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Investigation of Beta-2 microglobulin Levels of Workers Who Exposed to Lead

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***Abstract*—**Lead is a common metal in environment both in nature and in industry because of common usage. Clinical, experimental and epidemiological many studies have proved that lead exposure causes renal damage. In our study we aimed to investigate the tubulary function marker urinary beta-2 microglobulin levels in workers who exposed to lead. A total number of 336 workers of different occupational groups who refered to Ankara Occupational Diseases Hospital toxicology polyclinic for periodical examination were included in the study and separated into two groups; group 1(n=177) and group 2 (n=159) ; whose blood lead levels were >10µg/dL and <10µg/dL, respectively. Lead levels were measured by Agilent 7700 series ICP-MS device, serum blood urea nitrogen and creatinine levels were analyzed by Vitros 5.1 FS device, beta-2 microglobulin levels in 24 hours urine were estimated by micro-ELISA method. SPSS for Windows 18 version was used for statistical analysis. Significance between groups was analyzed by Mann-Whitney U test.

Even though 24 hours urine beta-2 microglobulin median levels in the group 1 were higher than the group 2, there was not a statistically significant difference between groups (median: 0.23, 0.21, respectively p=0.713). No significant difference was found between groups by means of serum blood urea nitrogen and creatinine levels (p=0.365; p=0.130 respectively). As a conclusion we did not find a significant difference in blood urea nitrogen and creatinine levels and in beta-2 microglobulin levels in lead exposure.

***Key words*—**Lead exposure, kidney function, beta-2 microglobulin,

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I. INTRODUCTION

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Lead is a naturally occurring toxic metal found in the Earth's crust. Its widespread use has resulted in extensive environmental contamination, human exposure and significant public health problems in many parts of the world. Lead is a cumulative toxicant that affects multiple body systems such as brain, liver, kidney and bones.

Lead has been known since ancient times. It is a soft, malleable and corrosion resistant material. It was used to make water pipes, some of which are still in use today. It is used to line tanks that store corrosive liquids, such as sulfuric acid (H_2SO_4). Its high density makes it useful as a shield against X-ray and gamma-ray radiation and is used in X-ray machines and nuclear reactors. Lead is also used as a covering on some wires and cables to protect them from corrosion. Most of the lead used today is used in the production on lead-acid storage batteries, such as the batteries found in automobiles.

Important sources of environmental contamination include mining, smelting, manufacturing and recycling activities, and in some countries, the continued use of leaded paint and leaded gasoline. Lead is also used in many other products, for example pigments, paints, solder, stained glass, crystal vessels, ammunition, ceramic glazes, jewellery, toys and in some cosmetics and traditional medicines.

People can become exposed to lead through occupational and environmental sources. This mainly results from inhalation of lead particles generated by burning materials containing lead, e.g. during smelting, informal recycling, stripping leaded paint and using leaded gasoline, and ingestion of lead-contaminated dust, water (from leaded pipes), food (from lead-glazed or lead-soldered containers). The use of some traditional cosmetics and medicines can also result in lead exposure.

Lead causes long-term harm in people. Although at lower levels of exposure that cause no obvious symptoms, lead is now known to produce a spectrum of injury across multiple body systems. Lead exposure also causes anaemia, hypertension, renal impairment, immunotoxicity and toxicity to the reproductive organs. The neurological and behavioural effects of lead are believed to be irreversible (WHO).

Health effects of chronic exposure to heavy metals such as lead, cadmium, and mercury are widely documented, yet few

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data exist about the renal impact of low environmental exposure to these metals, especially lead [1-4].

Beta-2 microglobulin is a low molecular weight protein that is found in the membrane of nucleated cells. It is released to blood particularly by tumor cells and lymphocites. It can be filtrated from glomerular membrane because of its small size. Normally it is eliminated less than 1%, because of its proximal tubulary reabsorption. It increases in urine in renal tubulary diseases, nephrotoxicity, renal toxicity because of exposure to heavy metals, lymphoma, leukemia, myeloma and AIDS. Its measurement in urine can be used to assess renal tubulary injury. Toxic elements such as lead, cadmium and mercury, which cause renal tubulary injury, increase the excretion of beta-2 microglobuin [4, 5, 6].

In our study we aimed to investigate the effect of lead on kidneys in the chronic low exposure of lead. We assessed lead exposure by measuring blood lead concentrations and renal tubulary injury by measuring urinary beta-2 microglobuin levels.

II. MATERIALS AND METHODS

A total number of 336 workers of different occupational groups who refered to Ankara Occupational Diseases Hospital toxicology polyclinic for periodical examination were included in the study and separated into two groups; group 1 (n=177) and group 2 (n=159) ; whose blood lead levels were >10µg/dL and <10µg/dL, respectively. Lead levels were measured by Agilent 7700 series ICP-MS device, Serum creatinine levels were studied by enzymatic method and blood urea nitrogen levels were studied by colorimetric method with Vitros 5.1 FS device (Ortho-Clinical Diagnostics, Rochester NY), beta-2 microglobulin levels in 24 hours urine were estimated by micro-ELISA method in Abbott (IMX, Abbott Park, IL).

Statistical analysis

Statistical analysis of data was made by using SPSS (Version 18.0) (SPSS Inc, Chicago, IL, USA) package program. Coherence to normal distribution analysis was made by using Kolmogorov-Smirnov test. Values were presented as mean±SD or in the case of non-normally distributed data, as median (range). The presence of a statistically significant difference between the groups in terms of continuous variables was examined with Student's t test for

parametric variables and Mann–Whitney U test for non-parametric variables

III. RESULTS

Even though 24 hours urine beta-2 microglobulin median levels in the group 1 were higher than the group 2, there was not a statistically significant difference between groups (median: 0.23, 0.21, respectively p=0.713). No significant difference found between groups in serum blood urea nitrogen and creatinine levels (p=0.365; p=0.130 respectively) (Table 1).

IV. DISCUSSION

Beta-2 microglobulin, a low molecular weight protein that is found in the membrane of nucleated cells, can be used to assess renal functions. While serum beta-2 microglobulin indicates glomerular impairment, urinary beta-2 microglobulin indicates tubulary injury. Toxic elements such as lead, cadmium and mercury which cause tubulary injury, increases the excretion of beta-2 microglobuin.

In many studies the association between heavy metal exposure and renal functions were investigated. There are different findings in literature in such studies. Cabral et al. investigated the lead concentrations and its effects on oxidative stress biomarkers and nephrotoxicity in humans in their study. They measured blood and urine levels of lead, biomarkers of oxidative stress and urinary renal biomarkers in lead exposed and control subjects. They found significantly higher levels of lead in blood and urine levels in exposed subjects than in control subjects. This caused in exposed subjects a decrease in antioxidant defence system and an increase in lipid peroxidation by inducing excessive production of reactive oxygen species. Futhermore nephrotoxicity markers suggested signs of impaired renal function for the exposed group [1].

In another study among 400 children and 600 adults, de Burbure et al. evaluated renal parameters who lived in lead polluted area, comparing their results with age and gender-matched controls of living in neighboring with unpolluted soil. They assessed renal function by measuring the urinary excretion levels of total protein, albumin, transferrin, beta-2 microglobulin, retinol-binding protein, brush border antigen, and the enzyme N-acetyl-beta-D-glucosaminidase. They found lead levels significantly increased in boys, girls, and women living in the polluted area. They didn't find a significant difference in the

renal parameters between control and exposed groups [2].

Hambach et al. indicated that lead increased the impact of cadmium exposure on early renal biomarkers in 122 metallurgic refinery workers examined in a cross-sectional survey [3].

Chaumont et al., found significant association between urinary beta-2 microglobulin and urinary lead, at the low exposure levels, in their cross-sectional study performed on 736 adolescents [4]. There are other studies suggesting that urinary total protein, beta-2 microglobuin and N-Acetyl-beta-D-glucosaminidase increased by blood lead concentration dose-dependently [5, 6]. However Roels et al. didn't find a significant relationship between blood lead concentration and urinary beta-2 microglobuin in their study [7]. Moreover in a study among traffic policemen no correlation was found between lead levels in blood, urine, hair and nails, and urinary excretion of beta-2-microglobulin and serum beta-2 microglobulin [8]. But Tian et al. suggested that urinary lead was associated with the increase of urinary N-Acetyl-beta-D-glucosaminidase activity, together with increase of urinary beta-2 microglobulin or total protein and those could reflect the status of renal damage in lead-exposed workers [9]. Another study stated a positive association between lead exposure and renal dysfunction. It suggested the use of urinary albumin, alpha-1 microglobulin, beta-2 microglobulin, retinol-binding protein and N-acetyl-beta-D-glucosaminidase as early markers of lead nephropathy [10].

Staessen et al. investigated the health effects of environmental exposure to cadmium and lead in 2327 participants in a cross-sectional study and concluded that environmental exposure to cadmium and lead was associated with alterations in renal function [11]. Vyskocil et al. observed a significantly increased excretion of beta 2-microglobulin in rats. Their study's results suggested that lead exposure caused impairment of renal tubular function in developing rats [12]. Chia et al. examined the urinary alpha-1 microglobulin, beta-2 microglobulin and retinol binding protein in chronic exposure of lead and concluded that urinary alpha-1 microglobulin might be the most sensitive of these markers because of its higher molecular weight [13]. Kawada et al. found in their study that urinary lead was

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the only predictor variable of beta-2 microglobulin [14].

Kumar et al. observed that urinary N-acetyl-beta-D-glucosaminidase activity and beta-2 microglobulin levels were significantly increased in auto garage mechanics with blood leads of 30-69 µg/dL, but they didn't find a significant correlation between blood lead levels and urinary beta-2 microglobulin levels [15]. Also Gerhardsson et al. found no correlations between concentrations of urinary albumin, beta-2 microglobulin, and N-acetyl-beta-D-glucosaminidase activity and the concentrations of blood lead, cumulative blood lead index, urinary lead and lead concentrations in the calcaneus and tibia, among lead workers and controls [16]. We found the median levels of 24 hours urine beta-2 microglobulin in the group 1 higher than the group 2, but there were no statistically significant difference between groups.

TABLE 1. Comparison between worker groups who exposed to lead. Group 1: workers with blood lead levels >10µg/dL, Group 2: workers with blood lead levels <10µg/dL.

Parameters	Group 1 (n=177)	Group 2 (n=159)	P
Lead (µg/dL)	30.95 (88.42)	2.8 (9.80)	<0.001
B2 microglobulin (mg/L)	0.23 (5.02)	0.21 (4.86)	0,713
Blood urea nitrogen (mg/dL)	13 (21)	13 (24.1)	0,365
Creatinine (mg/dL)	0.90 (0.70)	0.90 (0.90)	0,130
Age	36.01±8.65	36.41±11.39	0,102

Values are represented as median(range) or mean±SD

Also there was not a significant difference in serum blood urea nitrogen and creatinine levels between groups (Table 1).

Because of the variety of the findings in literature, it is confusing whether blood lead concentrations and urinary beta-2 microglobulin levels can be in association

or not and whether they can be used as a biomarker or not in case of chronic and low dose exposure. We think that it is needed to make prospective studies among more subjects. We assessed the association between blood lead concentrations and 24 hours urinary beta-2 microglobulin levels of workers who refered to Ankara Occupational Diseases Hospital toxicology polyclinic for periodic examination retrospectively. We

were restricted as the study was retrospective. We couldn't assess

smoking habits, intake of medications, and comorbidity. Other markers of tubulary injury like urinary N-acetyl-beta-D-glucosaminidase, retinol-binding protein, and markers of glomerular impairment like urinary albumin, serum beta-2 microglobulin, and creatinine clearance were not evaluated. Researchers can design more expanded studies about this issue.

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