



## Increase of Histamine Concentration in the Sputum of Exposed Workers a Case-control Study

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### Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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### ABSTRACT

**Background:** The key aim of this study was to determine the relation between possible changes in the lung function and the concentration of histamine in the sputum of exposed workers and control group. The research aimed to establish possible correlation between participants exposed to air pollutants at workplaces, especially participants who are smokers and non-smokers, workers in industrial - mining basins and mines. This case-control study assessed the COPD risk attributable to occupational exposures among mine workers.

**Methods:** The participants in this case control study included 420 workers out of which 60 represented the control group. The study determined, histamine concentration in the sputum, pH,

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arterial partial oxygen pressures ( $\text{PaO}_2$ ) and carbon dioxide ( $\text{PaCO}_2$ ) in capillary blood and, spirometric parameters  $\text{FVC}/\text{FEV}_1$  using "Godart" pulmo-test model spirometer. Airways resistant ( $\text{Rt}$ ) and intrathoracic gas volume (ITGV) were measured using a 'Siemens' model Body Plethysmograph. Specific resistance ( $\text{SRt}$ ) was calculated using the formula ( $\text{SRt}=\text{Rt} \times \text{ITGV}$ ). Qualitative exposure indicators were developed based on both, work duration and exposure histories.

**Results:** Histamine presence in sputum was at a significant level ( $F=10, 59, p<0.0001$ ) just for the whole group of exposed workers compared to the control group. However, significant values were found for the smokers' category only in the case of Leposavić participants, respectively at the level ( $p<0.05$ ). Apparently the obtained values for partial pressures at level  $\text{PaO}_2$  ( $F = 13,387, p<0.001$ ) and  $\text{PaCO}_2$  ( $F = 10,79, p<0.001$ ), where the lowest value of  $\text{PaO}_2$  was at participants of Leposavić basin, namely 8.91 kPa, whereas the highest was at the control group, RS 10.04 kPa (SD5.3).  $\text{PaCO}_2$  was also the lowest to the workers in Leposavić, 4.53 kPa (SD2.6), while the highest was in Ajvalia 5.01 kPa (SD5.4). Hence we consider that these findings are not just casual but they are rather in a direct correlation with increased values of histamine in sputum of the participants. At the same time spirometric parameter values were at a significant level [Tiffneau Index ( $p<0.001$ ),  $\text{FEV}_1$  ( $p<0.0001$ ),  $\text{SRt}$  ( $p<0.0001$ )]. Hence, these results suggest that histamine might participate in the pathogenesis of functional disorders in exposed workers.

**Conclusions:** Mine workers are at increased risk for COPD as a result of broad and complex effects of many exposures acting independently or interactively. Control methods should be implemented to prevent workers' exposures, as well as smoking cessation should be promoted. "Hermetization" of technology processes, which is currently a world trend in "dirty" technologies, practically disables pollutants' emission at working places and the atmosphere.

*Keywords: COPD; mine workers; occupational risks; vapours; gasses; dusts; fumes; smoking; attributable risk.*

## 1. INTRODUCTION

Chronic obstructive pulmonary disease (COPD) causes a significant health burden worldwide, in terms of morbidity and mortality. COPD is characterized by progressive and not fully reversible airflow limitation. It is a chronic airway inflammatory disease with a systemic component related to repeated inhalation of noxious gas and particles, in particular tobacco smoke [1]. The huge discrepancies found between the respiratory functioning indices have been considered as a sustainable criterion between the exposed workers and control group, and in this case the former have been considered as a group with potential risk of COPD disease development. The aim of this case control study was focused on eventual finding of the correlation of increased histamine concentration at the sputum of participants with direct and indirect lung functioning parameters. As a result of exposure to various pollutants at workplaces on the one hand and smoking on the other hand, as eventual possibilities of interacting and potentiating of the common and harmful effects in causing COPD.

Bronchial asthma and Chronic Obstructive Pulmonary Diseases (COPD) are common

diseases characterized by inflammation of the airways and disturbed integrity of the epithelial cell layer of the airways [2]. Macroscopic responses to airway inflammation include airway obstruction, and mucus hypersecretion by exocytose of submucosal glands and surface epithelial goblet cells [3]. The quality, as well as the quantity of mucosal secretions differs between healthy subjects and patients with respiratory diseases [4]. During periods of hypersecretion, the mucus shifts from having a protective to a potentially harmful role due to increase in viscosity which may impair mucociliary clearance with resulting accumulation of mucus in the airways [4].

Histamine released in allergic reactions as well as various harmful effects of non-antigen factors, in addition to its direct effect on smooth muscles, which stimulates irritating receptors of the airways, stimulates cholinergic bronchoconstriction mechanisms and leads to a reflex that narrows airways [5]. In addition to smooth muscles contraction, histamine causes increased wall permeability of blood vessels and stimulates bronchial secretion [6]. Histamine can be found also in bronchial secretion. Increased concentration of histamine in sputum has been found in patients with asthma and obstructive

bronchitis [7]. However, although this fact is known, the relation between histamine concentration in the sputum and change in the lung function parameters has not been well studied enough in Kosovo and countries of the south-eastern Balkans. Public health programs and policies that focus on tobacco-use prevention and cessation, reducing occupational exposure to dusts and chemicals, and reducing other indoor and outdoor air pollutants are critically important for health of workers in regard to undertaking all appropriate preventive measures and for their personal and environmental protection.

## 2. METHODOLOGY

The study was carried out at the Pathophysiology Institute of the Faculty of Medicine, University of Prishtina. The study recruited 420 participants divided in 7 groups. Out of the seven groups, six (6) groups with a total of 360 were exposed mining workers to: Lead and Zinc Smelter (60 participants), Pit Mine - Ajvalia (120 participants), Lead and Zinc Concentrate Processing - Leposavić (30 participants), Magnesite Mine - Magure (30 participants), Gasification (60 participants), Surface Coal Mine in Belačevc, Obilić Power Plant (60 participants). The control group of workers (60 participants) included workers from the construction company GK from Prishtina, who practically were not exposed to the noxious elements to which miners at industrial plants of "Trepča" complex, Magure, open pit mine in Belačevc and Obilić Power Plant were exposed.

### 2.1 Criteria for Inclusion

Workers working at least for 5 years continuously in the workplaces within the abovementioned enterprises, or in cumulative manner for 10 years, at least in the period of last 20 years.

### 2.2 Criteria for Exclusion

Workers who had any other pulmonary illness, and which could have repercussions on examined spirometry parameters.

All participants, including the control group were subjected to the following examinations:

### 2.3 Spirometry Determination

Dynamic spirometry is one of the first tests for measurement of lung volume. Testing of forced

expiratory flow was measured by "Godart" pulmo-test spirometer. Spirometric measurements were made after the purpose methods and the purpose were clearly described to the participants. Forced expiration was analysed, where one of variables (volume or time) was fixed. In our case time was fixed at the x-axis, so that the obtained volume from the acquired curve is described as expiratory forced volume for a certain time, e.g. Forced expired volume in the first second ( $FEV_1$ ). Measurements were carried in the standing or sitting position. The participants were wearing a nose clip, and slowly started to inspire starting from functional residual capacity (FRC) to the total pulmonary capacity (TPC) followed by a full and forced expiration to the residual volume (RV). Several measurements were conducted until we did not obtain two reproducible curves. Forced volume capacity (FVC) was calculated from the forced expiration volume curve. Forced expired volume in the first second  $FEV_1$ ,  $100 \times FEV_1 / FVC$ , and forced expiratory flow at 50% of FVC ( $FEF_{50}$ ), forced expiratory flow between 25 and 75% of FVC ( $FEF_{25-75}$ ), forced expiratory flow at 75% of FVC ( $FEF_{75}$ ) [8].

### 2.4 Body Plethysmography

Body plethysmography is used to measure static lung volumes and airway resistance. Study was carried in the cabin according to Boyle's law, which states that the product of volume and pressure is constant at the same temperature; respectively, when you know the volume of gas in the lungs, the corresponding changes in alveolar pressure can be calculated. Airway resistance was measured according to the air flow, as well as its consequences hyperinflation. Determination of total airway resistance (Raw) was done based on Ohm's law. While breathing spontaneously, changes of air flow were recorded simultaneously at Y-axis, whereas the changes of pressure in the cabin (PC) at X-axis of the XY recorder of Hewlett-Packard make. Afterwards upon closure of electromagnetic valve at the end of expiration, alpha angle was recorded. The same procedure was repeated during shallow and rapid breathing (in an approximate breathing speed of a respiratory cycle per second). Intrathoracic gas volume (ITGV) was calculated based on Boyle-Mariotte law: a constant ratio of lung volume and pressure that occurs in the lungs during breathing movements in short stop valve flow rate [9]. At least three curves were recorded, out of which the average value was calculated. The specific

resistance ( $SRT = R_t \times ITGV$ ) was calculated from measured values of  $R_t$ ,  $ITGV$  [9].

## 2.5 Determining the Concentration of Histamine in Participants' Sputum

Histamine was determined by biological method as follows: In the bath for isolated organs with Tirod's solution, with aerated gas mixture (5%  $CO_2$  and 95%  $O_2$ ), at the temperature of  $37^{\circ}C$ , a part of guinea pig's ileum was placed that was sacrificed by cervical dislocation exsanguination. The segment ileum, of about 2 cm long, was fixed on the holder by its lower end, while the upper part was fixed by nonexpendable thread connected to a transducer (Statham UC 2). Thirty minutes after the preparation was set, known concentrations of histamine was added and a smooth muscle response was registered on multichannel writer Watanabe HSE 6600. Doses of histamine were changed every 15 minutes during which the effects of added doses were observed 3 minutes after. The preparation was then rinsed several times with fresh Tirod's solution and once the tonus returned to the initial value, the next concentration was added, namely 1 ml of sputum's homogenate. The values of histamine in sputum have been calculated from the obtained deflection size, and comparing it with standard known histamine concentration. At least  $24^h$  before participants gave their sputum, they did not take bronchodilation agents nor corticosteroids.

## 2.6 Sampling Sputum of Participants

Sampling for determining the concentration of histamines in the saliva of participants was done as follows: Firstly, special 200 gram bottles were prepared and provided with hygienic closure which were well cleaned and then sterilized a day earlier, every single day. Participants were given the explanation how to collect their 24 hours sputum, kindly asking them for a proper cooperation. Collected experimental material was a subject of determination of histamines in sputum of participants.

## 2.7 Ethical Consideration

Informed consent to participate in the study was obtained from all participants after the purpose and methods were clearly explained; and participants were assured that they could withdraw from the study at any time without any consequences. The experimental animals were

treated ethically and the Institute's ethics committee approved the content of our study protocol and granted ethical clearance.

## 2.8 Determination of Acid-alkaline Status and Respiratory Gases in Capillary Blood

The respiratory gas was done at a standstill form with arterial puncture, (previously hyper-immunized with butylnicotine capsaicin) from which the parameters of the partial pressure of oxygen  $pO_2$ , partial pressure of carbon dioxide  $pCO_2$ , oxygen saturation of haemoglobin and acid base status of the blood, using analyzer IL-213 few minutes after the samples were taken. Standard vials solutions pH,  $PaO_2$  and  $PaCO_2$  have been used as standards for verifying the measurement accuracy. The ointment residue was removed 10-15 minutes later. Every two heparinized tubes were filled with capillary pressure without squeezing them. Sample taking time is about two minutes.

## 2.9 Statistical Data Processing

Comparison of the groups of participants was analysed by ANOVA statistical method. Whilst the computer program INSTAT-3 and STATISTICA FOR WINDOWS was used for data processing.

## 3. RESULTS

Results of examinations for both, exposed and control group of workers were shown in tables and charts. The chart method represents concentration values of determined histamine in sputum of the participants, partial pressures for  $PaO_2$  and  $PaCO_2$  as well as  $FVC/FEV_1$  and specific resistance ( $SRT$ ).

Table 1 gives general characteristics of the participating workers based on their age, body height, body weight, Brocca index and years of working experience.

Table 2 gives of subjects according to the smoking habits.

The results of histamine concentration in sputum analysis have shown that histamine concentration was the highest to the workers at smelter in Zvečan (lead and zinc smelter) and the workers at Leposavić mining area (lead and zinc concentrate processing).

Table 1. Basic characteristics of participating workers

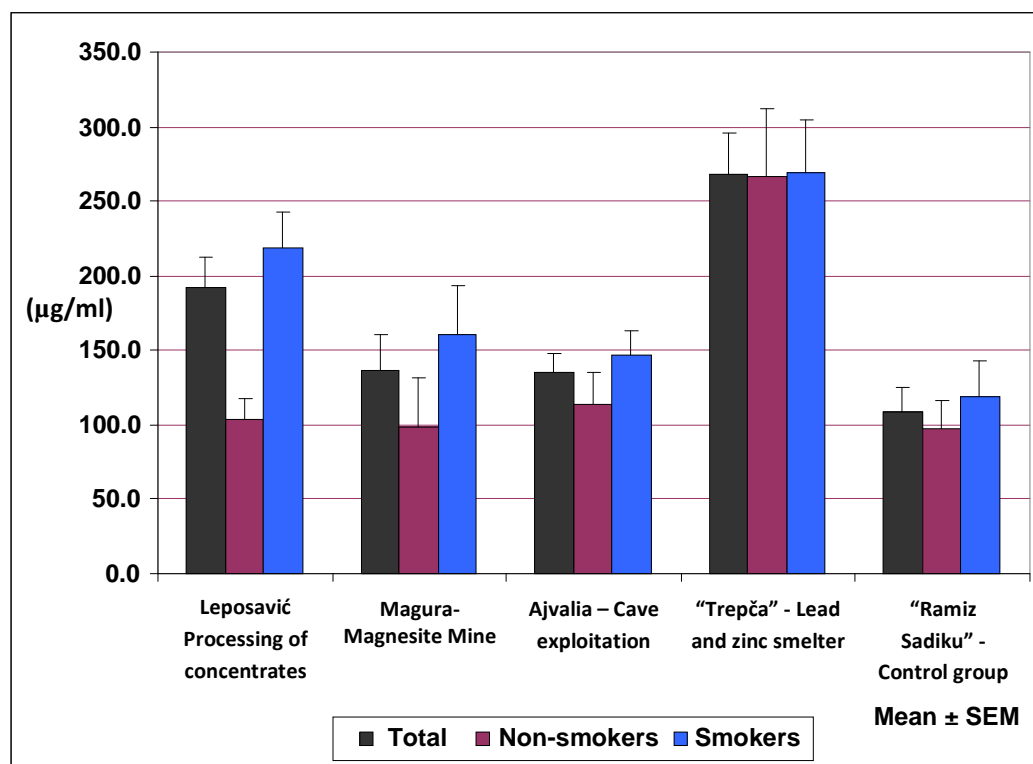
	Age (years)			Body height (cm)			Body weight (kg)			Relative weight (Broca index)			Length of service (years)		
	Mean	SD	SEM	Mean	SD	SEM	Mean	SD	SEM	Mean	SD	SEM	Mean	SD	SEM
Obilić surface coal seam/power plant	44.6	9.2	1.09	170	6.1	0.72	74.4	11.6	1.36	100.3	15.9	1.88	13.3	7.2	0.85
Obilić - gasification	35.5	10.7	1.29	169.1	6.6	0.8	67.7	10.2	1.24	97.5	12	1.46	15.5	9.4	1.14
Leposavić processing of concentrates	46.5	6.3	0.9	173.5	6.9	1	77	11.9	1.72	106.1	16.9	2.44	21.4	7.6	1.1
Magura-Magnesite mine	45.1	5.9	1.15	173.3	5.9	1.15	73.2	9.5	1.86	100	11.9	2.32	19.9	8.5	1.67
Ajvalia – cave exploitation	46.6	7	0.65	171.8	6.2	0.57	73.2	11.5	1.05	100.7	16.3	1.49	23.5	7.3	0.67
“Trepča” - lead and zinc smelter	40.6	7.7	0.98	171.8	6.8	0.86	74.8	14.9	1.89	102	12.2	1.55	15.6	8.3	1.06
“Ramiz Sadiku” - control group	39.8	8.5	1.31	170.5	5.8	0.66	71.6	9.1	1.03	101.9	14	1.59	14.2	11.9	1.35
One way ANOVA	F=18.23, p<0.0001			F=4.193, p<0.001			F=2.362, p<0.05			F = 1.879, p>0.05			F = 19.414, p<0.001		

By comparing histamine concentration in sputum of the participating workers, it has been found that histamine concentration in sputum of participating workers has shown a significant difference ( $p < 0.0001$ ) in certain groups of participants, in accordance with their workplace. The values of histamine concentration in sputum of both, participating workers smokers and non-smokers, excluding concentration to a worker at Leposavić ( $p < 0.05$ ), the rest of categories linked

to smoking habits have not shown a statistically significant difference [Magure - Magnesite Mine ( $p > 0.05$ ), Ajvalia - Mine exploitation ( $p > 0.05$ ), "Trepča" - Lead and Zinc Smelter ( $p > 0.05$ ), "Ramiz Sadiku" - Control group ( $p > 0.05$ )], thus statistically important differences were displayed only in relation to working place, and not in relation to smoking habit with only one exception, (Chart 1).

**Table 2. The total number of participants and categories of subjects according to the smoking habits**

Group of industrial workers	Non-smokers		Smokers		Total	
	N	%	N	%	N	%
Obilić surface coal seam/power plant	34	56.9	26	43.1	60	100
Obilić -gasification	24	39.7	36	60.3	60	100
Leposavić processing of lead & zinc concentrates	7	22.9	23	77.1	30	100
Magura-Magnesite mine	12	38.5	18	61.5	30	100
Ajvalija – cave exploitation	42	35.3	78	64.7	120	100
"Trepča" - lead and zinc smelter	22	37.1	38	62.9	60	100
"Ramiz Sadiku" - control group	26	43.6	34	56.4	60	100
$X^2$ -test	$X^2=16.23, p < 0.05$					



**Chart 1. Histamine concentration (µg/ml) in the sputum of groups of participating workers**

The analysis of respiratory gases partial pressures in arterial blood has shown a difference between workers at concentrate processing in Leposavić (lead and zinc concentrate processing). Differences were found by analysis of variance (One Way ANOVA), along with statistical significance at the level ( $p < 0.001$ ).

As to the values for pH among certain groups, we didn't find significant differences ( $p > 0.05$ ). But, the values of partial pressure in capillary blood for  $PaO_2$  and  $PaCO_2$  to exposed workers and control group workers we got significant statistical differences ( $p < 0.001$ ). The Chart 2 shows values for partial pressure in capillary blood ( $PaO_2$ ) which was the lowest to workers in Leposavić 8.91 kPa (SD 6, 0), whereas the highest was to workers in control group RS 10.04 kPa (SD 5, 3). Partial pressure in capillary blood ( $PaCO_2$ ) was the lowest to the workers in Leposavić 4.53 kPa (SD 2, 6), and the highest was to participants workers from the mine Hajvalija 5.01 kPa (SD 5, 4).

Results of spirometry parameters for FVC (L) and  $FEV_1$  (L) was at the level of statistical significance of ( $p < 0.0001$ ) for the workers participants in relation to their workplaces, while as to the category of smokers and nonsmokers, with exception of a worker smoker at the mine

Hajvalia ( $p < 0.05$ ), to the other groups of exposed workers we did not obtained statistically significant differences ( $p > 0.05$ ) Chart 3.

Values for Tiffneau Index in relation to workplaces were statistically significant at the level ( $p < 0.001$ ), while for the category of workers smokers and nonsmokers, there were no significant differences for the Tiffneau Index ( $p > 0.05$ ).

While reviewing direct indicators for pulmonary function such as resistance in breathing paths ( $R_t$ ), intrathoracic gas volume (ITGV) and specific resistance ( $SR_t$ ), significant differences in relation to various workplaces have been shown.

Comparability of values for  $SR_t$  found at all participating groups, through analysis of variance, significant statistical difference has been obtained ( $p < 0.001$ ) between the value of  $SR_t$  (specific resistance in breathing paths) in exposed groups of miners in relation to the nature of workplace. Extremely low value of  $SR_t$  was recorded at participating workers in Obilić open pit mines (1.1 value), but concerning the category of smokers and non-smokers, we didn't find any significant statistic differences in all basins was ( $p > 0.05$ ) Chart 4.

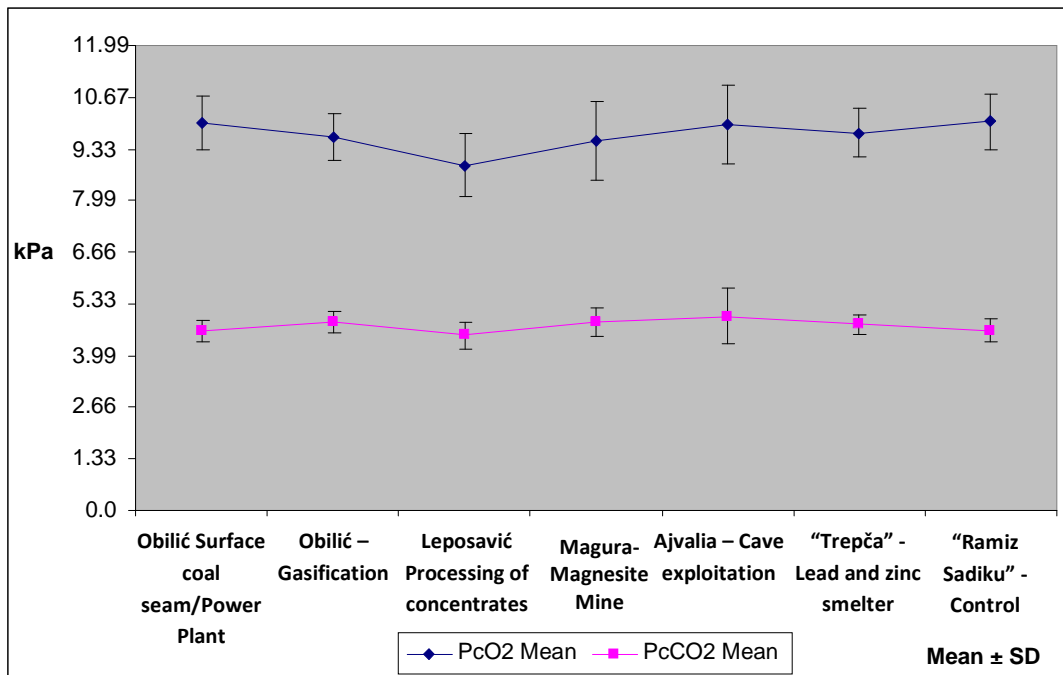


Chart 2. Partial pressures of respiratory gases

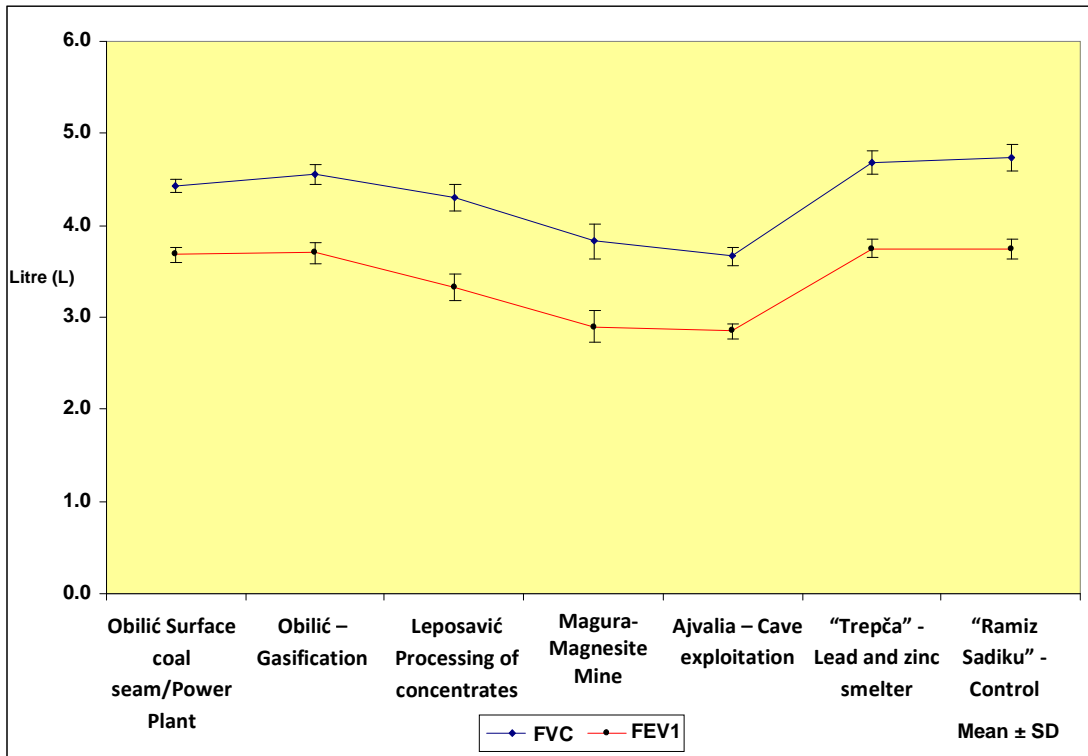


Chart 3. Lung function parameters for the examined working units at industrial pools in Kosovo

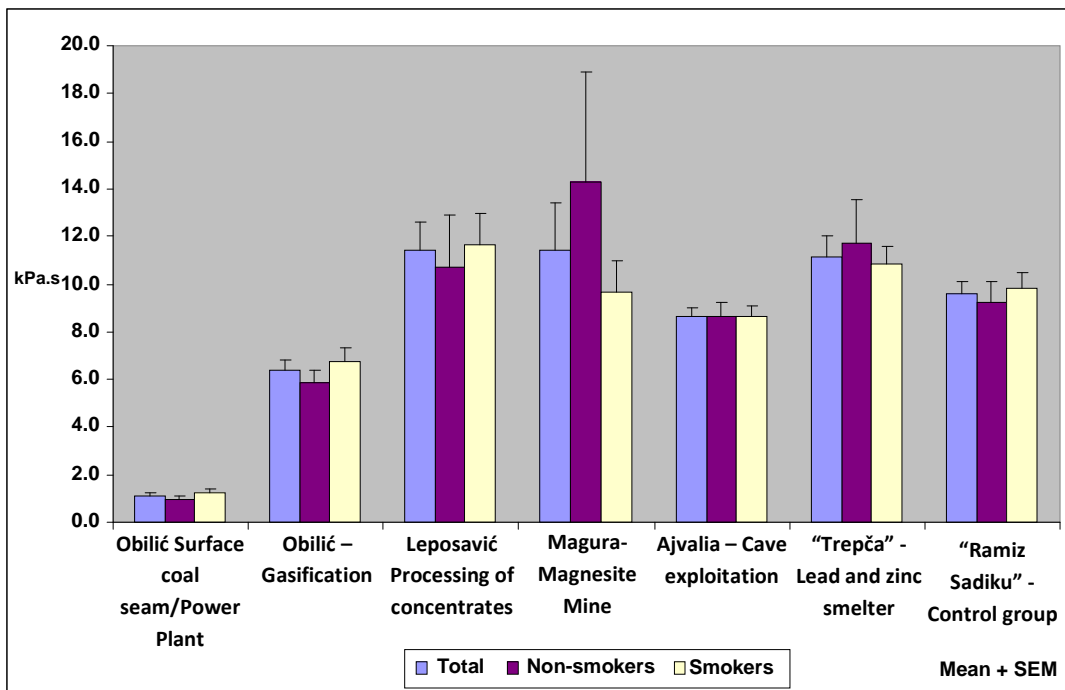


Chart 4. SRt (kPa.s) for participants by groups, as well as the categories for smokers and non-smokers



#### 4. DISCUSSION

Results of the participants' respiratory tract analysis have shown the presence of changes which could be placed in direct link between cause and effect with long-term breathing pollutants at the work place. Examined groups were not significantly different by social, anthropologic, cultural characteristics, which could significantly change the results of measured and examined parameters. Smokers comprised approximately 60% of each group, so regarding this habit the groups were not significantly different. This should be particularly stressed because examined parameters were disproportionally different, although participants have smoked for several years, along with simultaneously inhaling pollutants from their workplaces. The exposed group consisted of participants in the study who worked in places where they were exposed to pollutants such as vapours, gases, dusts and fumes (VGDF). While the workers who represented the control group in our examinations considering that they have not been exposed to any of the pollutants which were a characteristic for the groups exposed to industrial basins in question. Increased COPD risk, and increased COPD mortality, has been observed among workers exposed to "vapours, gases, dusts, and fumes" (VGDF) [10-12]. Both large and small airway effects from VGDF exposures are suggested in the literature [13]. Increased COPD risk has been associated with some specific occupational exposure agents, including: coal dust [14]; silica [14]; welding and cutting gases and fumes [15,16]; Epidemiology researches carried out with the aim to examine the prevalence of COPD, especially in the last decades have shown that factors contributing to larger prevalence of this illness lead to inability to work [17-19]. Factors responsible for developing pulmonary changes are: smoking, air pollution in community environment, particularly in larger industrial centres, air pollution at the workplaces with activities where intensive air pollution comes from gases, dust and smoke, which are released in the working process, unfavourable climate conditions [20,21]. Chronic obstructive bronchitis and its consequences in many countries are amongst leading cause of death. Unfortunately, there are not accurate data available yet regarding prevalence of this illness in Kosovo and in south-eastern Balkans. The data on regular health statistics very often is not reliable, because, in addition to adopted diagnostic criteria, this illness is inadequately recorded and diagnosed. As a result, chronic bronchitis

prevalence is best detected by specific epidemiology researches of certain population groups [22,23]. This study gave the importance to sulphur dioxide effect and other accompanying noxious elements at the lead and zinc smelters as well as lead and zinc concentrate processing, powdered noxious elements released during lead and zinc ore exploitation, fine dust released at surface coal mines, gasification process at power plant with abundant gases of sulphur dioxide, nitrous oxide etc. as well as processing magnesite ore which all could be the cause of chronic obstructive pulmonary disease occurrence. Partial pressures of blood, and increased histamine concentration in the sputum of exposed group of participants in relation to control group, we obtained significant statistical differences at the level ( $p < 0.001$ ). Partial pressure of ( $\text{PaO}_2$ ) the lowest was to the participants of Leposavić 8.906 kPa, while the highest was to the participants of control group 10.039 kPa. Partial pressure of ( $\text{PaCO}_2$ ) was the lowest to the participants of Leposavić 4.533 kPa, while the highest was to the participants of Ajvalia 5.013 kPa. The FVC and  $\text{FEV}_1$  was statistically significant ( $p < 0.0001$ ) related to their workplaces, with one exception of a worker smoker at the mine Ajvalia ( $p < 0.05$ ), to the other groups of exposed workers we did not obtained statistically significant differences ( $p > 0.05$ ). Tiffneau Index in relation to workplaces were statistically significant ( $p < 0.001$ ), while for the category of workers smokers and nonsmokers, there were no significant differences for the Tiffneau Index ( $p > 0.05$ ). The value of  $\text{SRt}$  was statistically significant ( $p < 0.001$ ) in relation to the nature of workplace.

#### 5. CONCLUSIONS

1. This research was carried out among workers exposed to "vapours, gases, dusts, and fumes" (VGDF), where particular importance was given to the effect of sulphur dioxide, gasification process known for abundant gases of sulphur dioxide, sulphur trioxide, nitrous oxide, released fine dust at surface coal mine, as well as processing of magnesite ore all of which could be the cause for occurrence of COPD.
2. Measurements of histamine concentration in sputum of participants of all exposed groups have shown statistical significance ( $F=10, 59, p < 0.0001$ ), compared to control group of workers. However, differences were noted between the exposed groups

themselves in the total number of exposed workers where the highest determined values of histamine were as follows Trepca>Leposavic> Magura>Ajvalia. While in only one case in the category of exposed smoking workers in Leposavić at the significant level of ( $p<0.05$ ).

3. "Warm technological plants" for lead and zinc processing generate primary inflammatory reaction of respiratory system in the first place, respectively over the time it causes increased concentration of histamine in sputum as an inflammatory mediator. By which we may conclude that there is a link between the level of pulmonary function damage and increased histamine concentration in the sputum. Increased histamine concentration can also be considered as the cause of accompanying inflammatory bronchial changes as well as increased bronchial secretion and bronchial hyper-responsiveness.
4. We believe that histamine concentration in sputum of smoking participants is always higher than at non-smoking participants, although in our case it was shown only at Leposavic workers ( $p<0.05$ ). Nevertheless, we believe that an additional provoking possibility exists from smoking effects in straining the inflammatory processes where histamine as one of the substances released in these reactions necessarily contributes to creation of extra conditions for strengthened interaction of smoke with harmful pollutants at workplace, for what more research is needed in the future.
5. Significant values of histamine concentration determined in the sputum of exposed workers in relation to control group can be the cause of appearance of more considerable obstructive changes in airways being a characteristic for exposed groups, referring to obtained spirometric parameters, such as  $FEV_1$  which are at threshold or lower than 80%, where values of Tiffeneau Index ( $100 \times FEV_1/FVC$ ) are at threshold or lower than 70%.
6. By fall of partial pressure ( $PaO_2$ ) respectively raise of partial pressure ( $PaCO_2$ ) from one side, and increased histamine concentration in the sputum of exposed group of participating workers in relation to control group, statistical significance was ( $p<0,001$ ). Nonetheless, it is not just casual that values of partial pressure ( $PaO_2$ ) was the lowest to the

workers in Leposavić 8.91 kPa (SD6.0), while the highest was to the control group workers RS 10.04 kPa (SD5.3). Furthermore partial pressure ( $PaCO_2$ ) was the lowest to the workers in Leposavić 4.53 kPa (SD2.6), while the highest was to the examined workers from the mine in Ajvalia 5.01 kPa (SD5.4). Results of histamine in sputum of smoking workers in Leposavić suggest a potential synergic interaction of smoke and pollutants at workplace.

7. In this case control study a particular emphasis was given to the presence of histamine in sputum of participants and correlation with direct parameters of pulmonary functions at exposed workers. This is attributed to changes of specific resistance and intrathoracic gas volume (SRT, ITGV), and it is closely related to nature of workplaces. However, no changes have been noticed for smoking participants. It would be preferable to conduct testing of pulmonary hyper-responsiveness in such studies.
8. As a long-term measure directed toward preventing respiratory tract damage to the workers exposed to pollutants from industry – mining areas, regular monitoring of their concentration at the surrounding area is recommended, and microenvironment at the workplaces, technological processes of "hermetization" is needed.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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