



Comparison of Heavy Metal and Trace Element Levels in Inferior Nasal Concha of People Living in Rural and Urban Regions

Original Investigation

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Abstract

Objective: Heavy metal exposure has recently become a problem due to the increasing environmental pollution as urbanization expands. This prospective cross-sectional study was conducted to compare levels of heavy metals in the nasal concha of the patients living in urban and rural who underwent partial inferior concha resection.

Methods: Sixty-seven patients were divided into two groups: 38 rural patients and 29 urban patients. Partial inferior turbinate resection was performed in these patients with turbinate hypertrophy, and these tissues were examined for heavy metal levels. Lead (Pb), cadmium (Cd), zinc (Zn), copper (Cu), and manganese (Mn) levels were measured in inferior nasal concha by inductively coupled plasma- optical emission spectrometry.

Results: The levels of Cu (0.24 ± 0.048 vs. 0.06 ± 0.019 µg/g) and Zn (3.29 ± 0.69 vs. 0.44 ± 0.14 µg/g) of the rural patients were significantly higher compared to urban patients ($p < 0.001$). There was no significant difference in the Cd level between groups. Pb (0.024 ± 0.009 vs. 0.008 ± 0.0002 µg/g) and Mn (0.273 ± 0.01 vs. 0.174 ± 0.05 µg/g) levels of urban patients were significantly higher than rural patients ($p < 0.001$). Significance was considered at $p < 0.05$.

Conclusion: Heavy metals accumulate in the nasal concha at different rates in rural and urban areas. In pathologies with unclear pathophysiology and potential for heavy metal accumulation, such as air pollution, it may be helpful to indicate the presence of heavy metals in the nasal turbinate's and measure their amounts for diagnostic purposes.

Keywords: Air pollution, heavy metals, nasal mucosa, spectrophotometry, turbinates, inductively coupled plasma-optical emission spectroscopy

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Cite this article as: Öner F, Kurt N, Üçüncü H.

Comparison of heavy metal and trace element levels in inferior nasal concha of people living in rural and urban regions. Turk Arch Otorhinolaryngol. 2024;62(4):161-167

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Received Date: 24.09.2024

Accepted Date: 30.12.2024

Epub: 27.03.2025

Publication Date: 28.03.2025

DOI: 10.4274/tao.2024.2024-9-4

Introduction

Environmental pollution is a severe problem in industrialized and metropolitan cities, threatening public health (1,2). Each year, 4,2 million people die earlier from heart and respiratory diseases triggered by air pollutants (World

Health Organization-2008) (3). Pollutants that cause the problem and disturb the natural balance include organic substances, industrial wastes, petroleum derivatives, synthetic agricultural fertilizers, detergents, radiation, pesticides, inorganic salts, synthetic organic chemicals, and waste heat. All of these, directly and indirectly,



cause air pollution. Heavy metals are found in almost all of them, mostly in industrial wastes and pesticides.

Elements are present in the human body in pure form or compounded form. Although some elements are essential for human physiology, some of them are toxic, such as lead (Pb), mercury (Hg), and cadmium (Cd). Generally, intoxication occurs through accumulation as a result of prolonged exposure. Heavy metals cause the dysfunction of enzyme systems by binding oxygen, nitrogen, and sulfhydryl groups to proteins, revealing their toxic effects (4). For instance, metalloproteins in the organism contain large amounts of thiol ligands. These ligands have a high affinity for binding elements such as Cd, copper (Cu), and zinc (Zn). Factors such as heavy metal particle size, duration of heavy metal exposure, and age of individuals determine the degree of heavy metal intoxication (5,6).

The nose is the main entrance gate of polluted air to the body (7). Many heavy metals can enter the body through inhaled air. Detection of heavy metal presence in nasal concha tissues may mean that heavy metals in ambient air cause accumulation in nasal mucosal and submucosal tissues by inhalation. Due to the mucociliary activity of the nasal mucous membranes, inhalation and absorption of pollutants can weaken local immune responses in the airways. This study compared heavy metal levels in nasal concha tissues of patients from urban and rural areas.

Methods

Patients and Study Design

Sixty-seven patients (24 females, 43 males) were administered to the otorhinolaryngology outpatient clinic with nasal obstruction. Most of the selected patients had compensatory nasal concha hypertrophy accompanying nasal septum deviation, and partial resection of the inferior concha was scheduled. The patients were divided into rural (n=29) and urban (n=38) groups according to their living areas of at least 15 years after verbal and written informed consent. The prospective cross-sectional study was initiated after obtaining approval Atatürk University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (decision no: B.30.2.ATA.0.01.00/56, date: 28.11.2014) and was conducted in accordance with the Declaration of Helsinki.

Living in a village was taken as a rural area, and living in the city center was taken as an urban area. As those living in the city center and villages of the districts, we would set our patient population target. Among the patients diagnosed with nasal concha hypertrophy and experiencing nasal congestion due to this condition, those scheduled for partial concha resection surgery and agreed to participate in the study were included after verbal and written consent was

obtained. Before the surgery, each patient was evaluated with an anterior nasal endoscopic examination and paranasal sinus computed tomography.

The study was conducted in a tertiary university hospital's otorhinolaryngology-head and neck surgery and biochemistry clinics. Patients with diseases that could affect the presence of heavy metals in the nasal concha were excluded. The exclusion criteria were as follows:

- Smokers/ex-smokers,
- Patients under the age of 18 and over 55,
- Patients with nasal polyps or polyposis,
- Patients with allergic rhinitis,
- Patients with nasal involvement of systemic diseases,
- Patients using medication continuously,
- Patients who had undergone any previous surgical intervention (septoplasty, concha radiofrequency ablation, partial resection) in the nasal cavity,
- Patients working in the industry sector,
- Patients working in the city and commuting to the village or vice versa, were excluded from work.

Surgical Procedure

Partial resection of the inferior concha with septoplasty was performed in 58 patients, and only partial resection of the inferior concha was performed in nine patients. All patients were operated on under general anesthesia by the same surgeon, and a standard procedure was performed. Local anesthetic was not applied to the concha tissue before resection. The inferior nasal conchas were first medialized with the Cottle elevator, and then the lower-medial parts were cut using concha scissors. We washed the resected concha pieces with distilled water, removed the mucus, and attached particles mechanically. The tissues taken were transferred to the sterile tubes without contact anywhere and stored at -80 °C (Figure 1).

Measurements of Metal Concentrations

Nasal concha tissues were let to thaw at room temperature. First, conchal bones, if any, were dissected and removed. From the deboned mucosa and submucosal parenchyma tissue, fragments weighing 0.5 g were transferred into a tube and added with 3 mL of acid mixture (HClO₄+HNO₃, 5:1). The samples were incubated at 95 °C for one hour (8). Solid conchal tissues were hydrolyzed with acid and became liquid at the end of three hours. Solutions were diluted with distilled water to measure heavy metals (Cu, Zn, Cd, Pb, and Mn) spectrophotometrically using the Inductively coupled plasma-optical emission spectrometry (Perkin-

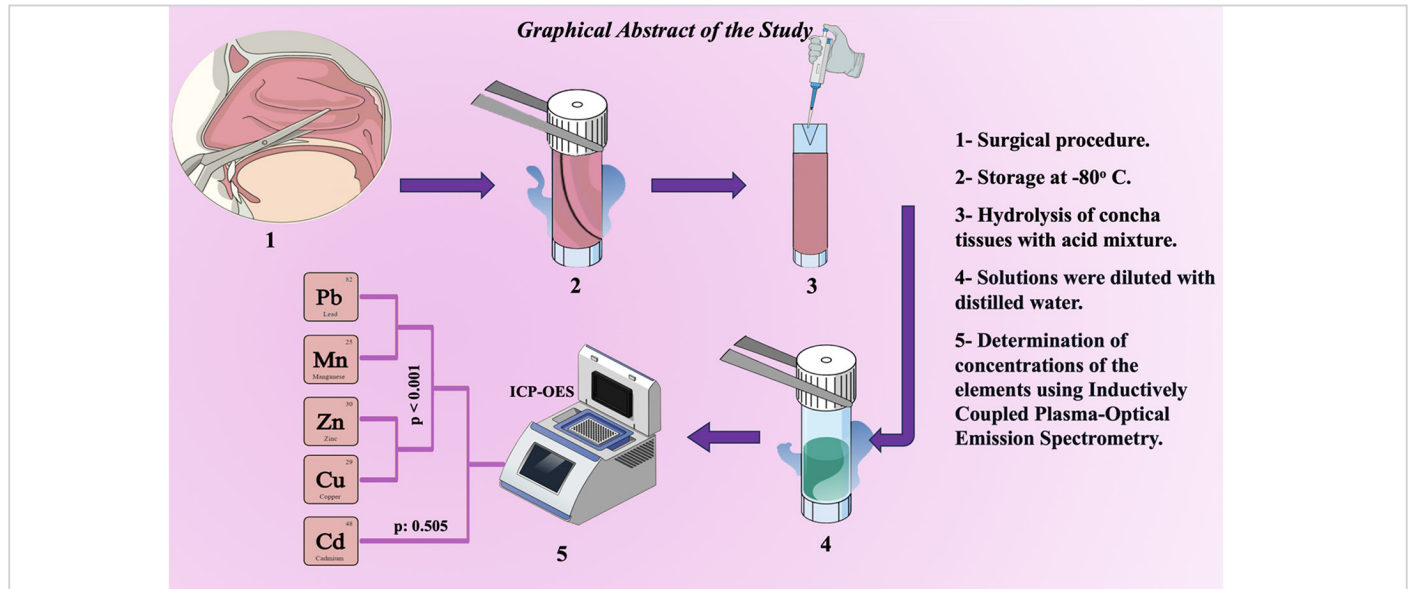


Figure 1. The graphical abstract provides a step-by-step overview of the study, including the surgical procedure, the storage of tissues at -80 degrees, the hydrolysis of tissues with an acid mixture, the schematic representation of the spectrophotometric analysis process with ICP-OES ICP-OES: Inductively coupled plasma-optical emission spectroscopy, Pb: Lead, Cd: Cadmium, Zn: Zinc, Cu: Copper, Mn: Manganese

Elmer, Optima 4300 DV, inductively coupled plasma/optical emission spectroscopy, Waltham, MA). Since the conchal tissues we received were 0.5 g, all results were multiplied by two, and we calculated the heavy metal level in 1 g nasal concha tissue in micrograms (µg).

Statistical Analysis

After confirmation of the normal distribution of the data in the Kolmogorov-Smirnov test, an Independent Samples t-test was used in the comparisons of patient age and Cd, Pb, Cu, Mn, and Zn levels by the patient group (SPSS, version 22, Chicago, IL). Data are presented as a number, percentage, mean, and standard deviation. For the comparisons of individuals according to gender, the Independent Samples t-test was used for continuous variables and the chi-square test for categoric variables. Independent Samples t-test was used to analyze age by gender, Cd, Pb, Cu, Mn, and

Zn in both groups. The Pearson correlation test was used to examine the relationship between continuous variables. Significance was considered at p<0.05.

Results

There was no difference in the mean age (p=0.991; Table 1) and gender distribution between the groups (p=0.991; Table 1). The age distribution of the rural group was 18-52 (29.3±9.4), and the urban group was 18-55 (29.1±9.8). There were 17 males (58.6%) and 12 females (41.4%) in the urban group, 26 males (68.4%) and 12 females (31.2%) in the rural group.

Cu (0.24±0.048 µg/g) and Zn (3.29±0.69 µg/g) levels of rural patients were significantly higher than Cu (0.06±0.019 µg/g) and Zn (0.44±0.14 µg/g) levels of urban patients (p<0.001, p<0.001, Table 2). The Cd (0.034±0.014 µg/g) level of the rural patients was similar to the Cd level (0.032±0.013 µg/g)

Table 1. Comparison of gender and age distribution between groups

	Female, n=24	Male, n=43	p-value	
Age, mean±SD	28.67±9.323	29.37±9.759	0.774*	
Urban	12 (31.6%)	26 (68.4%)	0.407**	
Rural	12(41.4%)	17(58.6%)		
ELements (µg/g)	Cd, Mean±SD	0.03±0.014	0.032±0.013	0.792*
	Pb, Mean±SD	0.016±0.009	0.014±0.010	0.555*
	Cu, Mean±SD	0.157±0.101	0.164±0.090	0.790*
	Mn, Mean±SD	0.101±0.078	0.114±0.085	0.541*
	Zn, Mean±SD	1.840±1.518	2.172±1.515	0.394*

*Independent Samples t-test, **Chi-square test, SD: Standard deviation, Pb: Lead, Cd: Cadmium, Zn: Zinc, Cu: Copper, Mn: Manganese

of the urban patients ($p=0.505$, Table 2). Pb (0.024 ± 0.009 $\mu\text{g/g}$) and Mn (0.273 ± 0.01 $\mu\text{g/g}$) levels of the urban group were significantly higher than Pb (0.008 ± 0.0002 $\mu\text{g/g}$) and Mn (0.174 ± 0.05 $\mu\text{g/g}$) levels of the rural group ($p<0.001$, $p<0.001$, Table 2, Figure 2).

Heavy metal levels in rural and urban patients were independent of age and gender. When the two groups were compared, we detected that the difference between the heavy metal levels occurred due to the residence difference (Table 3).

Discussion

Air pollution is considered a general health hazard. Technologies that facilitate our current world release various pollutants into the atmosphere. Technological products increase the concentration of air pollutants in the atmosphere, containing heavy metals harmful to plants, animals, and humans. When specific risk factors such as genetics, diet, and lifestyle come together with environmental factors, the negative impact of air pollution on human health is

likely to increase (9). For the individual risk assessment of environmental hazards, showing the physical presence of the substances in the body or the negative functional results is essential. The nasal cavity is a usual gateway to the human body for air pollutants and is a well-known target site for toxicity caused by air pollutants (7). This study reported comparison of levels of heavy metals in nasal conchal tissues in patients living in rural and urban areas.

Few studies examine the relationship between nasal mucous membranes, air pollution, and heavy metals. Şenvar (10) compared serum Cu and Zn levels in the patients with atrophic rhinitis and healthy people and reported higher serum Cu levels and lower serum Zn levels in the patient group. A study compared (11) trace elements on the nasal lower concha and septum. There was an age-related increase in Pb levels in both tissues and decreased Zn levels. In another study (12), exposure to urban pollution in adults in Mexico has increased the proliferation rate in nasal cells, a risk factor for developing neoplasia.

Table 2. Element levels in inferior nasal concha tissues by rural and urban residence

Elements	Rural*	Urban*	t	p-value**
Cd	0.034±0.014	0.032±0.013	0.67	0.505
Pb	0.008±0.0002	0.024±0.009	-8.55	<0.001
Cu	0.24±0.048	0.06±0.019	19.25	<0.001
Mn	0.174±0.05	0.273±0.01	17.45	<0,001
Zn	3.29±0.69	0.44±0.14	24.19	<0.001

*Mean±standard deviation, **Independent Samples t-test, Cd: Cadmium, Cu: Copper, Mn: Manganese, Zn: Zinc, Pb: Lead

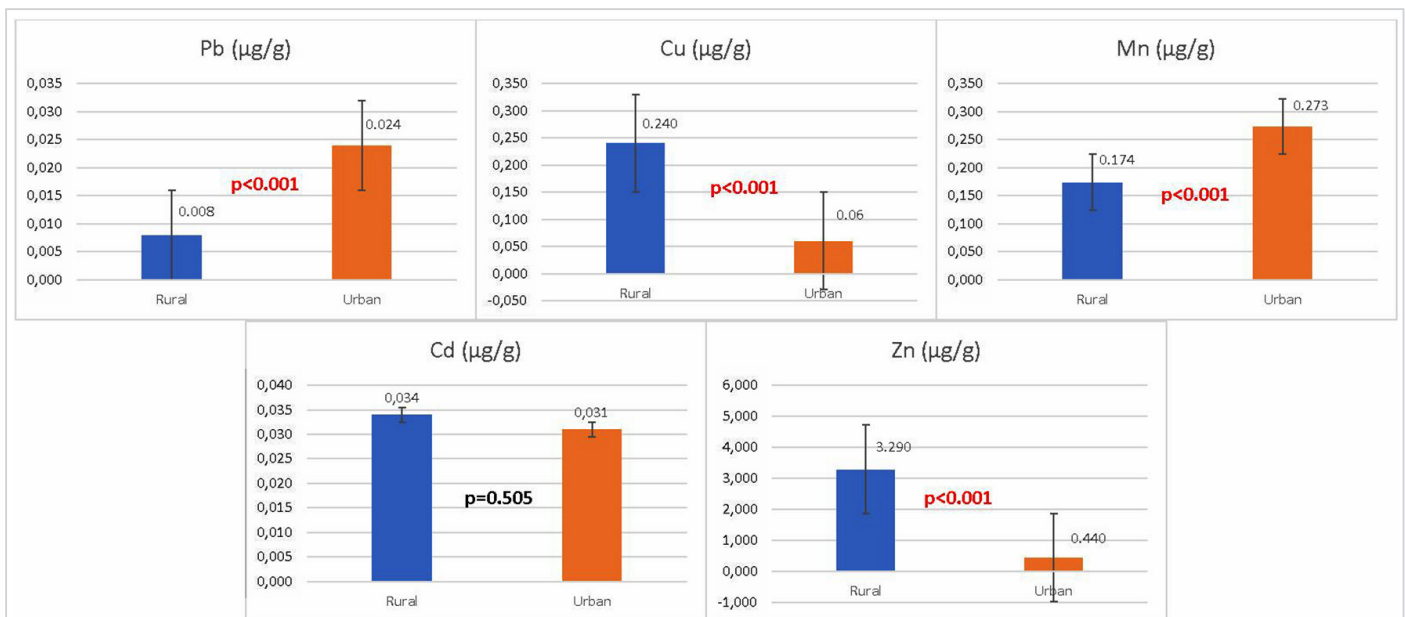


Figure 2. This is a graphic representation of heavy metal levels of Pb, Cu, Mn, Cd and Zn, where there is a statistically significant difference between the levels of the two groups
Pb: Lead, Cu: Copper, Mn: Manganese, Cd: Cadmium, Zn: Zinc

Table 3. Correlation between age and element levels

Age	Cd	Pb	Cu	Mn	Zn
r	-0.14	-0.05	-0.02	0.01	0.01
p-value*	0.26	0.67	0.87	0.99	0.97

*Pearson correlation test, Pb: Lead, Cd: Cadmium Zn: Zinc, Cu: Copper, Mn: Manganese

Calderon-Garciduenas et al. (13), found significant differences in biopsies from nasal mucosa of children exposed to outdoor pollutants compared with a healthy control group. Children exposed to polluted air had more complaints about upper airways, such as epistaxis, nasal congestion, dryness, and crusting. As expected in ENT examinations, abnormal nasal mucosal findings such as increased hyperemia and bleeding points in the nasal mucosa, purulent mucus, and sinusitis were observed. The authors reported basal cell hyperplasia, a decrease in ciliary epithelial cell and goblet cell count, submucosal neutrophil infiltration, squamous metaplasia, and dysplasia histopathological analysis of nasal mucosa biopsies of children exposed to air pollutants.

In rural regions, air pollution is rare and may be caused by pesticides and fertilizers in the agricultural sector (14). Metropolitan locations have more air pollution than rural areas owing to cars, industry, and industrial facilities. Traffic density and diesel and gasoline engine exhaust emissions are the primary sources of air pollution in densely populated metropolitan areas (15,16). CO, SO₂, ozone, NO₂, and lead are major outdoor air pollutants (14). Ultrafine particles are abundant in city air pollution, and their health effects are unknown (16,17). Glück et al. (18) examined the cytopathology of the nasal mucosa of individuals chronically exposed to diesel engine emissions. They detected goblet cell hyperplasia and an inflammatory response caused by increased leukocytes and defined this condition as chemical-induced rhinitis.

The major heavy metal in polluted air is Pb (19). Air pollution is caused by exhaust gas, and heavy metals enter the body mainly through inhalation (20). Yilmaz and Zengin (21) investigated heavy metal levels in the leaves of trees in the city center and countryside. The amount of Pb in the samples of the city center was significantly higher than in rural areas, and they associated these higher Pb levels with exhaust gas and air pollution. In another study (22), Suchodoller found that the amount of Pb accumulated in the barley and corn planted next to the road was high. They reported that the amount of Pb in the plants decreased as they moved away from the road, and the effect of traffic was not noticed 30-40 m away from the road. Similarly, in our study, Pb levels in the tissues of rural patients were significantly higher than in rural patients (p<0.001). Yousaf et al. (23) evaluated tree barks as a bioindicator to monitor air pollution in downtown Toronto and found high Pb and Mn levels in roadside trees with heavy traffic. Our investigation indicated considerably

higher Mn and Pb levels in the urban group.

People are not only exposed to polluted air outdoors. The best-known effect is cigarette smoke, which is an air pollutant inside. In an experimental study (24), significant changes were observed in the nasal mucosa of animals exposed to tobacco smoke. In the study conducted by Öner et al. (25) in which the heavy metal levels in the inferior nasal concha of smokers and non-smokers were compared, heavy metal levels were found to be significantly higher in the smoker group. Disruptions in intercellular tight junction complexes, significant structural changes in cell membranes, and increased infiltration of neutrophils on the nasal mucosa surface had been demonstrated in exposed animals. Cigarette smoke or occupationally exposed smoke is inhaled directly into the body along with the heavy metals it contains and causes the levels of heavy metals in the blood to rise (26). In the present study, patients who were smokers and ex-smokers were excluded.

Exposure to passive smoking is almost as harmful to the upper airway as active smoking (27-29). In the study by Elwany et al. (30), biofilm formation with *S. aureus* was seen in the nasal mucosa of 11 out of 20 children who had been exposed to passive smoking, but only one child in the control group had this happen. In the study conducted by Habesoglu et al. (31), mucociliary clearance was observed to be affected in those exposed to passive smoking. We did not exclude exposure to passive cigarette smoke in our study. We can acknowledge this as a limitation of our study.

Heavy metals inhaled with polluted air cause accumulation in the human body. Heavy metals trigger oxidative stress in the organism, increase reactive oxygen species, lipid peroxidation, and inflammatory cytokines, and exhibit harmful effects (4,32,33). Heavy metal accumulation in the nasal concha can lead to oxidative stress and inflammation in mucosal tissues, weakening immune responses and increasing the risk of infection. This accumulation may serve as a biological indicator for assessing the impact of air pollution on respiratory health. Oxidative stress plays a role in the etiopathogenesis of many diseases. It is a challenge to show the harmful effects of exposure to air pollution on human health with evidence. It is necessary to present the pollutant at the same time above the acceptable concentration in ambient air and human tissue, which is a challenging application in the normal population.

Liu et al. (34) showed that silver, a heavy metal, accumulated in the brain tissue of rats given an intranasal spray form. Another study suggested that Cd could pass from the nasal cavity to the brain via the olfactory nerve and show its neurotoxic effects (35). Again, it is predicted that Mn could cause accumulation via nasal uptake (31). As stated in such studies, demonstrating the presence of heavy metals in the nasal cavity could be helpful in shedding light on the etiology of related diseases.

We only measured five heavy metals, which limits our study. Due to technical constraints, this number is small but can be used for future research on heavy metal alterations. Additionally, the absence of simultaneous measurements of heavy metal levels in patient's blood samples and indicators of heavy metal air pollution in their urban and rural areas can be considered.

One limitation of this study is the absence of histopathological analysis of inferior nasal concha tissues. Including histopathological evaluation could provide insights into cellular or tissue-level alterations associated with heavy metal accumulation. This would allow a deeper understanding of the clinical implications and pathological changes from metal exposure. Future studies could enhance these findings by better correlating histopathological results with metal concentration levels to assess the potential impact on nasal and respiratory health. The study's inability to consider passive smoking status despite excluding active smokers and ex-smokers needs improvement.

Conclusion

When we attribute the cause of a condition to air pollution, but the underlying mechanisms are not yet completely understood, showing the presence of heavy metals in the nasal mucosa can be beneficial. In clinical scenarios where there is evidence of heavy metal accumulation and a clear link to diseases, we can mitigate the occurrence of the diseases by implementing preventive measures in urban areas.

Ethics

Ethics Committee Approval: This study was conducted in accordance with the Atatürk University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (decision no: B.30.2.ATA.0.01.00/56, date: 28.11.2014) and the Declaration of Helsinki.

Informed Consent: All participants provided written informed consent for the surgical procedures and study participation.

Acknowledgements

The authors thank to; Professor Adem Kara, PhD for his assistance in the preparation of the samples, PhD Adem Güneş for his help in measuring heavy metal, and Sultan Keskin Demircan, Md for statistical analysis.

Footnotes

Authorship Contributions

Surgical and Medical Practices: F.Ö., H.U., Concept: F.Ö., N.K., H.U., Design: F.Ö., N.K., H.U., Data Collection or

Processing: F.Ö., N.K., Analysis or Interpretation: F.Ö., N.K., Literature Search: F.Ö., N.K., Writing: F.Ö., H.U.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Main Points

- Air pollution is more prevalent in urban areas than in rural areas.
- Heavy metals in the inhaled polluted air can accumulate in the nasal mucosa and turbinate tissues.
- The determination of heavy metals in the inferior nasal concha can be considered an indicator of air pollution, and spectrophotometric examination of nasal mucosal tissues can aid in the differential diagnosis of associated diseases.

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