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Manifestation of Bronchial Reactivity in Mining Workers who are Exposed to different Pollutants

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Abstract

In this paper the impact of air pollution on the bronchial reactivity of mine workers in Leposaviq - Kosovo with toxic metals such as: (SiO_2, Pb, Zn, Particulate matter-PM) has been studied. Since body plethysmography is a highly sensitive and precise technique in the research of phenomena affecting bronchial reactivity, we have defined lung function with Body Plethysmography. Airway resistance (Raw) was recorded and Intrathoracic Gas Volume (ITGV) was measured and Specific Airway Resistance (SRaw) and specific conductance (SGaw) were calculated. The control group consisted of 35 healthy people. In our case we used histamine as a provocative test, which did not cause significant changes in bronchomotor tone ($p > 0.1$). In the experimental group, 59 workers of the Leposaviq - Kosovo mine were included. The results obtained from this research show that the mean Specific Resistance (SRaw), and specific conductance (SGaw) values significantly underwent changes in the experimental group compared to the control group ($p < 0.01$). The study also found that smoking favors the adverse effects of air pollution on workers' health. To the workers exposed to high concentrations of air pollution found change in lung function, increased bronchial reactivity, and impaired lung function at the level of gas exchange, namely a decrease in O_2 partial pressure and an increase in pacific CO_2 pressure in arterial blood. We also have a reduction in carbon monoxide transfer factor ($p < 0.01$).

Keywords: Leposaviq - Kosovo mine workers, Respirable noxae of SiO_2, PM Ores, Pb, Zn

1. Introduction

Disruption of environment emerged with the modern technological development of civilization, which cause serious impact on human health. Various damaging agents that are released into the air by the development of heavy industries pollute the air, land, water. The air we breathe is polluted with substance in all the aggregate states in the form of dust, gas, smoke and fog which we inhale from the atmosphere in the form of an aerosol. Inhalation of air that contains other particles can directly or indirectly damage the human body: various poisons or substances that damage the body allow other triggers (mainly bacteria and viruses) to continue the process of damaging. It is very difficult to talk about all the factors involved, especially the specific effect of each agent, because it depends on the interplay between the cause and the human organism, the cause and the work environment as the medium where this reaction takes place[1].

One of the factors that cause bronchial hyperreactivity and Chronic Obstructive Pulmonary Disease (COPD) is the inhalation of harmful noxae in the environment such as: harmful noxae released from mines, smelting plants, smoking, etc.). Due to increased lung ventilation during physical activity, the amount of inhaled air and harmful particles is much higher; the particles increasingly penetrate the respiratory system causing structural abnormalities of the lungs parenchyma resulting in increased static volume of the lungs and decreased arterial pressure of oxygen in arterial blood. Workplace environmental pollution and adverse climatic conditions further complicate chronic obstructive

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pulmonary disease and cause occupational asthma and lung emphysema[2].

Bronchial hyper-reactivity and COPD are major causes of mortality and morbidity in the adult population. The global prevalence of this disease is between 4 to 10%[3]. COPDs are the 5th leading cause of death worldwide. Given the increasing prevalence and limitation of therapeutic treatment, it is predicted that by 2020 this disease will take the 3rd place in the leading mortality list[4]. It is characterized by restriction of air flow through the respiratory tract, which is not completely reversible. This restriction of airflow is progressive and is accompanied by abnormal lung inflammatory responses because of harmful noxae and various gases released into the atmosphere. Although they primarily affect the lungs, and cause COPD, they also produce important systemic consequences[5].

Dangerous contaminants for human health are toxic metals such as: SiO_2, Pb, Zn, PM_{10}, $PM_{2.5}$, Ag, Au, Bz, K, Cu (copper). Very dangerous to health are also the radioactive waste which is gradually released from earlier explosions. One of the pollutants in certain environments are also persistent free radicals - tiny particles discharged into the atmosphere that cause cardiovascular problems and complications[6–8].

In addition to examining air pollutant quotas in certain areas through various chemical and toxicological methods, it is appropriate to consider other pathophysiological indicators that speak of improving human health as a result of improved air quality in these environments. In this respect, the examination of bronchial reactivity is a very effective indicator in assessing interventions aimed at reducing air pollution in those environments. Such a methodology was followed by the authors Wong et al.,[9], in which case by measuring the reduction of bronchial reactivity level they proved the efficacy of the intervention in reducing the air pollution.

For the above mentioned reasons, we have approached the study of the working environment of workers working in the Leposaviq - Kosovo ore mines from the extraction of Pb, Zn ore and the release of very harmful noxae to the human body: $PM_{2.5}$, PM_{10}, and various gases especially SiO_2.

2. Material and Methods

Periodic controlled examinations of the respiratory system in accordance with MRC (Medical Research Council) have been performed to verify increased bronchial reactivity and chronic obstructive pulmonary disease[10,11]. Measurement of airway resistance (Raw) and Intrathoracic Gas Volume (ITGV) was performed using body plethysmography technique. From the obtained results, calculated the specific resistance (SRaw) as well as the specific conductance (SGaw). Spirometry technique and body plethysmography have been applied. Obviously in our case body plethysmography is essential, as spirometry is known to be only an initial procedure during pulmonary function measurements and as such does not provide satisfactory information on respiratory parameters, especially when dealing with bronchial reactivity studies. On the other hand, body plethysmography is a very sensitive and precise technique in the research of phenomena affecting bronchial reactivity. The values of partial pressures of (pO_2) gases, and oxygen saturation linearly decrease from younger to older ages, which is not present at diffusive capacity and pH. The results indicate a reduction in the transfer factor for CO. The research was carried out in two groups: in the control group, 35 persons are included; whereas the experimental group included 59 workers at the mine in Leposaviq-Kosovo. Individual selection was randomized, and all research participants were informed about the procedures and purpose of the research. All individuals' part of the research has been informed in time to not take any medicines at least 48 hours prior to examination so as not to interfere with the results of our tests. According to international consensus, long-term therapeutic treatment of bronchial asthma and COPD is performed in three important stages: Continual-based treatment; Treatment by regional system; Properuse of medicines.Continual-based treatment- it is directly dependent on the severity of the disease itself. Thus, the doses applied in these cases show respective variability. Patient follow-up is done subjectively and objectively.Treatment by regional system- the purpose of this system is to inform the patient about the nature of his illness and to ensure co-operation with the physician during therapeutic treatment. This recognition also consists in the permanent monitoring of the patient's own respiratory state by measurements made with the PEF-meter.Properuse of medicines– medicines that have been used in the treatment of bronchial asthma and COPD have been: bronchodilator drugs, and anti-inflammatory drugs. Anti-inflammatory drugs: corticosteroids, antihistamines, antileukotrienes. Bronchodilator drugs: beta-2 adrenergic agonists, methylxanthines and

anticholinergic drugs. Since medication treatment of these diseases is limited, therefore, the only option to avoid them is to take preventive measures[12–16].

2.1 Statistical Analysis

In this scientific study we are dealing with the difference between the two research groups. On this basis we used the t-test as a differentiation mechanism regarding the level of significance between the two comparison groups. The work was carried out between the two working groups: the control group and the experimental group. When comparing the significance between the control group and the experimental group we used the t-test for independent samples (Unpaired t-test), because we were dealing with two separate and independent groups. The results of the t-test were processed with the help of a statistical program called GrafPad Prism.

3. Results

3.1 Concentration of SiO_2 in the Environment of the Leposavic, Koporic and Kopaunik Mines

In Flotation, air pollutants vary depending on jobs and technological processes, so the ratio of free SiO_2 to air in the Flotation environment is 62% at the location where the ore is extracted. The maximum concentration exceeds 1-4%. Noise and vibration from machinery in all areas where the ore is extracted is higher than the maximum permissible concentration which further contaminates the air, whereas in areas where this machinery is not applied but hand-operated, the noise and vibrations do not exceed the allowed maximum concentration values.

In the Leposaviq mine, the airflow velocity and temperatures are kept at normal limits. In some areas of the mine, the presence of free SiO_2 in the air has been over 26% higher than normal. This means that the maximum permissible concentration has exceeded 1.7 to 3 times the normal values, while the air humidity has exceeded the maximum permitted concentrations by 20%.

At the work site of the so-called "Koporiqin" mine in Leposaviq, SiO_2 emission has gone up to 30%, which means that the maximum allowable concentration has been over 3 times. Air humidity has been conditioned by atmospheric conditions, as the ore is superficial; this is also true for temperature and airflow, which is again dependent on the seasons.

At the "Kopaunik"-Leposaviq mine site, measurements of SiO_2 (free silicon dioxide in the air) have also been performed. The measurements have also been performed on the space walls where the workers worked, then measured humidity and air velocity, temperatures and noise emitted by machinery in the mine area. In some areas, it can be concluded that the percentage of SiO_2 in the air where the workers worked in the mine area varied from 11%-20%. Presence of the dust in relation to free SiO_2 exceeds the maximum permissible concentration for 2-3 times, and relative humidity of air exceeds 31%. See Figure 3.

All general data of the people of both groups are given in Tables 1 and 2.

3.2 The difference between control and Experimental Group Values

We will first present the results measured by body plethysmography to the control group with the aim of eliminating suspicions about the presence of bronchial reactivity in this group. The statistical calculation for SRaw, which was made between the control group and the experimental group, shows that there is a significant difference between these two groups. This is also confirmed by the obtained values ($p < 0.01$). The results indicate the presence of emphasized bronchial reactivity

Table 1. General characteristics of the researched people

Group	N	Age (vitet)	Height (cm)	Weight (kg)	VC (L)	FEV_1 (L)
Control	35	44.9± 0.44	177±1.40	70.6±1.8	4.04±0.16	3.72±0.13
Experimental	59	46.5±0.90	173.5±1.0	77.0±1.72	43±0.14	3.3±0.14

– Generalized mean values for: Control group n = 35, X ± SEM; Experimental group n = 59, X ± SEM. The general starting values for: VC (L) and FEV1 (L) are also given.
– VC =Vital capacity expressed in liters,
– FEV_1 - Enhanced expiratory volume in the first second, expressed in liters.

Table 2. Body-plethysmography features of the researched people

Group	N	Raw (kPa x s/L)	ITGV (L)	SRaw (kPa x s)	SGaw (kPa x s)
Control	35	0.24±0.3	3.0±0.1	0.80±0.04	1.25±0.12
Experimental	59	2.1±0.24	3.2±0.13	6.72±1.12	0.14±0.01

- Raw (kPa × S/L); ITGV (L); SRaw = Raw × ITGV; SGaw = 1/SRaw.
- Raw - Airway resistance expressed in kilo pascal/second/liter,
- ITGV - Volume of intrathoracic gas expressed in liters,
- SRaw - Specific airway resistance which is the relationship between resistance and the volume of intrathoracic gas,
- SGaw - expresses the relationship between 1/specific resistances. SGawcan also be referred to as specific airway passage or conductivity.

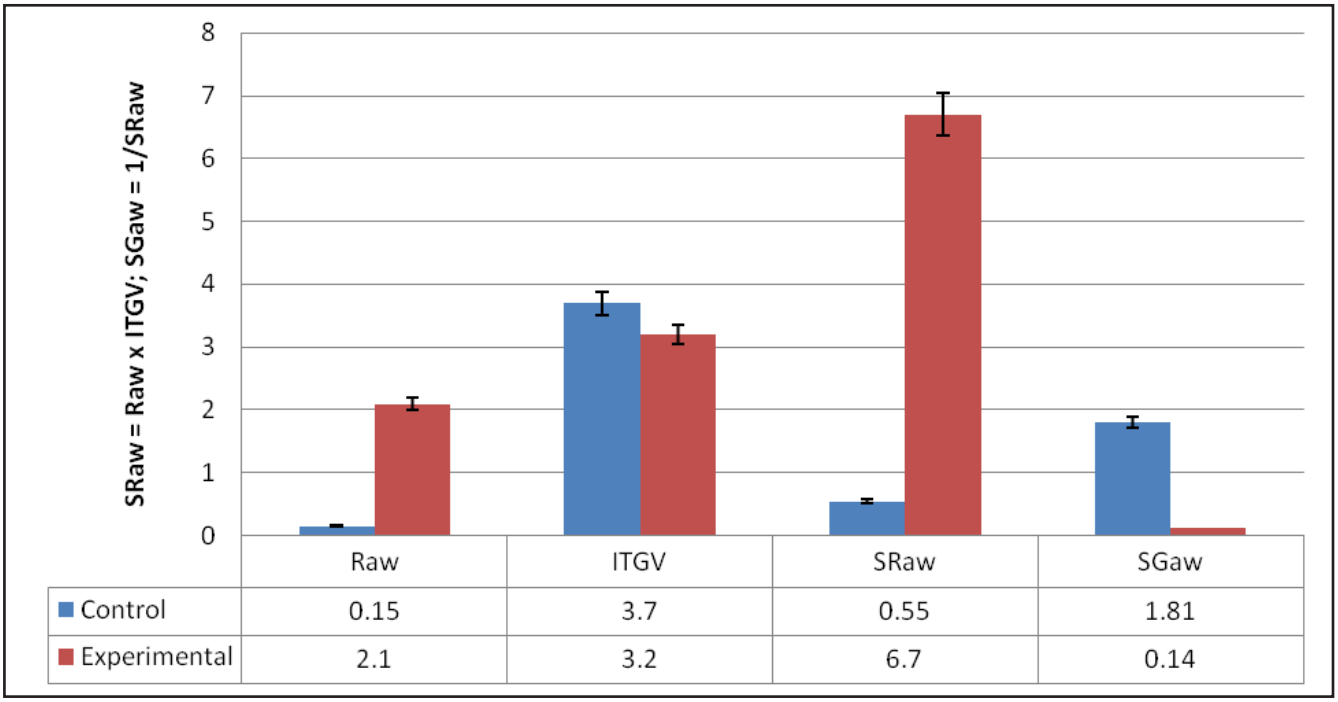


Figure 1. Comparison of values of control group (n=35; X±SEM) and experimental group (n=59; X±SEM). (p< 0.01).

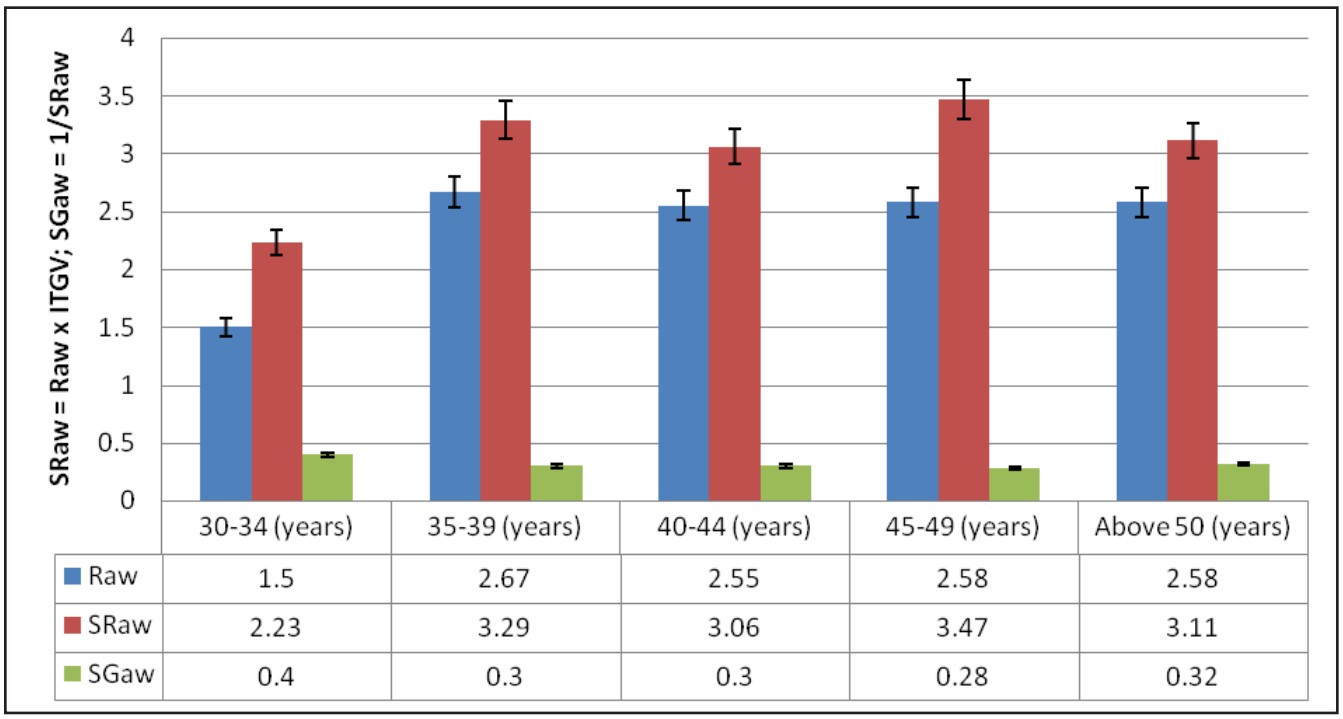
in the group of workers working in the Leposaviq-Kosovo mine. The parameters, SRaw and SGaw, for both groups analyzed and are shown graphically in Figures 1 and 2.

3.3 The Influence of Exposure on Bronchial Reactivity

Workers who work in mines regardless to age also increase their susceptibility to harmful particulates released into the air during ore mining. Changes are significant starting from age 30 to age 50 (p <0.01), see Figure 2.

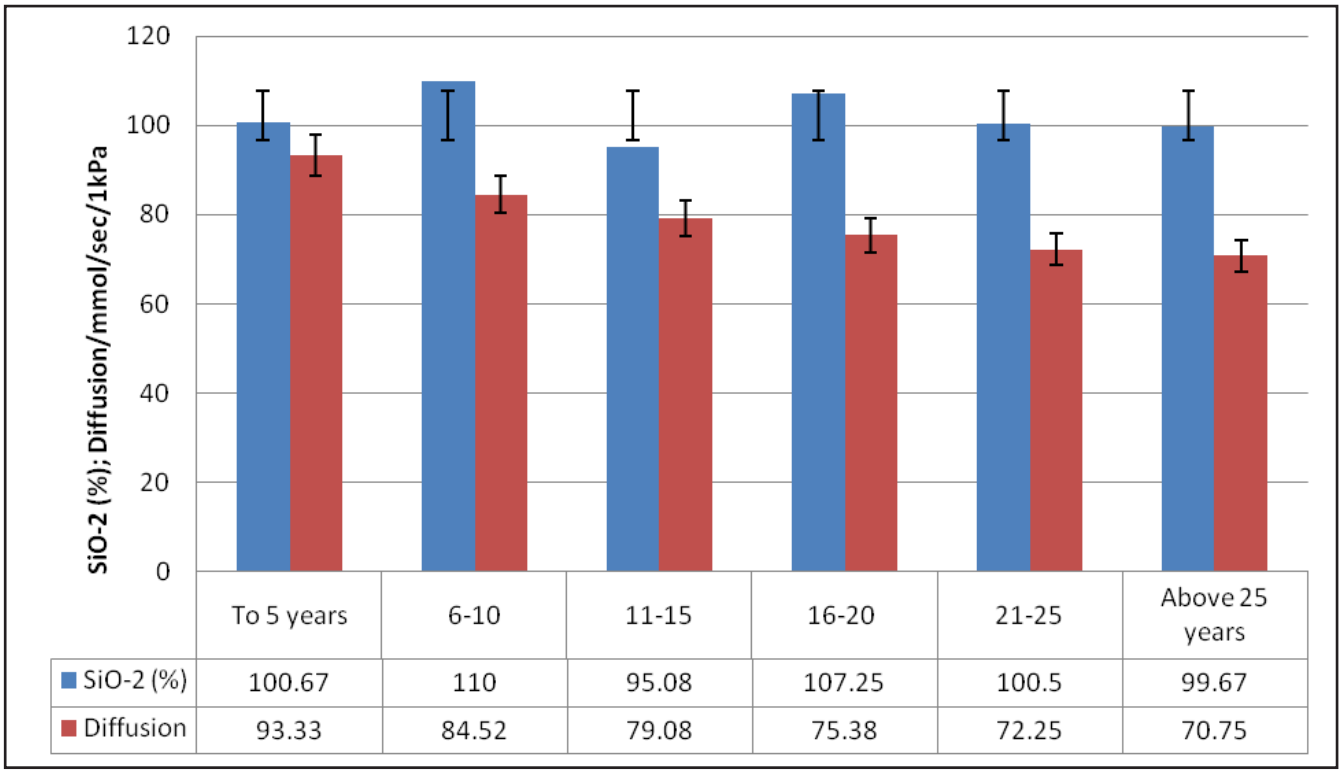
3.4 The Role of Transfer Factor in the Passage of Gases through the Alveolar Membrane

We also have a reduction in Carbon Monoxide (CO) transfer factor. Decrease of transfer factor, which represents difficulty in circulation of gases through the alveolar-capillary membrane, results in changes statistically significant in the group of workers exposed to noxae, compared with the control group (p <0.01).



	30-34 (years)	35-39 (years)	40-44 (years)	45-49 (years)	Above 50 (years)
Raw	1.5	2.67	2.55	2.58	2.58
SRaw	2.23	3.29	3.06	3.47	3.11
SGaw	0.4	0.3	0.3	0.28	0.32

Figure 2. Lung function values researched with body plethysmography depending on exposure age (SRaw and SGaw). (X ± SEM; n=59), ($p < 0.01$).



	To 5 years	6-10	11-15	16-20	21-25	Above 25 years
SiO-2 (%)	100.67	110	95.08	107.25	100.5	99.67
Diffusion	93.33	84.52	79.08	75.38	72.25	70.75

Figure 3. The values of SiO_2 and diffusion per (CO) depending on the age of exposure. (X ± SEM; n=59). ($p < 0.01$).

3.5 Gas Change in Arterial Blood

Analysis of respiratory symptoms, alteration of lung function, and bronchial reactivity in workers exposed to high concentrations of air pollution indicated impaired lung function at the level of gas exchange, namely decreased partial pressure of O_2 and elevated partial CO_2 pressure in the arterial blood of the study groups, the changes being statistically significant ($p < 0.01$). See Figure 4.

3.6 Pletizmographic Values Depending on the Age of the Workers

With the increase in exposure duration after 20 years of age, bronchial reactivity and obstructive pulmonary syndrome have undergone significant changes ($p < 0.01$), see Figure 5.

4. Discussion

Regardless of the large number of researches in this field, there are still open questions concerning the relevance of pathological changes and the effect of harmful noxae in the workplace. When assessing the causes of chronic non-specific lung and knee disease in the workplace, criteria must be established to assess the degree of damage and the effects of true triggers in relation to damage to structures and disorders caused to the health of workers as a result of individual or combined effect of harmful noxae in the workplace. The study also evaluated the effect of silicon dioxide and trioxide as well as of sulfur dioxide and other associating noxae in the lead and zinc smelting sectors and processing of this concentrate, which may be a major cause of COPD development[17–19].

The effect of silicon dioxide and sulfur dioxide on the respiratory system of humans and animals is the object of the study of many researchers, both locally and worldwide. The researched were mainly exposed to the pollutants mentioned above.SiO_2 is mostly present in "heat technology" in foundries and power plants. The main physiological response to inhalation of these pollutants and other similar irritants is broncho constriction. This is observed in the measurements of increased airway resistance. These findings have also been observed in series of experiments performed in cavities and other experimental animals, as well as in humans. These results have been experimentally obtained with short exposure, with varying concentrations of SiO_2. Accelerated exposure of human beings to particulates of 10×10^6 (i.e., 10 ppm)

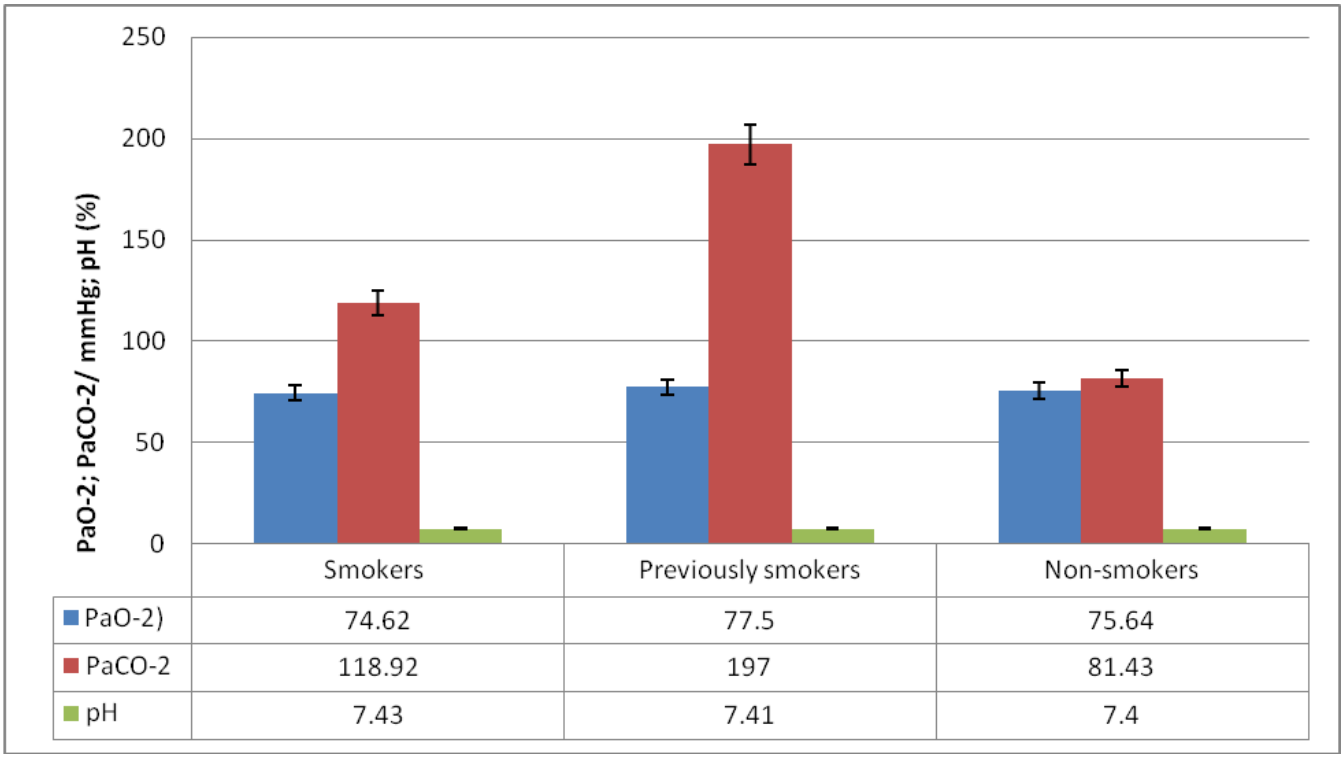
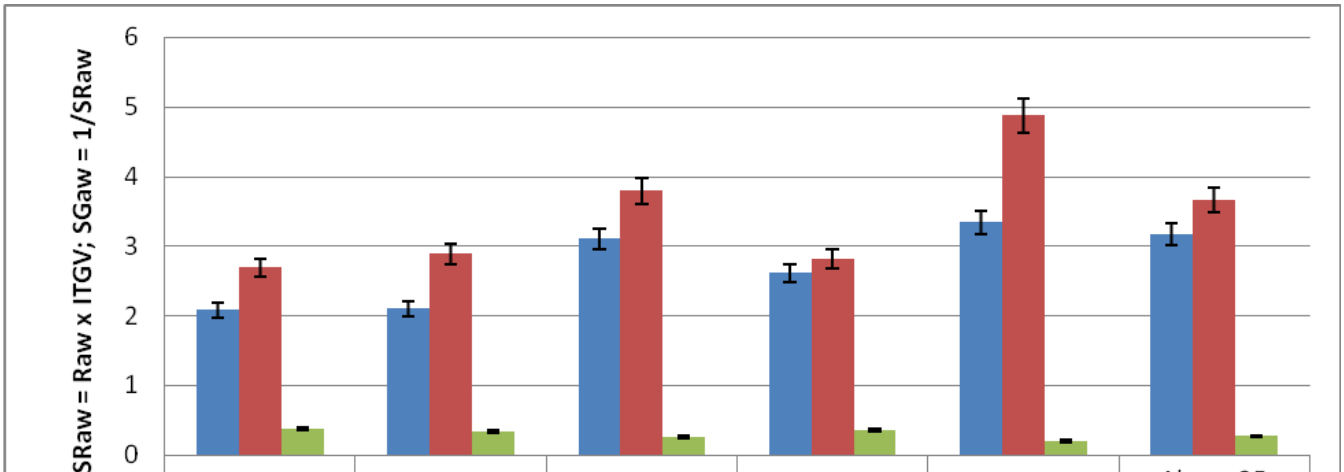


Figure 4. Analysis of arterial blood gases depending on smoking habit. (X ± SEM; n = 59). ($p < 0.01$).



	To 5 years	6-10	11-15	16 - 20	21 - 25	Above 25 years
Raw	2.08	2.1	3.1	2.61	3.34	3.17
SRaw	2.69	2.89	3.79	2.82	4.87	3.66
SGaw	0.37	0.34	0.26	0.35	0.2	0.27

Figure 5. Lung function values researched with body plethysmography depending on the age of exposure to SiO_2. (X ± SEM; n=59). ($p < 0.01$).

showed no changes in lung function. Exposure of 3 ppm also did not register maximal effects and expiratory airflow, but exposure of 5 ppm resulted in a decrease in maximal expiratory volume flow, as well as an increase in airway resistance. The exposure time of these experiments was 1-5 minutes. Toxicological research has shown that sulfuric acid and certain specific sulfates, such as oxidizing products of sulfur dioxide, have a much greater irritant effect than sulfur dioxide. The harmful effects that are still caused are unclear [20–24]. The presence of these particles in high concentrations both in the workplace and in the premises of the industrial complex "Leposaviqi" has been confirmed by several measurements.

Analysis of the partial pressure of the respiratory gases in the arterial blood has shown differences among the workers working in the Leposaviq mine, which is rich in lead and zing. It is about reducing the partial pressure of oxygen, but to the same worker has been present hypercapnia. Changes were observed with analysis of variance (One Way ANOVA), indicating statistical significance ($p < 0.01$). Whereas in relation to the results of the transfer factor analysis across the groups of workers researched, it has been observed that to these workers transfer factor are significantly reduced. These results suggest that the persistent absorption of contaminated air into the processing (lead and zinc) sectors primarily cause respiratory system inflammatory reactions (release of chemical mediators such as: histamine, serotonin, bradykinin, Leukotrienes LTD_4, PGF_2-alpha, SRS, prostacyclin, etc., namely reduction of the transfer factor (inflammatory changes) of the alveolarcapillary membranes, especially of the terminal membranes, respectively of the respiratory bronchioles. As a result of inflammatory reaction are also plethysmography facts that parameters of the airway permeability (Rt, ITGV, SRT, SGaw) had statistically significant changes ($p < 0.01$). Restriction of airflow through the respiratory tract as a result of the effect of harmful oxides and gases, especially those found on the working premises. In some cases, these changes in environmental contamination are associated even by smoking[25–27].

Nonspecific hyperactivity to histamine has been present in those researched who have been exposed to toxic noxae which have at the same time generated inflammatory processes of the tracheobronchial trunk. The reactivity has been proportionally decreasing with time of exposure of the respiratory system to various noxae. Since bronchial reactivity is determined by genetic property, it virtually means that every person has something to do with inheritance, and it is not to

be expected that life can change significantly. Bronchial reactivity is mainly determined by the increased sensitivity of the smooth muscle in parsmembranacea of the tracheobronchial system. Genetic determination gives little room for these changes when exposed to any adverse conditions for the respiratory system. One comment on this increase in bronchial reactivity is the presence of inflammatory reaction throughout the tracheobronchial system, except in the pars membranacea. Any tissue is involved in the inflammatory reaction if it is well involved with vascularization. Any inflammation causes hyperemia reactions for which the only rational explanation is the finding that it is about a bronchial reactivity, respectively bronchial asthma[28].

The process of change is dynamic related to the duration of exposure to noxae, but the constitutional predisposition of each person individually depends very much on the habit of smoking. However, preventive action is more efficient (effective reduction of environmental pollution by using technical equipment such "air purifiers", "aspirators", "adsorbents", "hermitization of technological processes". Permanent air monitoring is a prerequisite for taking correction action. On the other hand, permanent monitoring of the parameters of malfunction (plethysmography, spirometry, bronchial reactivity, changes in transfer factor, respiratory gases, extraction and analysis of extracted substances, nitrous oxide analysis, NO), can provide timely taken therapeutic measures for the treatment of the condition, namely other measures that are necessary for the protection of workers in the workplace.

Analysis of the noxae in the atmosphere, their effect on the respiratory system, changes in the body (damage, inflammatory reactions, remodeling of the respiratory tract and alveolar-capillary membranes, decisions on preventive measures, diagnostic or therapeutic treatment), are necessary as interdisciplinary actions on the whole issue of the impact of air pollutants on the health of workers and the general population. For this reason, it is necessary to include many experts of different profiles, from the fields of toxicology, ecology, pathophysiology, clinical biochemistry, pathohistology, immunology, pharmacology, pharmaceutical technology (for the preparation of adequate medicine forms for treatment of respiratory tract diseases), when it comes to protecting the health of workers who work their whole lives in polluted environments. On the other hand, it is necessary to involve experts of the relevant field (technologist, engineer, ecologist), who are capable that based on the analysis obtained with the condition monitoring, in time take appropriate measures to improve the technology which will minimize emission of noxae in the environment.

5. Author Contributions

DSH and PI conducted the literature search and determined studies for exclusion and inclusion. HI extracted data from the studies included, performed the meta-analysis, and drafted the manuscript. ZI conceived the idea for the study, designed the study, and critically revised the manuscript for content. All authors contributed to the data analysis, drafting and revising the article, and gave their final approval to the version to be published, and agreed to be accountable for all aspects of the work.

6. Disclosure

The authors report no conflicts of interest in this work.

7. Summary

These researches undoubtedly show that workplace exposure to harmful noxae such as: silicon dioxide, silicon dioxide and trioxide, cause inflammatory reactions and increase the release of chemical mediators. Increased bronchial reactivity reduces carbon monoxide (CO) transfer factor. Research has shown significant correlations between the duration of exposure to the harmful agent and morbidity by the respiratory system, following the presence of respiratory symptoms, changes in parameters measured by body plethysmography, decreasing factor transfer, and increasing presence of general inflammation syndrome. Based on the research done, and the results obtained, it can be concluded that permanent monitoring of the respiratory system condition is necessary, especially in terms of the presence of inflammatory reactions that develop after a long-term inhalation of harmfulnoxae. Therefore, these workers need to monitor bronchial reactivity more often by provoking them with histamine or acetylcholine to intervene early to initiate therapeutic treatment. Patients with bronchial hyper reactivity especially show a predisposition to the development of long-term changes in the respiratory

tract, therefore this group of workers should be treated as a high-risk experimental group. In conclusion, this study demonstrates the need for continuous monitoring of macro and microclimates to determine the level of concentration of harmful oxides in order to detect different organism reactions in the event of increased and sudden emissions of oxides due to any reason.

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