

Biological Monitoring Among Workers Exposed to Inorganic Lead and Its Compounds

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Abstract

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Key words: Blood lead level; aminolevulinic acid dehydratase; aminolevulinic acid; biological markers; occupational exposure; toxicity.

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Objective: To explore the association between lead biomarkers and their deviations in the circumstances of occupational exposure, and influence of life style factors.

Material and Methods: We performed cross-sectional study using 60 workers occupationally exposed to lead compared with 60 controls. All examinees were assessed by Questionnaire, and laboratory testing concerning blood lead level (BLL), activity of delta-aminolevulinic acid dehydratase (ALAD) in blood, concentration of delta-aminolevulinic acid (ALA) and coproporphyrin in urine, reticulocytes and erythrocytes with basophilic stippling (EBS).

Results: The mean values of BLL and ALA were significantly higher, and mean ALAD activity was significantly lower in lead workers than in controls. Lead workers also had a higher rate of abnormal BLL, ALAD, and ALA, significant for BLL and ALAD. The average BLL values among exposed workers and controls in men were significantly higher. There was strong inverse correlation between distribution of ALAD values in exposed workers due to their BLL values. Significant correlation with mean ALAD values was shown for alcohol consumption, form of compounds, and use of protecting equipment, whereas with mean BLL values was shown for age, gender, exposure duration, smoking, and alcohol consumption.

Conclusion: The data confirmed the association between occupational exposure and lead biomarkers abnormalities.

Introduction

Lead is a naturally occurring element used by mankind almost since the beginning of its civilization. Human activities contributed for wide environmental spreading of the lead within air, water, soil, plants, animals, and manmade constructions [1]. Therefore, lead exposure is an international and global issue. Many developing countries still have problems associated with mining, smelting and refining of lead, as well as the use of leaded gasoline in motor vehicles, so exposed individuals could receive substantial lead exposure [2].

The contact with lead and its compounds within different conditions and circumstances can result in acute and chronic occupational lead poisoning, and non-occupational lead poisoning [3].

Within the last few decades, concentrations of lead in the atmosphere have been significantly decreased all over the world, having in mind the fact that more and more countries have chosen, and obliged themselves, to remove tetraethyl lead as additive from gasoline [4]. Workers engaged in the industries for lead smelting, refining, and manufacturing products containing lead

experience the highest and perhaps the most prolonged occupational exposures to lead [5].

Biological markers (biomarkers) are specific substances which can be identified and measured in the human biological media [6]. There are three kinds of biomarkers: biomarkers of exposure, biomarkers of effect (specific and non-specific) and biomarkers of susceptibility [7]. Biomonitoring for human exposure to lead reflects an individual's current body burden, as a function of recent and/or past exposure [8]. Adequate selection and measurement of biomarkers of lead exposure is very important for health care management purposes, public health decision-making, and future primary prevention activities [9]. It is well known that lead affects several enzymatic processes responsible for hem synthesis [10]. It directly inhibits the activity of the cytoplasmic enzyme delta-aminolevulinic acid dehydratase (ALAD), resulting in a negative exponential relationship between ALAD and blood lead level (BLL). There is also depression of coproporphyrinogen oxidase, leading to increased coproporphyrin activity [11]. These effects also result in modifications of delta-aminolevulinic acid (ALA) concentrations in urine (ALA-U), blood (ALA-B) and plasma (ALA-P), and coproporphyrin in urine (CP) [12]. Levels of these various metabolites in biological fluids may be used to facilitate diagnose of lead poisoning as complementary information to BLL, and are described as biomarkers for toxic effects of lead [13].

Since the beginning of the technological process in the lead melting plant in the municipality of Veles, many problems concerning occupational lead exposure have been raised. The melting plant uses lead and zinc sulfide and oxide concentrates, which are transported by the system of bands into the Sinter, while coke is placed in the pre-heaters in the facility called "high furnace" for charge preparation. The ore is sintered and fried in the Sinter machine, and then further crumbled into smaller granules. Alternately charging of sinter and coke is performed in the "high furnace" part, which results in production of lead and zinc after being refined. Some previous studies already explored the role of occupational exposure in lead toxicity development, which clearly impose the necessity of additional research in this area [14]. The aim of this study was to explore in depth the association between lead biomarkers of exposure and effect and their deviations in the circumstances of occupational exposure, and to examine possible influence of life style factors on biomarkers, as well as on the expression of lead toxic effects.

Material and Methods

Study design

We performed cross-sectional study using examined group of 60 workers occupationally exposed to inorganic lead compared with a group of 60 controls at the Institute for Occupational Health of RM, Skopje. The examined and control groups were the same cohorts that were have used in our previous study [14]. All study subjects were assessed by a specially designed Questionnaire for lead exposure and toxic effects assessment, and toxicological laboratory testing concerning BLL, as a biomarker of exposure, and activity of ALAD in blood, concentration of ALA in urine, coproporphyrin concentration in urine, reticulocyte count, and count of erythrocytes with basophilic stippling (EBS) as biomarkers of lead toxic effects.

Questionnaire for lead exposure and assessment of possible toxic effects

Within the study we have used a specially designed questionnaire that contained demographic data, job history (occupation, workplace, duration of exposure, and total duration of employment, workplace hazards), smoking status (current smoker, ex-smoker, non-smoker, cigarettes per day, duration of smoking), alcohol consumption (quantity and duration), risk information, work organization, absenteeism, and use of preventive workplace equipment. The questionnaire was helpful in receiving data about the existing occupational risks in exposed workers, association between lead exposure and lead biomarkers deviation, as well as possible influence of life style factors on biomarkers and expression of lead toxic effects.

Subjects

The exposed group consisted of 60 lead workers engaged in production and refining in the lead smelting plant in Veles, occupationally exposed to inorganic lead; 51 men and 9 women, aged 45.1 ± 7.6 years, total employment duration of 22.8 ± 9.2 years, exposure duration or years on the current workplace of 19.2 ± 7.8 years. The control group consisted of 60 workers employed in different services and industries in Veles, without any occupational exposure to lead; 50 were men and 10 women, aged 42.2 ± 8.7 years, with total employment duration of 18.9 ± 9.7 years.

The groups were matched in demographic characteristics, environmental exposure, total duration of employment, smoking habit, and alcohol consumption.

All of the study subjects volunteered for the research and gave their signed consent. The study was approved by the bioethical committee and performed according to the Declaration of Helsinki. The basic criteria for determining occupational risk factors in the study were data collected by the questionnaire for lead exposure and toxic effect assessment. Nobody among the study subjects was diagnosed nor with occupational chronic lead poisoning, neither with any other disease or disorder associated with exposure to inorganic lead or its compounds. The limitation of the study is the lack of data about environmental lead exposure.

Laboratory testing

Blood lead level was determined using PERKIN ELMER 4100 HGA 700 atomic absorption spectrometer (AAS) with an auto-sampler AS-70, in the Institute for Public Health of RM-Skopje. For this purpose, a venous blood of about 2 mL was taken into a sterile vacutainer with K₂EDTA 1.5 mg/mL of blood and transported at +4 °C on the same day. The extraction of lead was made by a mixture of HNO₃ and HCl using a microwave furnace PAAR PHYSICA-PERKIN ELMER [15, 16, 17]. The method detection limit is on the order of about 1 ng/L. Determination of biomarkers of lead effect was performed at Institute for Occupational Health of RM, Skopje by venous blood and urine spot samples. ALAD activity was determined in 0.2 mL venous blood samples with heparin by the spectrophotometric method within 24 hours of sampling because of its instability. In order to facilitate a reaction between ALAD and its substrate ALA, an ALA substrate was added to the haemolysed blood, which resulted in the forming of porphobilinogen. ALAD activity was quantified by porphobilinogen, which was previously determined by spectrophotometry at 555 nm after adding p-dimethyl amino benzaldehyd [18, 19]. ALA concentration in the urine was determined by condensing 1 mL spot urine samples with acetyl acetone into a pyrrole compound. This pyrrole compound together with paradimethy-aminobenzaldehyd gave a red colored complex that was determined by spectrophotometric method at 553 nm [20]. Coproporphyrin concentration in urine spot samples was determined by spectrophotometric absorption measurement at 401 nm of the urine extract by ether and HCl [19]. Reticulocyte count was determined in blood sample [21], and count of erythrocytes with basophilic stipplings (EBS) was carried out using two mixtures: 2 g boric acid + 1 g methylen blue and 0.28 g NaOH in 100 mL of distilled water. This mixture was used to paint the blood sample on the microscopic glass, fixed and analyzed by microscope [22].

Statistical analysis

We have analyzed the obtained data using descriptive and inferential statistical methods by the statistical package STATISTICA for Windows release 7. Descriptive statistical analysis included tables and figures containing statistical series according to the defined variables. Continuous variables were expressed as mean values with standard deviation (SD), while nominal variables as numbers and percentages. The chi-square test (or Fisher's exact test) was used for testing differences in frequency. The differences between two groups and multiple group means were compared by the ANOVA. Regression analysis was used to determine the correlation of continuous variables, by using them as dependent variables, with several independent variables that are considered as possible confounders. Statistical significance was considered when *P*-value was below 0.05.

Results

Characteristics of the study subjects are given in Table 1.

Table 1: Characteristics of the study subjects [14].

Variable	Exposed workers (n=60)	Controls (n=60)
Sex / M/F ratio	5.6	5.0
Age / yrs	45.1 ± 7.6	42.2 ± 8.7
BMI / kg m ²	25.3 ± 3.4	26.4 ± 3.6
Duration of employment/yrs	23.1 ± 7.2	18.9 ± 9.7
Duration of exposure/yrs	18.8 ± 7.5	/
Daily smokers	25 (41.6 %)	26 (43.3 %)
Smoking experience/yrs	10.8 ± 11.5	11.9 ± 12.1
Cigarettes per day	8.1 ± 10.2	11.1 ± 14.4

Numerical data are expressed as means with standard deviations; the frequency of active smoking as number of subjects with certain variable; M: male; F: female; BMI: body mass index.

Mean values of biological markers of exposure and effect are given in the Figure 1.

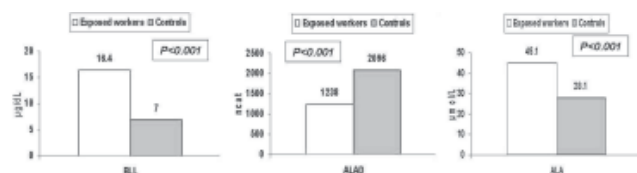


Figure 1: Mean values of BLL, ALAD and ALA among exposed workers and controls. *Compared by independent-samples t-test; BLL - blood lead level; ALAD - delta-aminolevulinic acid dehydratase; ALA - aminolevulinic acid.

The mean values of BLL and ALA were significantly higher, while mean values of ALAD were

significantly lower in workers occupationally exposed to inorganic lead than in controls ($P<0.05$).

Higher prevalence of BLL, ALAD and ALA deviation was obtained in exposed workers, but statistical difference was registered for BLL and ALAD. The percentage of coproporphyrine, reticulocytes, and BPE deviation were equal or even lower than those in controls ($P>0.05$) (Figure 2).

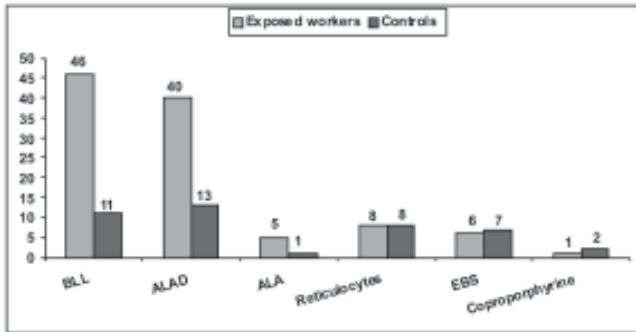


Figure 2: Deviation in biological markers in exposed workers and controls. Data are expressed as number of subjects with certain variable; Data are tested by chi-square test; * Statistical significance; BLL - blood lead level; ALAD* - delta-aminolevulinic acid dehydratase; ALA - aminolevulinic acid; EBS - erythrocytes with basophilic stippling.

Figure 3 shows distribution of numbers of exposed workers having BLL in certain intervals with particular range ($\mu\text{g/dL}$).

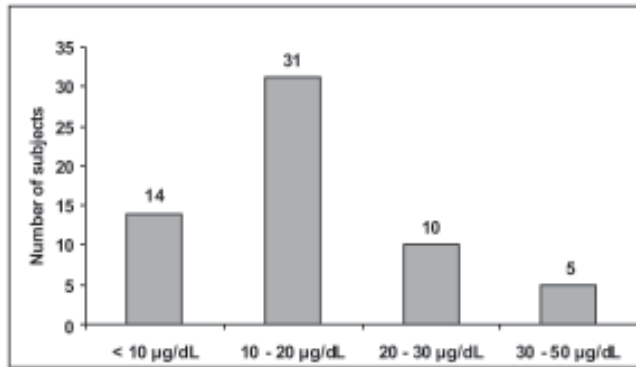


Figure 3: The distribution of exposed workers with respect to different BLL intervals. BLL - blood lead level.

The figure shows that most of the exposed workers (31) have BLL within the range 10-20 $\mu\text{g/dL}$.

Figure 4 presents the distribution of BLL values and average ALAD activity values according to the duration of the total employment and duration of employment on the actual workplace in exposed workers and controls.

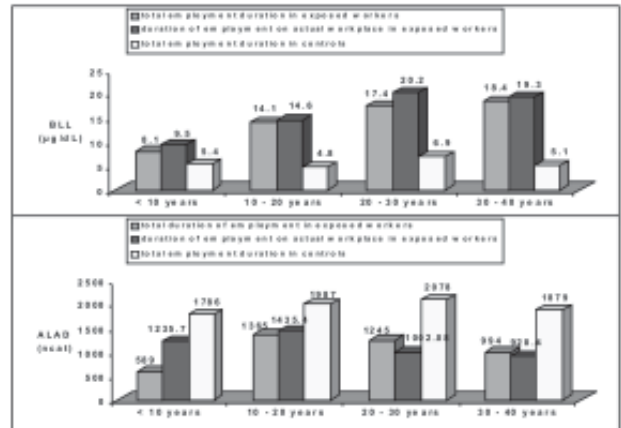


Figure 4: Distribution of BLL values and average ALAD activity values according to the total employment duration and duration of employment on the actual workplace among exposed workers and controls. BLL - blood lead level; ALAD - delta-aminolevulinic acid dehydratase.

The figure shows that increasing of the total employment duration among exposed workers contributes for the increase of the average BLL values. The average BLL values were also higher with longer duration of employment on the actual workplace in exposed workers. The figure presents no certain regularity in the decrease of ALAD activity with increase of total duration of employment in exposed workers, and with the duration of employment on the actual workplace. There is no regularity both in BLL and ALAD in controls according to total employment duration.

Figure 5 gives an overview of the distribution of average BLL values and average ALAD activity due to the gender among exposed workers.

The average BLL values among exposed workers in men were significantly higher compared to those in women ($P<0.05$). The average values for ALAD activity among exposed workers were significantly lower

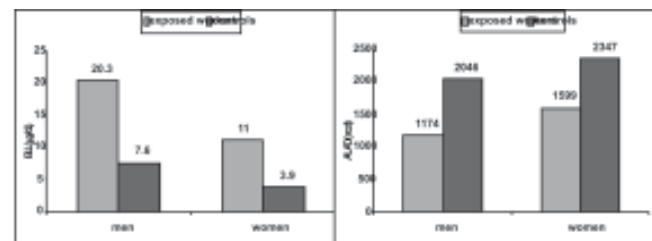


Figure 5: Distribution of average BLL values and average ALAD activity according to gender among exposed workers and controls. BLL - blood lead level; ALAD - ä-aminolevulinic acid dehydratase; * Statistical significance; BLL (*both exposed workers and controls); ALAD (*exposed workers).

in men compared to those in women ($P<0.01$). The average BLL values were significantly higher in men, with no significance found for average ALAD activity according to gender in controls.

Figure 6 presents distribution of average values for ALAD activity and ALA according to the BLL average values in exposed workers, given by intervals.

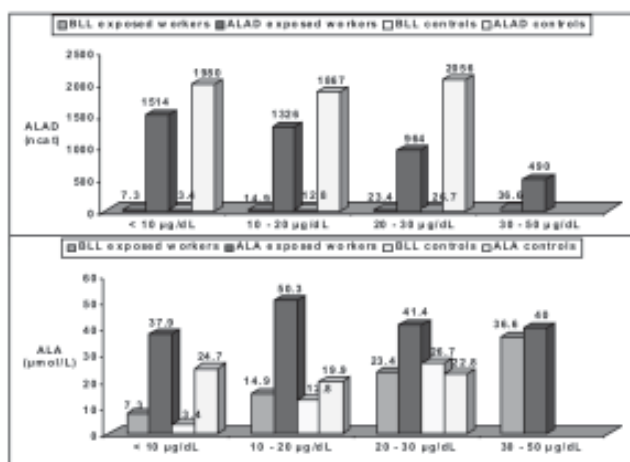


Figure 6: Distribution of average values for ALAD activity and ALA according to the BLL average values in exposed workers and controls by intervals. BLL - blood lead level; ALAD - delta-aminolevulinic acid dehydratase; ALA - aminolevulinic acid.

There was strong inverse correlation ($P<0.01$) between distribution of ALAD activity values according to average BLL values expressed in intervals among exposed workers. There was a clear positive correlation ($P<0.05$) between the values of ALA among exposed workers in accordance to their BLL values in intervals. No correlation was found between distribution of ALAD activity and ALA due to average BLL values in intervals among controls.

Figure 7 gives an overview of the distribution of average ALAD activity values and average BLL values due to the smoking habit and alcohol consumption in exposed workers.

There was significant difference ($P<0.05$) in the average values of ALAD activity according to alcohol consumption among exposed workers, and no significant difference ($P>0.05$) in average ALAD activity values according to the smoking status among exposed workers, although ALAD activity was lower in smokers compared to non-smokers.

There was no significant difference ($P>0.05$) in the average BLL values due to the smoking status and

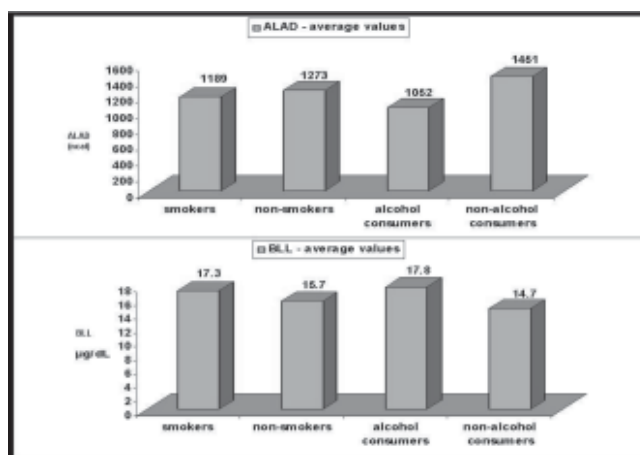


Figure 7. Distribution of average ALAD activity values and average BLL values due to the smoking habit and alcohol consumption in exposed workers. BLL - blood lead level; ALAD - delta-aminolevulinic acid dehydratase.

alcohol consumption habit among exposed workers. Analysis showed that most of the smokers and alcohol consumers had BLL values in the interval 10-20 µg/dL.

Table 2: ANOVA - Univariate Tests of Significance for ALAD and BLL in exposed workers.

	ALAD				
	SS	Degree of freedom	MS	F	p
Gender	1381526	1	1381526	3.4316	0.069051
Duration of exposure/years	11097312	21	528443	1.4728	0.146638
Smoking habit	101881	1	101881	0.2399	0.626115
Smoking experience/ylrs	6370787	17	374752	0.85723	0.623059
Cigarettes per day	1568205	3	522735	1.2638	0.295638
Alcohol consumption	2375274	1	2375274	6.1623	0.015967*
Al. consumption experience/ylrs	6574488	15	438299	1.06212	0.416236
Form of chemicals	8503440	6	1417240	9.4101	0.001240**
Work influence on health	1185521	1	1185521	2.01528	0.176171
Use of personal protecting equipment	2419910	1	2419910	4.78267	0.045003*
	BLL				
	SS	Degree of freedom	MS	F	p
Gender	301.716	1	301.716	4.41940	0.039885*
Duration of exposure/years	2234.228	21	106.392	1.9943	0.031475*
Smoking habit	38.37	1	38.37	0.5270	0.470801
Smoking experience/ylrs	1985.064	17	116.768	2.1544	0.022072*
Cigarettes per day	184.441	3	61.480	0.8445	0.475352
Alcohol consumption	146.83	1	146.83	2.0697	0.155621
Al. consumption experience/ylrs	1906.213	15	127.081	2.3741	0.013261*
Form of chemicals	181.966	6	30.328	0.71061	0.649524
Work influence on health	11.710	1	11.710	0.2942	0.595506
Use of personal protecting equipment	20.320	1	20320	0.51798	0.482769

Level of statistical significance: * $P<0.05$; ** $P<0.01$; Tested by ANOVA; ALAD - delta-aminolevulinic acid dehydratase.

Table 2 gives univariate tests of significance for mean ALAD activity values and mean BLL values in exposed workers tested by ANOVA.

Significant correlation with mean ALAD activity values was shown for alcohol consumption ($P<0.05$), form of chemicals used at the workplace (lead compounds) ($P<0.01$), and use of personal protecting equipment ($P<0.05$). Significant correlation with mean BLL values was shown for gender ($P<0.05$), duration of exposure/years (without grouping) ($P<0.05$), smoking experience/years ($P<0.05$), and alcohol consumption/years ($P<0.05$).

Table 3. Multiple linear regression analysis for BLL, ALAD and ALA in exposed workers.

	BLL		ALAD		ALA	
	Beta	P-level	Beta	P-level	Beta	P-level
Age	-2.62446	0.121232	2.95081	0.001385**	-3.44076	0.003855**
Duration of employment/hrs	3.36294	0.104570	-3.62681	0.001274**	3.47857	0.008086**
Duration of exposure/hrs	-0.11792	0.823212	-0.03764	0.827764	0.14886	0.564336
Smoking habit	-0.10960	0.784101	0.43036	0.017980*	-0.48969	0.043767*
Smoking experience/hrs	-0.48060	0.847952	2.88417	0.014055*	-1.58565	0.225382
Cigarettes per day	-0.65652	0.418811	0.55742	0.071449	-0.79529	0.077702
Alcohol consumption	0.71095	0.785622	-3.12869	0.011965*	1.44650	0.279679
Alcohol consumption experience/hrs	-0.59854	0.450921	0.82990	0.018101*	-1.87427	0.003162**
Form of chemicals	-0.17357	0.716590	0.02378	0.878702	0.53902	0.056079
Work influence on health	0.00753	0.992137	-0.44036	0.123838	-0.11628	0.753341
Use of personal protecting equipment	-0.18397	0.810731	-0.10128	0.689193	0.31437	0.411612
	BLL		ALAD		ALA	
Multiple R	0.821937		0.9824		0.96160	
Multiple R ²	0.675580		0.9651		0.92468	
Adjusted R ²	-0.038144		0.8884		0.75898	
F(11,5)	0.946556		12.5838		5.58052	
ρ	0.566242		0.0059**		0.03525*	

Level of statistical significance: * $P<0.05$; ** $P<0.01$; Tested by Multiple Linear Regression Analysis; BLL - blood lead level; ALAD - delta-aminolevulinic acid dehydratase; ALA - aminolevulinic acid.

To control for confounding factors influencing the BLL, ALAD, and ALA, the possible influencing factors (age, duration of employment/years, duration of exposure/years, smoking habit, smoking experience/years, cigarettes per day, alcohol consumption, alcohol consumption experience/years, form of chemical, work influence on health, use of personal protecting equipment) that could affect BLL, ALAD, and ALA were used for multiple linear regression analysis. Table 3 shows multiple linear regression analysis for BLL, ALAD and ALA in exposed workers.

Statistical significance was determined for ALAD (age, duration of employment/years, smoking habit, smoking experience/years, alcohol consumption, alcohol consumption experience/years), and ALA (age, duration of employment/years, smoking habit, alcohol

consumption experience/years), while no significance was found for BLL.

Discussion

Even though perhaps lower than usual value for lead smelters, the average value of BLL in exposed workers was statistically significant ($P=0.000$) compared to measured average value of BLL in controls, which must be taken into account according to occupational exposure. The relatively low average BLL value, in some extent, was due to the proper use of personal protective equipment, and relatively good working conditions within the exposed workers. The 95th percentile for BLL of 5.20 $\mu\text{g/dL}$ for adults aged 20 years and older was obtained by the data collected as part of the US National Health and Examination Survey (NHANES) [23]. Many other studies have reported statistically significant associations between BLLs and various adverse health effects. However, some of them have been statistically weak, with a relatively small magnitude of the effect. According to Hu et al. [24], such association weaknesses may occur because BLL is not a sufficiently sensitive biomarker of exposure or because the relationships involved are biologically non-relevant and found mostly because of an uncontrolled confounding factor [25]. Moreover, in view of the kinetics of lead distribution within the body (the cycle between blood, bone, and soft tissues), differentiation of low-level chronic exposure from a short high-level exposure is not possible on the basis of a single BLL measurement [24]. Therefore, there is renewed and increased interest in alternative biomarkers that could facilitate better diagnosis and understanding of the lead exposure extent. Such alternatives include lead determinations in plasma/serum, saliva, bone, teeth, feces, and urine [26].

Since lead is still used in Macedonia as a gasoline additive (even though lately in trace quantities of tetraethyl lead), there is still increased risk in urban areas which also may be connected to such high values of BLL. Values of BLL and ALAD depend on many factors, including genotype variants but also environmental factors [27].

The average value of ALAD in exposed workers was statistically significant ($P=0.000$) compared to average value of ALAD in controls.

Our data showed that increasing of the total employment duration as well as duration of employment on the actual workplace among exposed workers

contributes for the increase of the average BLL values. On the other hand, there was no certain regularity in the decrease of ALAD activity with increase of total duration of employment or increase of the duration of employment on the actual workplace in exposed workers. Similar findings had some other studies showing increase in biomarkers of lead effect with age and duration of employment [28], unlike some other with no significant association found between either BLL or erythrocyte ALAD activity and duration of service [29].

The average BLL values among exposed workers in men were significantly higher compared to those in women ($P < 0.05$), whereas average values for ALAD activity among exposed workers were significantly lower in men compared to those in women ($P < 0.01$). In controls, the average BLL values were significantly higher in men, but no significance was found for average ALAD activity according to gender. Kemal et al [28] in the analysis to assess the impact of sex on urinary delta-ALA levels among workers in lead acid battery repair units of transport service enterprises in Ethiopia, failed to show any significant sex-related differences, although levels in males tended to increase than females. Interestingly, Popovic et al. recently reported very different long-term lead kinetics between men and women, with pre-menopausal women appearing to retain lead more avidly or release lead more slowly compared to postmenopausal women and men [30].

Strong inverse correlation ($P < 0.01$) was found between distribution of ALAD activity values, and a clear positive correlation ($P < 0.05$) between the values of ALA according to average BLL values expressed in certain intervals among exposed workers, confirming the role of increased BLL values in development of ALAD and ALA deviations. Some studies confirmed the role of different chemical properties of lead in distributional patterns of the metal in different blood components (whole blood or plasma), and its influence on observed correlation between BLL and ALAD activity [31].

There was significant difference ($P < 0.05$) in the average values of ALAD activity according to alcohol consumption among exposed workers, and no significant difference in average ALAD activity values according to the smoking status among exposed workers, although ALAD activity is lower in smokers compared to non-smokers. This is similar with findings of Kemal et al [28]. No significant difference was registered for the average BLL values due to the smoking status and alcohol consumption habit among exposed workers, which is similar to the findings of Karita et al [32] showing that

length of service, smoking, face washing and wearing gloves have no significant correlation with the BLL.

When the analysis of variances (ANOVA) was performed for ALAD and BLL in exposed workers, the results showed significant correlation between mean ALAD activity values and alcohol consumption ($P < 0.05$), form of chemicals used at the workplace (lead compounds) ($P < 0.01$), and use of personal protecting equipment ($P < 0.05$). Significant correlation with mean BLL values activity was shown for gender ($P < 0.05$), duration of exposure/years ($P < 0.05$), smoking experience/years ($P < 0.05$), and alcohol consumption/years ($P < 0.05$). These findings confirm the role of exposure duration, gender, but also life style factors (smoking habit and alcohol consumption) and workplace organization among exposed workers in the incidence and development of deviations in the mean values of lead biomarkers. Mehdi et al [33] in the survey about the levels of some trace metals and related enzymes in workers at storage-battery factories in Iraq, using ANOVA, found significant negative correlations between BLL and ALAD, significant positive correlation was between BLL and duration of exposure, and no correlation between of BLL to age, smoking and alcohol consumption.

Using multiple linear regression analysis, statistical significance was determined for ALAD (age, duration of employment/years, smoking habit, smoking experience/years, alcohol consumption, alcohol consumption experience/years), and ALA (age, duration of employment/years, smoking habit, alcohol consumption experience/years), while no significance was found for BLL among exposed workers. This means that examined covariates or confounders (age, duration of employment, smoking habit, smoking and alcohol consumption experience) influence on the occurrence and extent of the ALAD and ALA deviations, as a biomarkers of lead effect. Examination of the possible impact by confounding factors showed no significant influence on the total BLL, as a specific biomarker of lead exposure. Occupational history of lead exposure and its duration, in multivariate logistic regression analyses, was found to be the major risk factors for high blood lead in both gender among general population in Taiwan apart from drinking water and factories in the neighboring areas, in the study of Chu et al [34].

However, our present study has some limitations. It has relatively small number of subjects, which may have certain implications on interpretation of data. Interpretation may also be affected by the fact that both exposed and control workers live in the environment with

emissions of the lead melting plant in Veles, and finally, the study lacks specific environmental monitoring data of lead workplace exposure, which may be relevant for evaluating the deviation in specific lead biomarkers and adverse health effects. On the other hand, this study is among the few ones, trying to assess health effects of occupational lead exposure in our country. Therefore, its strength is that by extensive examination of lead biological markers deviations, has made it possible to compare our results with other similar studies worldwide. Further investigations and continuous research in this area are necessary to better understand and interpret the issue and burden of lead toxicity. Identifying proteins prone to bind lead, its blood carriers and tissue deposition, can enable us to find appropriate, exact and accurate biomarkers of lead exposure and effect and identify susceptible individuals and groups [35].

Conclusion

As a result of the study dedicated to biological monitoring among workers exposed to inorganic lead we have managed to obtain data for the prevalence of deviation in specific biomarkers of lead exposure and effect in exposed individuals, engaged in the process of lead production and refining compared to controls, without occupational lead exposure. Also it was opportunity to further explore the relationship between occupational exposure and lead toxicity in exposed workers. Our data confirmed the associations between the specific biological markers of lead exposure and effect. On the other hand we had the chance to examine the possible difference due to certain life style factors (smoking habit and alcohol consumption), age, gender, duration of exposure, personal protecting equipment, and their influence on specific biomarkers of lead exposure and effect among exposed workers. Obtained data are helpful in recognizing the workplace preventive measures and activities in exposed individuals, intended to improvement in regulation of occupational lead exposure. Since the recognition of some life style factors, as well some intrinsic factors among exposed workers as modifiers of lead toxicity and biomarkers deviation extent, identification of susceptible individuals and population groups could improve regulation of occupational lead exposure and protect them by developing specific workplace oriented and broader public health interventions.

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