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ALTERATION OF THE IMMUNE FUNCTIONS AMONG WORKERS OF SECONDARY ALUMINUM SMELTING

By

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Abstract

Introduction: The immune functions could be altered due to the exposure to heavy metals. Although the impact of heavy metals on the immune system among human populations is poorly understood, however, several recent studies illustrated the immunological changes due to human exposure to Aluminum (Al) and Lead (Pb). **Aim of Work:** to study the alteration in some cellular and humoral immune components among some Egyptian Al smelter workers. **Materials and Methods:** The studied group was composed of 55 exposed male workers in Al smelter and a matched control group of 55 administrative subjects. Full medical and occupational histories, clinical examination, and laboratory investigations including (levels of serum Al, blood Pb, serum neopterin, TNF-α, IL-2, C3, C4, IgM, IgG, total IgE, and count of CD4+ and CD8+ T-lymphocytes) were performed for the Al smelter's workers and their matched controls. **Results:** Clinically, the exposed smelter workers showed a significant prevalence of some manifestations as allergy, inflammation, and infections, when compared with the control group. Besides, significantly elevated levels of Al, Pb, neopterin, total IgE, and CD8+ T-lymphocytes count in addition to significantly diminished levels of TNF-α, IL-2, C3, C4, IgM, IgG, and CD4+ T-lymphocytes count were detected among the exposed group compared to their controls. Moreover, all the investigated immune parameters were significantly correlated to the duration /years of employment and the levels of both studied heavy metals in the exposed smelter's workers. Moreover, the neopterin levels were significantly correlated with the parameters of cellular immunity (CD4+, CD8+ cells, and cytokines). **Conclusion:** There was a significant alteration in the cellular and humoral immune functions among the smelter workers occupationally exposed to Al and Pb. Additionally; neopterin could be considered a significant biomarker for the response of cell-mediated immunity.

Keywords: Immune Function, Neopterin, Aluminum, Lead and Smelters.

Introduction

The smelter's workers are occupationally exposed to various types of heavy metals as Aluminum (Al), Lead (Pb), Copper (Cu)….etc. ; that have been reported to potentially result in a broad range of harmful health effects. Inhalation and ingestion of metal fumes and dust, respectively, are considered the main routes of exposure where these metals get accumulated in the body. Although the impact of heavy metals on the immune system among human populations is poorly understood, however, several recent studies illustrated the immunological impact of human exposure to Aluminum (Al) and Lead (Pb) generously (Fenga et al., 2017; Pukanha et al., 2020 and Zuo et al., 2021).

It was reported that chronic exposure to Al could result in a wide variations in the T-lymphocytes proportions in peripheral blood and affect cellular immunity (Zhu et al., 2013). Additionally, exposure to Al could inhibit the production of various cytokines resulting in alterations in host immune function (Wei et al., 2001). The complement system could be activated, and its components might be depleted with serum treatment with Al, which compromises the body›s natural defense against infections (Guven et al., 2013). Aluminum-treated animals showed a significant reduction in the levels of immunoglobulins (IgM and IgG) (Liu et al., 2009). Additionally, the IgE level increased after animal injection with Al, which suggested that Al might result in type I hypersensitivity (Tater et al., 2005).

Various researches among Pb-exposed workers suggested that Pb could affect the expression of CD4+ and CD8+ T-lymphocytes (Wang et al., 2011) and could cause a significant decrease in cytokines (TNF-α and IL-2) production (Dobrakowski et al., 2016) and immunoglobulins (IgM & IgG levels), while an inverse relationship was observed for IgE (Raddam and Assad, 2019). Furthermore, exposure to Pb was shown to cause significant depletion of both C3 and C4 complement proteins (Ündeğer et al. 1996).

Searching for an innovative indicator for cellular immunity response, neopterin was acknowledged as a reliable biomarker for cell-mediated immunity and a mediator or modulator in the course of inflammatory and infectious processes. *Neopterin* is a pyrazino-pyrimidine compound

that is related to the pteridine group. It is formed by human monocytes/ macrophages and dendritic cells when stimulated with interferon-gamma (IFN), which is generated by activated T-helper lymphocytes. Increased neopterin levels in body fluids have been linked to a number of illnesses involving the activation of the cellular immune system, including some cancers, allograft rejection, autoimmune disorders, and different infections (Ünüvar and Aslanhan, 2019).

Exposure to Al (even at low levels) might alter the metabolic profile, resulting in elevated serum neopterin. Al causes inhibition of dihydroneopterin reductase (DHPR) which is an essential enzyme in the pteridine pathway (Pingle et al., 2015). Also, exposure to Pb may trigger neopterin production, as concluded by Sipahi et al. in 2017, because Pb could increase macrophage activity mainly induced by IFN-γ.

Aim of Work

To study the alteration in some cellular and humoral immune components among some Egyptian Al smelter's workers occupationally exposed to Al and Pb.

Materials and Methods

Study design: It is a comparative cross-sectional analytic study.

Place and duration of the study: The study had been performed in a secondary Al smelter which is a separate sector at one of the major Al factories in Helwan, Cairo, Egypt. This research was carried out between December 2019 and January 2020.

Study sample: This study included two groups: an exposed group and a matched control one. The exposed group involved 55 male workers in the production line of the secondary Al smelter. They work 8 hours per day for five days (40 hours) per week. The total number of workers engaged in the smelting process at the time of the study was 62 workers. Any worker who had been working in the smelter for at least one year was included in the study. Seven workers were excluded according to the preset exclusion criteria: workers who gave a history of receiving Al-containing antacids or experienced an autoimmune or allergic disease or recurrent infections and/or systemic inflammation before their employment in the smelter or having a relevant family history of those immunological diseases, diabetic workers and those suffering from chronic medical diseases such as liver and kidney diseases were

excluded from the study due to their expected compromised immunity. The control group involved fifty-five male subjects from the administrative department of the same factory who are away from the production line and had never been occupationally exposed to aluminum or lead. The same exclusion criteria were applied to the control group. Both groups were matched for sex, age, body mass index (BMI), socioeconomic status, smoking habit, and duration of employment.

Study methods:

I- A self admistrated questionnaire including full personal and occupational histories in addition to the medical history that included the present history of any recent complaint with emphasis on any manifestations suggesting compromising of the immune system as autoimmune diseases or allergy or recurrent and frequent inflammation or infections as pneumonia, bronchitis, sinus infections, ear infections, or skin infections. Past and family histories for the same diseases were also considered.

II- Clinical examination: A thorough clinical examination was also performed.

III- Laboratory investigations:

Blood sample collection for the study investigations: Under a complete aseptic condition, a dry plastic disposable syringe was used to collect ten ccs of venous blood from each participant. The blood was then separated into two tubes: a clean heparinized tube for measuring blood Pb levels and detecting T-lymphocyte subsets, and a plain tube where the blood was allowed to clot before being centrifuged to separate the serum for testing additional biomarkers. To get to the lab, all of the samples were carried in an icebox.

a- Determination of the levels of serum Al and blood Pb: This was performed using atomic absorption spectrometry (Thermo elemental M6, Cambridge, England).

b- Determination of serum neopterin level: It was estimated by a standard protocol of competitive enzyme-linked immunosorbent assay (ELISA) method using a commercially available kit (Kit-DRG International, Inc., USA Catalog No. EIA-2949).

c- Detection of T-lymphocyte subsets: PE-Cy7-CD4+ and PE-Cy7-CD8+ fluorescence-labelled mouse anti-human monoclonal antibodies were used. The number of lymphocytes and lymphocyte subsets was examined

by flow cytometric analysis.

d- Detection of serum cytokines (TNF-α and IL-2): They were measured by Enzyme-Linked Immunosorbent Assay (ELISA) using Quantikine kits (Thermos Fisher Scientific).

e- Estimation of complement components C3, C4, and serum immunoglobulins (IgM and IgG) was done using Quantitative Turbidometric Immunoassay while measurement of serum total IgE was done by standard ELISA method.

Consent

A written informed consent to participate in the research in addition to an agreement to take blood samples from each subject were acquired after explaining the purpose and the importance of the study.

Ethical Approval

The study protocol was approved by the Ethical Committee of the Occupational and Environmental Medicine Department, Faculty of Medicine, Cairo University.

Data Management

The statistical program SPSS version 25 was used to input and code the data. For quantitative variables, mean, standard deviation, median, minimum, and maximum were utilized, while frequencies (absolute numbers) and relative frequencies (percentages) were employed for categorical variables. Because all of the collected quantitative variables were not normally distributed, comparisons between groups were made using the non-parametric Mann-Whitney test. The Chi-square ($\chi 2$) test was used to compare categorical data. When the predicted frequency is less than 5 or more than 25% of cells, the Fisher's Exact test was applied instead. The Spearman correlation coefficient was used to calculate correlations between quantitative variables. *Statistical significance* was defined as a p-value equals or less than 0.05 ($p \leq 0.05$).

Results

Table (1): The general characteristics of the studied groups.

			Exposed group (Smelter workers) (No =55)		Control group (Administrative employees) (No =55)	
	Mean ± SD	**Median**	**Min-Max**	**Mean ± SD**	**Median**	**Min-Max**
Age (years)	43.07 ±9.65^{NS}	41	29-59	42.05 ±10.04	39	28-59
SI (pack. years)	6.31 ±7.39^{NS}	5	0-25	6.8 ±7.29	5	0-25
BMI (kg/m^2)	23.37 ±1.32^{NS}	24.2	20.8-25.3	23.19 ±1.41	23.6	20.2-24.9
Work duration (years)	12.35 ±7.32^{NS}	9	5-30	11.85 ±6.69	10	6-29

SI:Smoking Index (pack/year). BMI: Body Mass Index.

NS: Non-significant Mann Whitney-U tests, p-value (>0.05).

NB: The results of Mann Whitney-U tests were 1389, 1433, 1410 and 1459 for age, SI, BMI and work duration respectively (results are not tabulated).

Table (1) showed no statistical significant differences between both studied groups regarding their age, smoking habits, body mass index (BMI) and duration of employment.

Table (2): The frequency distribution of some clinical and immunological manifestations among the studied groups.

Manifestations	Exposed group (No =55)		Control group (No =55)		Chi²/ Fisher's Exact	p-value
	No.	(%)	No.	(%)		
H/O of Autoimmune diseases	4	(7.3)	1	(1.8)	1.886#	0.363
Skin allergy or other problems	7	(12.7)	1	(1.8)	4.853	**<0.001***
Bronchial asthma	15	(27.3)	4	(7.3)	7.698	**0.010***
Recurrent infections	9	(16.4)	2	(3.6)	4.949	***0.026**
Joint pain/ inflammation	9	(16.4)	2	(3.6)	4.949	**0.026***
Recurrent fever	7	(12.7)	1	(1.8)	4.853	**<0.001***
GIT problems	7	(12.7)	0	(0)	-	**-**
LNs enlargement	4	(7.3)	0	(0)	-	**-**
Fatigue	17	(30.9)	5	(9.1)	8.182	**0.008***

H/O: History GIT: Gastrointestinal tract. LNs: Lymph nodes.
#: Fisher's Exact test. *Statistically significant tests, p-value ≤ 0.05.

Table (2) showed that all the studied parameters were significantly higher among the exposed workers compared to the administrative control group except for history of autoimmune diseases.

Table (3): Comparison between the means ± SD, medians, minimum and maximum values of the results of the laboratory investigations of the studied groups.

	Exposed group (No =55)			Control group (No =55)		
	Mean ± SD	**Median**	**Min-Max**	**Mean ± SD**	**Median**	**Min-Max**
Serum Al (μg/L)	7.9±4.6*	6.2	4.1-25.3	2.72±1.84	3.2	0.33-6.3
Blood Pb (μg/dl)	13.68±5.21*	12.9	5.61-27.1	5.89±1.96	5.6	2.31-10.21
Neopterin (nmol/L)	11.53±2.03*	11.65	6.66-15.6	4.41±0.66	4.54	3.24-5.37
CD4+ (cells/mm^3)	616.56±71.33*	598	469-755	863.05±145	874	522-1123
CD8+ (cells/mm^3)	878.04 ±81.82*	865	701-1006	550.8 ±107.61	547	351-755
CD4+/CD8+ ratio	0.71 ±0.23*	0.69	0.47-1.01	1.63 ±0.42	1.58	0.91-2.73
TNF-α (pg/ml)	1.94±1.25*	1.55	0.1-4.6	6.94±0.86	7.12	5.14-8.1
IL-2 (pg/ml)	1.27±0.76*	1.2	0.2-3.2	4.46±0.57	4.65	3.59-5.11
C3 (mg/dl)	84.77 ±7.86*	82.5	75-112	119.68 ±21.72	120.3	89.3-160.01
C4 (mg/dl)	16.85±1.62*	16.9	13.87-20.1	5.6±37.11	37.4	25.3-45.6
IgM (mg/dl)	62.55 ±9.79*	62.3	39.9-85.6	221.83±27.65	214.01	178.3-263.2
IgG (mg/dl)	806.24±55.21*	800.3	711.2-896.3	1289.18 ±180.04	1300.2	954.3-1542.2
Total IgE (IU/ml)	108.17±8.97*	109.1	75.3-124.7	67.8±21.73	63.4	30.2-102.1

Al: Aluminum. Pb: Lead. TNF-α: Tumor Necrosis Factor Alpha.
IL: Interleukin. C: Complement. Ig: Immunoglobulin.
*:Highly significant Mann Whitney-U test, p value < 0.001.

Table (3) showed that the levels of serum Al, blood Pb, serum neopterin, serum total IgE and CD8+ T-cells count showed statistically significant elevation among the exposed smelter workers when compared with their controls. However, serum cytokines levels (TNF-α and IL-2), complement components (C3 and C4), and immunoglobulins (IgM and IgG) in addition to CD4+ T-cells count and CD4+/CD8+ ratio were significantly decreased among the exposed group in comparison with the administrative control group.

Table (4): Spearman's rank correlation coefficients (r) between the general characteristics and the laboratory investigations of the exposed smelter workers.

	Age (yrs)	SI (pack.yrs)	BMI (Kg/m^2)	Work duration (yrs)	Serum Al (µg/L)	Blood Pb (µg/dl)	Neopterin (nmol/L)
Serum Al (µg/L)	0.284	-0.009	0.055	**0.705***	-	**0.649***	**0.601***
Blood Pb (µg/dl)	0.096	-0.069	0.031	**0.543***	**0.649***	-	**0.596***
Neopterin (nmol/L)	0.046	0.011	-0.055	**0.593***	**0.601***	**0.596***	-
CD4+ (cells/mm^3)	-0.104	-0.168	0.056	**-0.553***	**-0.559***	**-0.538***	**-0.796***
CD8+ (cells/mm^3)	0.187	-0.028	0.099	**0.581***	**0.833***	**0.616***	**0.643***
CD4+/CD8+ ratio	-0.141	-0.123	0.016	**-0.651***	**-0.743***	**-0.603***	**-0.774***
TNF-α (pg/ml)	-0.075	0.081	-0.020	**-0.573***	**-0.567***	**-0.494***	**-0.495***
IL-2 (pg/ml)	-0.227	0.044	-0.080	**-0.813***	**-0.744***	**-0.554***	**-0.520***
C3 (mg/dl)	-0.081	-0.180	0.081	**-0.567***	**-0.542***	**-0.380***	-0.220
C4 (mg/dl)	-0.125	-0.169	0.047	**-0.596***	**-0.623***	**-0.613***	-0.253
IgM (mg/dl)	-0.137	-0.027	-0.093	**-0.627***	**-0.631***	**-0.651***	-0.247
IgG (mg/dl)	-0.123	-0.168	-0.084	**-0.608***	**-0.594***	**-0.440***	-0.274
Total IgE (IU/ml)	-0.188	0.082	-0.053	**0.708***	**0.791***	**0.760***	0.235

SI: Smoking index. BMI: Body Mass Index. Al: Aluminum. Pb: Lead.
TNF-α: Tumor Necrosis Factor Alpha. IL: Interleukin. C: Complement. Ig: Immunoglobulin (r), p-value > 0.05. *: Statistically significant Spearman's correlation coefficient (r), p-value < 0.05.

Table (4) showed non-significant correlations between all the performed laboratory investigations and the demographic characteristics (age, smoking index, and BMI). However, there were significant correlations between the duration of employment of the exposed group and all of the laboratory investigations. Also, the Al and Pb levels were significantly correlated with all of the measured immune parameters. Moreover, the neopterin levels were significantly correlated with the parameters of cellular immunity (CD4+, CD8+ cells & their ratio and cytokines), while no significant correlation was detected between neopterin levels and the parameters of humoral immunity (C3, C4 and the immunoglobulins).

Discussion

Several previous studies demonstrated that exposure to heavy metals such as Al and Pb, was associated with toxic effects on the immune system. Thus, the current study aimed to detect the alteration in some cellular and humoral immunological components among some Egyptian Al smelter's workers occupationally exposed to Al and Pb. It is worth mentioning that no such study was previously performed in Egypt among this type of workers.

Although both studied groups were matched for their demographic characteristics (Table 1), however, the exposed smelter workers showed a significant prevalence of manifestations that might suggest immune alteration when compared with their controls (Table 2). Four exposed workers gave history of autoimmune diseases (rheumatoid arthritis and psoriasis) after 2 to 4 years from their employment in the smelter. The relationship between exposure to Al and autoimmunity was discussed previously through several researches. It was reported that Al could trigger autoimmunity through a bystander effect by activating dormant autoreactive T cells in certain individuals (Tomljenovic and Shaw, 2012).

As for the skin problems, although Al is considered a weak allergen; however, contact allergy to Al had been reported in recent years (Siemund et al., 2022). Development of work-related asthmatic symptoms in Al pot room workers is defined as pot room asthma where fluoride compounds were suggested to be the leading agent. A significant occurrence of pot room asthma was observed among Al smelter workers. Inflammatory markers and eosinophils were detected in airway tissue and blood, as well as specific morphological presentations in bronchial biopsies (Kongerud and Søyseth, 2014).

Regarding the relationship between the compromised immune system and Al exposure, early studies observed altered immune responses after excessive Al exposure among Swiss-Webster mice, which showed an increased tendency to bacterial infection (Krewski et al., 2007). Another previous study among workers in an Al factory showed that they suffered from frequent sinus infections, prolonged fatigability, chronic joint pain, and signs of reactive airways dysfunction syndrome (Ordog, 2005). Joint and bony pains among exposed workers could result from inflammatory reactions. At the same

time, the increased prevalence of GIT problems as heartburn and abdominal discomfort is due to high incidence of infections and inflammatory processes. It was concluded that absorbed Al could enhance macroscopic and histologic GIT inflammation, inflammatory cytokines production, reduce the epithelial cell regeneration and impair the intestinal barrier function (Hao et al., 2022). The detected lymph nodes enlargement was most probably due non-specific inflammation of the submandibular and inguinal nodes.

Exposure to Pb and autoimmunity was previously emphasized by the capability of the heavy metal (Pb) to produce autoantibodies against the tissue proteins in the body; however, this is aided by genetic predisposition (Mishra, 2009). Also, chronic occupational exposure to Pb could harm the skin in the form of inflammation, reduced elasticity and hydration, and pigmentation (Rerknimitr et al., 2019). Recent studies correlated between Pb exposure and the occurrence and intensity of asthma through changes in oxidative stress, immunological, and inflammatory responses (Raddam and Assad, 2019). Regarding Pb exposure and increased tendency to infections, in 2016, Krueger and Wade observed the significant association between the elevated blood Pb level and the seropositivity for the three pathogens; Helicobacter pylori, Toxoplasma gondii, and Hepatitis B virus (HBV) infections. Also, Pb might disrupt the gut barrier and enhance gut permeability, allowing inflammatory cytokines, immunologic agents, and microbial metabolites, to easily enter the enterohepatic circulation (Liu et al., 2021).

Referring to the results of the laboratory investigations in Table 3, similar results of significant elevated serum levels of Al among the exposed Al smelter workers in comparison, with controls were obtained in 2018, by Samir and Rashed in their study which was done in Egypt.

As regards the immune profile in the current study, CD4+ or T-helper lymphocytes could stimulate the activation of T-lymphocytes and the induction of cellular immune responses (Table 3). Similar results were obtained by Zhu et al. (2013) on their study on the impact of Aluminum exposure on the immune system in China, showed that the proportion of CD4+ T lymphocytes in peripheral blood diminished in workers exposed to Al from about 2 to 16 years. On the other hand, CD8+ or

T-inhibiter lymphocytes have a cytotoxic effect and could suppress T-lymphocyte activity. Al initially reduce CD8+ T cells, but the organism compensates by increasing their number. Eventually, the organism loses its ability to compensate as the Al exposure duration increased and the fraction of CD8+ T cells drop. The present study results suggested that the studied workers might be still in the compensatory stage due to the significant elevation of the count of CD8+ T lymphocytes compared to the control group (Table 3).

Both cytokines; IL-2 and TNF-α work together to enhance the development of T- and B-lymphocytes, which helps to manage immune function. TNF-α regulates T-helper 1 (TH1) immune responses against intracellular bacteria and some viral infections (Mehta et al., 2018). The immunological results of the studied workers showed a potential diminution in the production of both cytokines (Table 3). Similarly, Wang and Li (2008) discovered that treatment of cultured chicken T-lymphocytes with $AlCl_3$ could reduce IL-2 and TNF-α synthesis.

Concerning humoral immunity, Al exposure could affect immunoglobins and complement levels in human and animal models. In a recent study, high Al exposure was associated with significant depletion of complement components among the studied anemic patients (Zuo et al., 2021). As for IgM and IgG levels, Synzynys et al. (2004) showed that their levels dramatically reduced after consuming a dosage of aluminum chloride (0.04 M), resulting in a severe immunosuppressive impact in mice. Additionally, according to Wang et al. (2000), IgM levels in the serum of aluminum casting industry workers were reduced substantially. Also, exposure to Al was proved to induce the production of total IgE in human and animal studies (Hoyt et al., 2017).

Furthermore, the levels of blood Pb also showed statistically significant elevation among the exposed group compared to the administrative controls (Table 3). It was previously shown in the United Kingdom that the maximum concentrations of workplace air pollutants at secondary Al smelters were for both heavy metals Al and Pb. This is because Pb has a melting point around half that of Al and is much lower than that of other metals. As a result, secondary Al smelting occurs at temperatures where Pb becomes volatile, resulting

in a high exposure proportionate to the degree of contamination (Healy et al., 2001).

As for the additional effect of Pb exposure on the expression of CD4+ and CD8+ T lymphocytes, Wang et al. (2011) reported that the percentage of CD4+ cells and CD4+/CD8+ ratio were significantly reduced among studied Pb-exposed workers. Also, it seemed that exposure to Pb might result in a significant additional reduction in both cytokines (TNF-α and IL-2) production (Dobrakowski et al., 2016). On the contrary, other studies declared that Pb exposure promotes inflammatory processes and could result in the production of higher levels of inflammatory cytokines but in a dose-dependent manner (Metryka et al., 2018; Turksoy et al., 2019).

Also, exposure to Pb might affect the humoral immune response by reduced antibody production. Basaran and Ündeğer (2000) showed that industrial exposure to Pb among male storage battery workers could result in a significant depression of T helper lymphocytes, IgM, IgG, and complement (C3 and C4) levels. Another study observed a significant linear association between the increased blood Pb and total IgE levels (Min and Min, 2015).

Regarding the serum neopterin, its level showed a significant elevation among the studied smelter workers compared with the non-exposed controls (Table 3). Likewise, Pingle et al. in 2015, found that serum levels of neopterin were significantly higher among bauxite dust exposed populations in some major Al producing bauxite mines in India, when compared with the control groups. Also, the neopterin levels were significantly higher among occupationally Pb-exposed workers with higher blood Pb levels than those with lower ones (Sipahi et al., 2017).

Spearman's correlation analysis revealed significant positive correlations between the duration of employment or exposure of the studied workers and the levels of both heavy metals (Al and Pb) (Table 4). Similar findings were obtained by Samir and Rashed in 2018 as regards the duration of exposure to Al and its serum levels among smelters workers. Moreover, a recent study detected a significant positive correlation between blood Pb levels and duration of Pb exposure among studied Indian workers involved in battery manufacturing or recycling

factories (Kumar et al., 2020).

The idea of dose-response relationship was emphasized by the observed effect of the duration of exposure and the level of each heavy metal (Al and Pb) on every studied parameter of the immune response (Table 4). An Italian review reported that the immunotoxic effects of the heavy metal could vary according to metal form, route, dose, time of exposure, host age, and genetic susceptibility (Fenga et al., 2017).

The current study revealed that the serum level of neopterin could be considered as a valuable biochemical marker for cellular immune response among the exposed smelter workers. Similarly, previous studies declared that neopterin levels were well correlated with counts of CD4+ and CD8+ T-cells and cytokines levels in the experimental populations (Hosp et al., 2000 and French et al., 2009).

Conclusion and Recommendations:

a significant alteration in the cellular and humoral immune function was observed in the smelter's workers occupationally exposed to Al and Pb. This alteration was significantly correlated with the years of exposure and the biological levels of both studied heavy metals. Additionally, serum neopterin could serve as a good biomarker for the response of cell-mediated immunity. Engineering and administrative control measures are highly recommended to diminish the exposure concentration and duration among smelters workers. Workers should be encouraged to use personal protective equipment (PPE) properly. Finally, additional studies involving a larger cohort of workers would be required to draw a more definitive conclusion.

Conflict of interest

The authors declared that there is no conflict of interest regarding authorship, and/or publication of this article.

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