to air pollutants have been increasingly well studied in recent years (Kathuria &Silverberg 2016, Krutmann et al. 2014, Mancebo &Wang 2015), with some researchers having linked changes in air quality and climatic conditions to skin aging and the incidence of eczema and atopic dermatitis (Ahn 2014, Kathuria &Silverberg 2016, Kramer et al. 2009, Li et al. 2015, Liu et al. 2018, Schafer et al. 1996, Suarez-Varela et al. 2013, Vierkotter et al. 2010). Urticaria is the most commonly reported skin condition, occurring in both chronic and acute forms. Affected patients present with regions of localized edema that are the result of increased vasopermeability within the skin and associated mucosa, resulting in red, circumscribed, red, itchy rashes that generally disappear within 24 h. These rashes can also recur on different parts of the body, and in severe cases can be accompanied by systemic symptoms such as fever, abdominal pain, vomiting, diarrhea, and dyspnea. Between 15% and 25% of people are estimated to experience urticaria at some point in their life (Zuberbier 2003).

Despite being a relatively common condition, the etiology of urticaria is complex and in many cases the precise cause is unknown. Few studies to date in China or abroad have examined whether urticaria may be aggravated or induced by changes in climate conditions or air pollution levels, leading us to explore that question in the present study.

Materials And Methods

Patients

All outpatient visit records for patients seeking care for acute urticaria and chronic urticaria records were obtained from the computerized database of Shengjing Hospital of China Medical University, Liaoning, China, during the time period from January 1, 2016, to December 30, 2018. these cases included both new patients and relapsed patients. All included patients were individuals that had lived in Shenyang for a minimum of 3 years and who were diagnosed as per the criteria of the International Classification of Diseases, 10th Revision.

Air Pollutants and Meteorological Data

Daily $PM_{2.5}$, PM_{10}, SO_2, and O_3 from January 1, 2016 to December 31, 2018 were obtained from the Shenyang Environmental Monitoring Center. Levels of these pollutants were monitored by eleven state-controlled environmental air quality automatic monitoring stations in Shenyang. Daily meteorological data including average temperature and relative humidity over this same study period were obtained from the Shenyang Meteorological Bureau.

Statistical Analysis

A time series is a set of dynamic sequences arranged in chronological order. Daily outpatient visits for acute and chronic urticaria were thus treated as time series for the present analysis, and a time series analysis was conducted to establish a predictive model based on the available data and to thereby predict future trends in that data series (Zeghnoun et al. 2001).

In the overall population, the number of daily outpatient visits for urticaria is regarded as a low-probability event, and as such its distribution was approximated to the Poisson distribution. A time series analysis was therefore conducted using a generalized additive model (GAM) to estimate associations between air pollutant levels and the number of daily outpatient visits for acute or chronic urticaria. This GAM approach was used to control for potential confounding variables such as long-term trends, weekends, and holidays, and was adjusted for variable meteorological parameters including daily mean temperature and relative humidity. The lag effect is a regression analysis that takes into account the health indicators from a given day (day 0) and air pollution levels on previous days in order to study the effects of pollution on previous days on future health ends. We separately examined O_3, $PM_{2.5}$, PM_{10}, and SO_2, using same day data (lag0) and data with a 1–6 day lag (lag1-lag6). We also tested the cumulative lag effects, denoted as lag01 - lag06 (the previous 1–6 days' moving average concentrations).

Odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated to assess the magnitude of the measured effect at an $\alpha = 0.05$. A P-value < 0.05 was regarded as the significance threshold for these analyses. Correlations between air pollutant levels and meteorological variables were assessed through Spearman rank correlation analyses. SPSS 20.0 and R 3.1.1, with the MGCV package (http://www.r-project.org), were used to conduct all analyses.

Results

Descriptive statistics

Demographic characteristics associated with outpatient visits during the study period are summarized in Table 1 by patient age and gender. Between January 1, 2016, and December 31, 2018, 35,305 total outpatient visits were recorded, including 20,884 visits associated with cases of acute urticaria and 14,421 visits associated with cases of chronic urticarial. The seasonal distribution patterns of these visits are shown in Fig. 1. Daily outpatient visit counts for acute urticaria were higher than for chronic urticaria, and counts for both were highest in the summer and lowest in the winter.

Mean concentrations of different air pollutants and meteorological factors in Shenyang over the 3-year (1,096-day) study period are summarized in Table 2. The daily mean concentrations of $PM_{2.5}$, PM_{10}, SO_2, and O_3 _8h over this period were 48.59 μg/m^3, 82.47 μg/m^3, 36.06 μg/m^3, and 94.40μg/m^3, respectively. The climate in Shenyang consists of four distinct seasons, each of which exhibited different levels of the analyzed air pollutants. Levels of $PM_{2.5}$, PM_{10}, and SO_2 were highest during colder seasons [Autumn (Sept-Nov) and Winter (Dec-Feb)] and lower in the warmer months [Spring (Mar-May) and Summer (Jun-Aug)], whereas O_3 exhibited the opposite trend. In all cases, these daily air pollutant concentrations remained below ambient air quality threshold values. The mean daily temperature and relative humidity in the study region were 8.14°C and 62.07%, respectively.

Analysis of correlations between airborne pollutant levels and meteorological factors

Next, Spearman's rank correlation analyses were used to gauge the relationships between airborne pollutant levels and meteorological factors during the study period (Table 3). Levels of $PM_{2.5}$, PM_{10}, and SO_2 were highly positively correlated with one another, with this correlation being strongest for $PM_{2.5}$ and PM_{10} (r = 0.901). In contrast, O_3 levels were negatively correlated with those of $PM_{2.5}$ and SO_2. Temperature and relative humidity were significantly negatively correlated with levels of $PM_{2.5}$, PM_{10}, and SO_2, with the strongest correlations for these meteorological variables being between temperature and SO_2 (r = -0.713), and between relative humidity and PM_{10} (r = − 0.201).

Time series analysis of associations between air pollutant levels and urticaria

The relationships between pollutant levels and outpatient visits for acute urticaria and chronic urticaria were next analyzed (Table 4). These analyses revealed that SO_2 levels were unrelated to outpatient visits for either form of urticaria. In contrast, daily mean O_3_8h concentrations were significantly positively associated with outpatient visits for both forms of urticaria. A 10 μg/m^3 increase in the daily mean O_3_8h concentration was associated with a 0.36% (95% CI, 0.31–0.41%), 0.35% (95% CI,0.30–0.40%), and 0.34% (95% CI, 0.29–0.39%) increase in the number of outpatients seeking care for acute urticaria on the same day (lag0), lagging day 1 (lag1), and lagging day 2(lag2), respectively. O_3 also exhibited a similar but weaker effect for patients seeking care for chronic urticaria, with respective lag0 and lag1 values of 0.28% (95% CI,0.22–0.33%) and 0.29% (95% CI, 0.23–0.34%). A 10 μg/m^3 increase in the daily mean O_3_8h concentration on cumulative lagging days was associated with an elevated excess risk of acute urticaria of 0.47% (95% CI,0.41–0.52%) and 0.46% (95% CI,0.40–0.51%). We additionally observed an estimated 1.23% (95% CI, 1.02–1.44%), 1.24% (95% CI, 1.03–1.45%), and 1.25% (95% CI, 1.04–1.46%) increase in the risk of seeking care for chronic urticaria following a 10 μg/m^3 increase in $PM_{2.5}$ concentrations on days 4, 5, and 6 after exposure, respectively (lag04, lag05, lag06). Similarly, PM_{10} exposure exhibited a significant but weaker effect on chronic urticaria on cumulative lagging days or 0.37% (95% CI, 0.21–0.52%) and 0.41% (95% CI, 0.25–0.57%).

Discussion

In the present report, we performed a time series analysis of the effects of air pollution on the incidence of acute urticaria and chronic urticaria in Shenyang, China, from 2016–2018. Over this time frame, the daily mean concentrations of $PM_{2.5}$, PM_{10}, and SO_2 were almost twice as high as levels outlined in WHO guidelines, indicating that additional focus on the air pollution situation in Shenyang is necessary. We found that acute urticaria and chronic urticaria-related outpatient visits exhibited a seasonal pattern, occurring more frequently in the summer relative to the winter, consistent with trends in O_3 levels, although the opposite trend was observed for $PM_{2.5}$, PM_{10}, and SO_2 concentrations.

Shenyang is a heavy industrial city in northeastern China that experiences cold winters. Air pollution sources in this region include vehicle exhaust, industrial emissions, construction site dust emission, and coal combustion. Overall, daily air pollutant concentrations were relatively stable with peak levels in the winter, likely because coal is the primary source of energy and heat during the colder months, and because lower temperatures are not conducive to air pollutant dispersal. In contrast, O_3 levels were higher during the summer, consistent with the intense solar radiation and higher temperatures during this season, which can increase photochemical reaction intensity and O_3 concentrations near the surface.

Rates of dermatosis are rising, and epidemiological studies suggest that short-term exposure to ambient air pollution can cause adverse effects on skin health (Ahn 2014, Kathuria &Silverberg 2016, Kramer et al. 2009, Li et al. 2015, Schafer et al. 1996, Suarez-Varela et al. 2013, Vierkotter et al. 2010). Herein, we found that exposure to three air pollutants ($PM_{2.5}$, PM_{10}, and O_3) significantly increased the risk of urticaria outpatient visits, with evidence of cumulative lag effects following such exposure. The impact of O_3 on acute urticaria was more significant than that on chronic urticaria, with the cumulative lag effect of O_3 exposure only remaining significant on 1 and 2 days post-exposure for acute urticaria outpatient visits. We observed no relationship between SO_2 exposure and urticaria outpatient visits. Our findings were similar to those of a study conducted in Shanghai, which found that elevated ground O_3 levels were associated with increased numbers of emergency medical visits for urticaria, eczema, contact dermatitis, and infectious skin diseases, whereas there was no significant relationship between these conditions and exposure to PM_{10}, NO_2 and SO_2 (Xu et al.). In another study conducted in Korea, Lee et al. determined that increases in daily mean O_3 concentrations were linked to increased hospitalization rates for patients with asthma and atopic dermatitis (Lee et al. 2010).

Many environmental pollutants have been shown to cause direct oxidative damage, including NO_2 and O_3, which can catalyze reactive oxygen species (ROS) production that can disrupt cutaneous redox homeostasis and cause skin cell damage (Cotovio et al. 2001, Ghio et al. 2012). Exposure to a range of O_3 concentrations can alter levels of IgE specific for plant pollen in humans (Beck et al. 2013, Garcia-Gallardo et al. 2013, Rogerieux et al. 2007). The sensitivity of the human body to such O_3 exposure is both dose- and allergen-specific. Exposure to high levels of O_3 on a daily basis may thus drive the incidence of urticaria, asthma, and other allergic diseases. In summary, exposure to lower levels of O_3 during warmer seasons may reduce the incidence of urticaria, although further research is necessary to confirm this hypothesis.

Particulate matter is primarily derived from vehicle and industrial exhaust sources, and is primarily composed of aromatic hydrocarbons and other organic compounds that can activate diverse biological processes and drive ROS production (Furue et al. 2014). ROS-mediated oxidative stress is thought to be linked to the pathogenesis of urticaria and other dermatological conditions (Kalkan et al. 2014). Previous studies have suggested that exposure to $PM_{2.5}$ and PM_{10} is linked to higher rates of acne vulgaris and atopic dermatitis in adults and children (Kathuria &Silverberg 2016, Kramer et al. 2009, Yunquan et al. 2016). Interestingly, we found that $PM_{2.5}$ exposure was associated with stronger cumulative effects on chronic urticaria incidence relative to PM_{10} exposure. Certain epidemiological analyses of PM exposure have linked the exposure to these pollutants to skin inflammatory response processes associated with dermatitis, acne, and psoriasis (Liu et al. 2018, Song et al. 2011, Tsuji et al. 2011, Yang et al. 2014).

While the mechanistic basis for our findings remains to be clarified, they are consistent with the result of a few prior studies. For example, Ono et al. found that polycyclic aromatic hydrocarbons (PHAs) in air organic pollutants can attach to the skin and cause damage thereto. The activation of aryl hydrocarbon receptor (AhR) signaling in keratinocytes can drive the production of inflammatory cytokines including IL-

6 and IL-8 (Ono et al. 2013). Researchers have also shown that metals on the surface of PM can additionally drive ROS production, lipid oxidation, and skin cell apoptosis in a dose-dependent manner (Lefebvre et al. 2016).

There are several limitations to this analysis. For one, this was a large-scale population-based study without any analyses of patients at the individual level, potentially introducing aggregation bias. In addition, Shengjing Hospital is a general hospital with a higher number of children as patients relative to other hospitals in this region. This may have increased the overall proportion of children in the study population. Differences in climate characteristics, air pollution composition, and personal behaviors may also limit the applicability of these findings to similar analyses conducted in other regions.

Conclusions

Herein, we identified a positive association between mean daily air pollutant concentrations and urticaria in Shenyang, China. Exposure to O_3 was identified as a risk factor associated with urticaria, with this relationship being strongest for cases of acute urticaria. $PM_{2.5}$ and PM_{10} levels were additionally associated with an increase in outpatient visits for chronic urticaria. Together, these analyses confirm the potential for air pollution-induced skin damage, and suggest that reducing such pollutant exposure during periods of extensive pollution may be a viable approach to reducing the incidence of urticaria.

Declarations

CONFLICTS OF INTEREST

The authors report no conflicts of interest in the publication of this work.

Ethics approval and consent

The paper is exempt from ethical committee approval, since all the information about people used in this study was obtained from computer databases.

Funding

This project was funded through a grant from the Provincial Key RESEARCH and Development Program of Liaoning, China (number2017225026).

Authors’ contributions

Xiuping Han designed the research. Jiawei Li and Guoqiang Song performed the analysis of this research. Zhenzhen Mu and Xiaoou Lan processed the data. Fan Yang and Lin Li wrote and revised the manuscript.

Availability of data and materials

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Conflicts of interest

The authors report no conflicts of interest in the publication of this work.

References

1. Ahn K (2014): The role of air pollutants in atopic dermatitis. J Allergy Clin Immunol 134, 993-9; discussion 1000
2. Beck I, Jochner S, Gilles S, McIntyre M, Buters JT, Schmidt-Weber C, Behrendt H, Ring J, Menzel A, Traidl-Hoffmann C (2013): High environmental ozone levels lead to enhanced allergenicity of birch pollen. PLoS One 8, e80147
3. Cho J, Choi YJ, Suh M, Sohn J, Kim H, Cho SK, Ha KH, Kim C, Shin DC (2014): Air pollution as a risk factor for depressive episode in patients with cardiovascular disease, diabetes mellitus, or asthma. J Affect Disord 157, 45-51
4. Cotovio J, Onno L, Justine P, Lamure S, Catroux P (2001): Generation of oxidative stress in human cutaneous models following in vitro ozone exposure. Toxicol In Vitro 15, 357-62
5. Furue M, Takahara M, Nakahara T, Uchi H (2014): Role of AhR/ARNT system in skin homeostasis. Arch Dermatol Res 306, 769-79
6. Garcia-Gallardo MV, Algorta J, Longo N, Espinel S, Aragones A, Lombardero M, Bernaola G, Jauregui I, Aranzabal A, Albizu MV, Gastaminza G (2013): Evaluation of the effect of pollution and fungal disease on Pinus radiata pollen allergenicity. Int Arch Allergy Immunol 160, 241-50
7. Ghio AJ, Carraway MS, Madden MC (2012): Composition of air pollution particles and oxidative stress in cells, tissues, and living systems. J Toxicol Environ Health B Crit Rev 15, 1-21
8. Hansel NN, McCormack MC, Kim V (2016): The Effects of Air Pollution and Temperature on COPD. COPD 13, 372-9
9. Kalkan G, Seckin HY, Duygu F, Akbas A, Ozyurt H, Sahin M (2014): Oxidative stress status in patients with acute urticaria. Cutan Ocul Toxicol 33, 109-14
10. Kathuria P, Silverberg JI (2016): Association of pollution and climate with atopic eczema in US children. Pediatr Allergy Immunol 27, 478-85
11. Kloog, Itai, Nordio, Francesco, Zanobetti, Antonella, Coull, Brent, A., Koutrakis (2014): Short Term Effects of Particle Exposure on Hospital Admissions in the Mid-Atlantic States: A Population Estimate. PLoS ONE 9, 1-7
12. Kramer U, Sugiri D, Ranft U, Krutmann J, von Berg A, Berdel D, Behrendt H, Kuhlbusch T, Hochadel M, Wichmann HE, Heinrich J, Giniplus, groups LIs (2009): Eczema, respiratory allergies, and traffic-related air pollution in birth cohorts from small-town areas. J Dermatol Sci 56, 99-105

13. Krutmann J, Liu W, Li L, Pan X, Crawford M, Sore G, Seite S (2014): Pollution and skin: from epidemiological and mechanistic studies to clinical implications. J Dermatol Sci 76, 163-8
14. Lee JT, Cho YS, Son JY (2010): Relationship between ambient ozone concentrations and daily hospital admissions for childhood asthma/atopic dermatitis in two cities of Korea during 2004-2005. Int J Environ Health Res 20, 1-11
15. Lefebvre M-A, Pham D-M, Boussouira B, Qiu H, Ye C, Long X, Chen R, Gu W, Laurent A, Nguyen Q-L (2016): Consequences of urban pollution upon skin status. A controlled study in Shanghai area. International Journal of Cosmetic Science 38, 217-223
16. Levinsson A, Olin AC, Modig L, Dahgam S, Björck L, Rosengren A, Nyberg F (2014): Interaction Effects of Long-Term Air Pollution Exposure and Variants in the GSTP1, GSTT1 and GSTCD Genes on Risk of Acute Myocardial Infarction and Hypertension: A Case-Control Study. Plos One 9, e99043
17. Li M, Vierkötter A, Schikowski T, Hüls A, Ding A, Matsui MS, Deng B, Ma C, Ren A, Zhang J, Tan J, Yang Y, Jin L, Krutmann J, Li Z, Wang S (2015): Epidemiological evidence that indoor air pollution from cooking with solid fuels accelerates skin aging in Chinese women. J Dermatol Sci 79, 148-54
18. Liu W, Pan X, Vierkotter A, Guo Q, Wang X, Wang Q, Seite S, Moyal D, Schikowski T, Krutmann J (2018): A Time-Series Study of the Effect of Air Pollution on Outpatient Visits for Acne Vulgaris in Beijing. Skin Pharmacol Physiol 31, 107-113
19. Mancebo SE, Wang SQ (2015): Recognizing the impact of ambient air pollution on skin health. J Eur Acad Dermatol Venereol 29, 2326-32
20. Miah AH, Sutradhar SR, Ahmed S, Bhattacharjee M, Alam MK, Bari MA, Tariquzzaman M, Mondol GD, Khan NA, Bari MS, Sarker CB (2012): Seasonal variation in types of stroke and its common risk factors. Mymensingh Med J 21, 13-20
21. Ono Y, Torii K, Fritsche E, Shintani Y, Nishida E, Nakamura M, Shirakata Y, Haarmann-Stemmann T, Abel J, Krutmann J, Morita A (2013): Role of the aryl hydrocarbon receptor in tobacco smoke extract-induced matrix metalloproteinase-1 expression. Exp Dermatol 22, 349-53
22. Rogerieux F, Godfrin D, Sénéchal H, Motta AC, Marlière M, Peltre G, Lacroix G (2007): Modifications of Phleum pratense Grass Pollen Allergens following Artificial Exposure to Gaseous Air Pollutants (O3, NO2, SO2). International Archives of Allergy and Immunology
23. Schafer T, Vieluf D, Behrendt H, Kramer U, Ring J (1996): Atopic eczema and other manifestations of atopy: results of a study in East and West Germany. Allergy 51, 532-9
24. Song S, Lee K, Lee YM, Lee JH, Lee SI, Yu SD, Paek D (2011): Acute health effects of urban fine and ultrafine particles on children with atopic dermatitis. Environ Res 111, 394-9
25. Suarez-Varela MM, Gallardo-Juan A, Garcia-Marcos L, Gimeno-Clemente N, Silvarrey-Varela AL, Miner-Canflanca I, Batlles-Garrido J, Blanco-Quiros A, Busquets-Monge RM, Dominguez-Aurrecoechea B, Arnedo-Pena A, Gonzalez-Diaz C, Aguinaga-Ontoso I, Martinez-Gimeno A, Llopis-Gonzalez A (2013): The impact of atmospheric pollutants on the prevalence of atopic eczema in 6-7-year-old schoolchildren in Spain; ISAAC Phase III. Iran J Allergy Asthma Immunol 12, 220-7

26. Tsuji G, Takahara M, Uchi H, Takeuchi S, Mitoma C, Moroi Y, Furue M (2011): An environmental contaminant, benzo(a)pyrene, induces oxidative stress-mediated interleukin-8 production in human keratinocytes via the aryl hydrocarbon receptor signaling pathway. J Dermatol Sci 62, 42-9
27. Vierkotter A, Schikowski T, Ranft U, Sugiri D, Matsui M, Kramer U, Krutmann J (2010): Airborne particle exposure and extrinsic skin aging. J Invest Dermatol 130, 2719-26
28. Xu J, Kan H, Song W, Xu F, Wu M, Zhao J, Li F, Xu X, Yan S Ambient ozone pollution as a risk factor for skin disorders.
29. Yang YS, Lim HK, Hong KK, Shin MK, Lee JW, Lee SW, Kim NI (2014): Cigarette Smoke-Induced Interleukin-1 Alpha May Be Involved in the Pathogenesis of Adult Acne. Annals of Dermatology 26
30. Yunquan, Zhang, Cunlu, Li, Renjie, Feng, Yaohui, Zhu, Kai, Wu (2016): The Short-Term Effect of Ambient Temperature on Mortality in Wuhan, China: A Time-Series Study Using a Distributed Lag Non-Linear Model. International journal of environmental research and public health
31. Zeghnoun A, Czernichow P, Beaudeau P, Hautemaniere A, Froment L, Le Tertre A, Quenel P (2001): Short-term effects of air pollution on mortality in the cities of Rouen and Le Havre, France, 1990-1995. Arch Environ Health 56, 327-35
32. Zuberbier T (2003): Urticaria. Allergy 58, 1224-34

Tables

Tables 1 to 4 are available in the Supplementary Files section

Figures

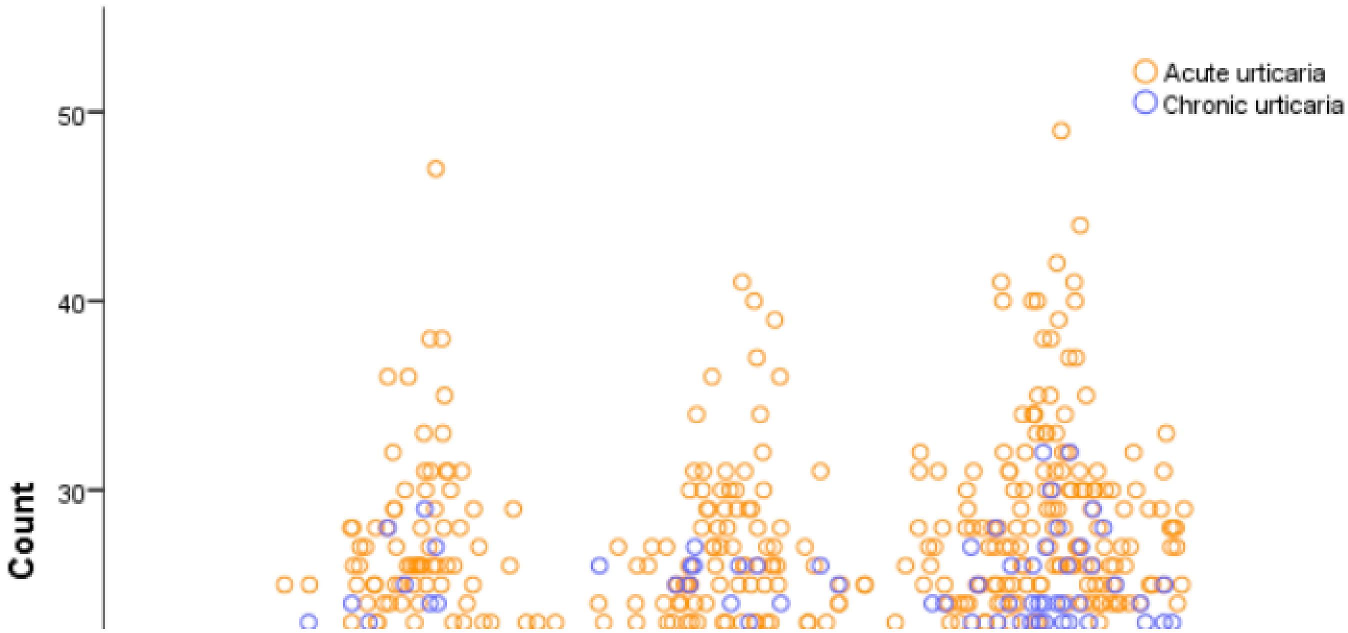

Figure 1

Legend not included with this version

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.pdf
- Table2.pdf
- Table3.pdf
- Table4.pdf