WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 6.647
Volume 6, Issue 12, 167-177 Research Article ISSN 2278 – 4357

STUDY OF THE EFFECT OF LEAD AND CADMIUM ON SOME IMMUNOLOGICAL AND HEMATOLOGICAL ASPECTS FOR SOME RESIDENTS OF BAQUBAH CITY.

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Article Received on
10 October 2017,

Revised on 30 October 2017,
Accepted on 20 Nov. 2017

DOI: 10.20959/wjpps201712-10609

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ABSTRACT

This study was designed to determine the amount of Lead and Cadmium pollution in Baqubah city and their effects on some immunological and hematological indicators. From several areas of Baqubah city, 120 blood samples were collected from apparently healthy individuals. Regarding sex, the results of this study indicated a highly significant difference (P≤0.01) in each level of Lead and cadmium in males when compared to female group, while the immunoglobin results were as follows: IgG levels showed a significant decrease in male group compared to female group (P≥0.01), a highly significant decrease was shown in IgM level in male group compared to female group (P≤0.01), while there was no significant difference in IgA level in the study groups. The results demonstrated a highly significant increase in the levels of (Hb),(RBC),(HCT),(MCV),(MCH) and (MCHC) in male group compared to female group, while the RDW-CV results showed a highly significant decrease in male group compared to female group (P≤0.01, whereas no significant difference was found in RWD-SV(P≥0.05) between male and female groups.

KEYWORDS:

INTRODUCTION

There have been many warnings in the last years of the twenty-first century about the fate of living organisms on the surface of the earth and has increased concern because of the use of

human means resulting from technological and industrial development and mining. In addition, scientific development and increased levels of intervention by humans became a threatening tool to environmental balance. In the past, the factories were small and undeveloped, so the increase in pollution was insignificant, but when these factories expanded and the industrial units increased, pollution became a matter of great importance, as most of the pollution on the earth can be attributed to industrial development (Shah, 2017). Metals are a group of naturally occurring elements that share certain properties, such as opacity, ductility, luster and electropositivity, so they tend to lose electrons, as well as thermal and electrical conductivity. Metal elements include regular metals and heavy metals (Ibrahim, 2009).

Heavy metals include: Pb, Cd, Hg, As, Cr, Cu, Se, Ni, Ag, Zn and less common metal pollutants are: Al, Cs, Co, Mn, Mo, Sr and U. The metals are classified by toxicity into low toxic metals (manganese, molybdenum and iron), medium toxic metals (chromium, zinc, copper, nickel and cobalt), highly toxic metals (silver, mercury, cadmium and lead) (Abudllah, 2017), The gravity of heavy metals comes from non-biodegradability and bioaccumulation in living organisms, causing various dangerous diseases (Nasrazadani *etal*., 2011).

Living cells need metal ions such as Cu, Ni, cobalt and Fe. These minerals are essential for all living organisms because they are used as cofactors and synthetic elements in enzymes and other molecules, while other elements that are considered unnecessary are toxic and have no vital role such as lead (Pb), mercury (Hg), cadmium (Cd), silver (Ag) and arsenic (As). The availability of these metals in the body lead to the damage of the DNA doubling, which causes cell death and damage or reduction in the central nervous system and damage to the blood structure, kidney, lung, liver and other organs (Shoeb, 2006). Most heavy metals are similar in many of their natural properties, but their chemical reactions are different, and this applies to their environmental effects. The danger of these minerals is due to two reasons: The first, is that these heavy metals are linked to functional groups in enzymes with stable bonds and in the form of complexes, thus disrupting the molecules that induce metabolic reactions. The second reason is that these minerals concentrate on the cell membrane, altering the structure of the cells and causing disruption of the exchange ions and organic substances essential for life, such as proteins and polysaccharides (Abdul Moneim and the Turkish, 2012), Lead is a toxic metal for many immune cells, which causes mutations of humoral and

cellular immunity. This metal has been recorded as immunosuppressant even in low concentrations, In addition, it causes dysfunction of the kidneys and the renal tubes. It inhibits its ability to re-absorb glucose, amino acids and phosphates. Lead poisoning causes hypertension and infertility in men and women (Weaver *etal.*, 2017). Cadmium is also a toxic carcinogen metal, where lung cancer is the main cancer caused by cadmium and a link was also found between this mineral and prostate and kidney cancer (IARC, 2012). It is toxic even at low concentrations when prolonged exposure to the metal causes kidney dysfunction because it causes damage to the renal tubules (Young, 2005).

The current study aims to determine the amount of Lead and Cadmium pollution in Baqubah city and the extent of the impact of these elements on some immunological and hematological parameters.

MATERIALS AND METHODS

The method of this study was based on collecting blood samples from different areas of Baqubah city to analyze and estimate lead and cadmium concentrations. From each individual 5 ml of venous blood was collected and 1 ml of blood was placed in test tubes containing anticoagulant (EDTA tube), while 4 ml of blood was put in plain test tubes and centrifuged to obtain serum samples. After that serum samples were kept in deep freeze at -20°C until use. The tests performed were as follows:

First: Measuring the concentration of both lead and cadmium by using the Flameless Atomic Absorption Spectrometer (FLAAS) at Ibn Sina Center.

Second: Immunological tests: (IgG, IgM, IgA) concentrations were measured by using single radial immunodiffusion plate (Recaesn etal.,2005).

Third: The BC-3000 plus (Mindray) device was used to measure the following indicators: Hb, RBC, HCT, MCV, MCH, MCHCH, RDW-CD, RDW-SD (Mindray BC-3000 Plus, 2012).

RESULTS AND DISCUSSION

The results of our study showed a significant increase in the Lead level in the male group (34.20 ± 11.20 ppb) compared to the female group (24.77 ± 8.96 ppb). For the total study group it was (29.49 ± 11.16 ppb) at ($P \leq 0.01$). The reason behind the higher amount of lead in

the male than that of the female group may be due to many causes including smoking and also due to different lifestyles as shown in (Table 1).

In a survey study conducted at the University of Baghdad / Market Research and Consumer Protection Center (Hussain, 2016), which has been conducted on electricity generator workers in Baghdad city and showed the percentage of blood pollution with some heavy metals found that the level of lead in the blood of workers was (0.72 mg/ml). While another study conducted at the University of Mosul by (Aljumaily *etal*., 2011) to determine the levels of some heavy metals in the serum of patients with explosive issues found that there was no significant difference in the level of lead. The study that was performed by (Algafari *etal.*, 2011) on the effect of lead and cadmium on men fertility with different occupations showed a significant increase in lead concentration in the blood of welders, car repairers and generator operators, while the results of Zubaidi and others (2016) in Najaf city found a significant increase in lead concentration in the blood of workers in the coal industry (0.0021±0.029 ppm) compared to the control group (0.0009±0.0035ppm) at (P≤0.01).

The results of cadmium were as follows: The study showed a significant increase in cadmium level in the male group compared to the female group as it reached (66.66 ± 46.63 ppb) while in females it was (43.81 ± 19.54 ppb). For the total study group it was (55.24 ± 37.40 ppb) at the level (P≤0.01) (Table 1). In a study carried out in (2016) by Hussain, it was shown that the amount of cadmium in the blood of the generators operators was (0.133 mg / ml) and the least significant difference was (0.044). The percentage of cadmium presence in the blood by inhalation and intake by the lungs increased by 30%. The limit of cadmium concentratio in the blood of non-smokers was 0.1 - 0.04 mg / dl (Alomer, 2000). Smoking also increases the level of cadmium in the blood of other smokers, semen and urine (Mansour, 2006). In a study conducted in Fallujah city by Hssani and others (2016) regarding the impact of heavy metals pollution on on male infertility, a significant difference was found between the study groups of cadmium, while Aljumaily and others (2011) found a significant difference in the levels of cadmium in the serum of patients with explosive issues compared to the control group. The study that was performed to show the effect of lead and cadmium on men fertility with different occupations by (Algafari *et al.,* 2011) found a significant difference in the concentration of cadmium in the blood of welders, car repairers and generator operators. It was found that cadmium level was significantly higher (0.003±0.1825 ppm) than the control

group (0.0030±0.0070 ppm) in the study that was carried out by Zubaidi and others (2016) in Najaf city.

Table (1) Shows the mean and standard deviation of lead and cadmium according to gender.

Gender		Pb (0.00)**	Cd (0.00)**
Male	**Mean**	34.20	66.66
	SD	11.20	46.63
	SR	1.45	6.02
Female	**Mean**	24.77	43.81
	SD	8.96	19.54
	SR	1.16	2.52
Total	**Mean**	29.49	55.24
	SD	11.16	37.40
	SR	1.02	3.41

Concerning the immunological findings, it was observed that the mean IgG level was significantly lower in the male group (730.16 ± 234.12 mg/dl) in comparison with the female group(857.87 ± 263.93 mg/dl) and for the total sample it was (794.02 ± 256.56mg/dl) (Table 2). The immunoglobulins have a variety of functions within the body and consist of two light chain series and a heavy chain and each series consists of folds or units of large proteins (Pasquier, 2006). Epidemiological data indicated that the main effect of lead is on the cellular aspects of the immune system, while the humoral indicators are relatively less sensitive, so the level of immunoglobulins (IgG, IgA, IgM) was within the normal level among workers exposed to lead (Kimber *etal*., 1986). However, a decrease in the level of immunoglobulins in serum exposed workers was noted (Castillo-Mendez *etal*., 1991). A negative correlation was found between the lead level and IgG level in serum exposed workers (Horiguchi *etal*., 1992). The results of the immunoglobulin IgM showed a significant decrease in the male group compared to the female group (126.18 ± 55.45 mg/dl), while the female level was (178.66 ± 81.27 mg/dl), while for the total study group reached (152.42 ± 74.12 mg/dl) (Table 2). IgM is the primary antibody produced by B cells and it is the largest antibody in the human circulatory system and it is the first line of defense against any infection(Bruce *etal*., 2002), The spleen-producing plasma cells are the largest producers of IgM and its properties are a five-component multi-component compound (Linked with five other antibodies) and molecular weight 970 Kda(Bours *etal.*, 2005) and that is why the spread of this antibody is somewhat difficult. The results of the immunoglobulin IgA showed a significant decrease in the male group(140.78 ± 82.32 mg /dl) compared to that of the female

group(145.07 ± 72.95 mg/dl), while for the total group was (142.93 ± 77.48 mg/dl) (Table 2). This result was identical to the result obtained by Ewers *et al*., (1982) who investigated the level of antibodies (IgG,IgM,IgA) and complement (C3) among lead workers and found a decrease in IgA level in saliva of workers. This type of antibody is most abundant in humans (Kerr, 1990). It is a monomer and is produced within the body of B lymphocytes in the bone marrow. In some lymphatic organs, humans produce large amounts of immune antibody IgA as well as immune antibody IgG, but most IgA is present in mucous secretions.

Table (2) Shows the mean and standard deviation of immunoglobulin (IgG, IgM, IgA) according to gender.

Gender		IgG (0.01)*	IgM (0.00)**	IgA (0.75)ns
Male	**Mean**	730.16	126.18	140.78
	SD	234.12	55.45	82.32
	SR	30.22	7.16	10.63
Female	**Mean**	857.87	178.66	145.07
	SD	263.93	81.27	72.95
	SR	34.07	10.49	9.42
Total	**Mean**	794.02	152.42	142.93
	SD	256.56	74.12	77.48
	SR	23.42	6.77	7.07

The results of hematological indicators in our study was as follows: The results of hemoglobin concentration showed a significant increase in the male group (15.61 ± 1.12 g/dl) compared to the female group(12.27 ± 1.84 g/dl), while for the total group it was (13.94 ± 2.26 g/dl) (Table 3). Nima and others (2009) found a significant difference in blood hemoglobin concentration level with a significant increase in lead levels of the study group compared to the control group in Kufa city, while in Ramadi city, the results of another study which was designed to estimate the concentration of some heavy metals and to study the hematological changes in the blood of the generators operators, found that the level of hemoglobin in the study group was (14.63), while in the control group was (13.14) (Fadel *etal.*, 2013). Lead inhibits the efficacy of d-amino levulinic acid dehydrogenase (d-AIAD) in the red blood cells and this enzyme is necessary in the process of formation of hemochlobin. Lead builds up in red blood cells in the form of blue pigmented spots, one of the important diagnostic properties of lead poisoning, thus, hampering the formation of hemoglobin Updated anemia Lead effect in protoporphyrin and this substance is the basis for the formation of the hemochlobin molecule. The appearance of Aminolivolinic acid in the urine indicates a deficiency in the synthesis of heme because of the impact of lead (Tandon etal.,

2002). The results of red blood cells were significantly higher in males than in females, as it reached in male group(5.29 ± 0.39), while in females it was (4.57 ± 0.49) and as for the total sample was (4.93±0.58) (Table 3). A number of studies have indicated that the target organ of the lead metal is bone marrow. Bone marrow is the main source of red blood cells, so lead works mainly to reduce the Haemocytoblast. The results of the haematocrit were significantly higher in males than in females, where it reached in male group(47.42 ± 3.22%) and in female group it was (38.48 ± 4.77%), but for the total sample it was (42.95 ± 6.05%) (P≤0.01) (Table 3). This result was on the contrary of Nima and others (2009), who found a significant difference at level (P<0.01) in hematocrite value, which is explained by the study that was done on children with iron deficiency anemia and found a significant increase in the level of lead in their blood. The amount of hematocrite in a study which was conducted in Ramadi city by Fadel and others (2013) was (45.62) for the study group, while the amount in the control group was (40.80). The impact of lead on the bone marrow, especially on the cell generators of red blood cells, causes a decrease in the number of red blood cells, which is reflected mainly on the the hematocrite values, which leads to the decline and this is referred to a number of studies that indicated the effect of lead in reducing hematocrite values (Mohamed etal., 1991). The results of the MCV were significantly higher in males than in females, where it reached in male group (89.85 ± 5.54 fL), while in females it was (84.69 ± 10.21 fL), whereas in the total group was (87.27 ± 8.58 fL) (P≤0.01) (Table 3). Nima and others (2009) found significant differences in their study of a group of children with iron deficiency anemia and the control group. Al-Saffar (2005) found that the volume of PCV cells decreased in all studied groups during periods of exposure (less than 10, 11-20 and over 20 years) by 18.2%. Our study showed that pcv is very similar in its variants with the concentration of hemoglobin in all studied groups and these results are identical with the finding of (Royce and Needleman, 1992) in their study on the effect of different proportions of lead in the health of adults and children. The results of the MCH were significantly higher in males than in females where it reached in male group (29.50 ± 2.01pg), while in females it reached (26.93 ± 3.96 pg), whereas in the total group it reached (28.22 ± 3.93 pg) (Table 3). In a study of Al-Azzawi (2015) Tikrit city, a significant increase was found in the proportion of MCH. Al-Jafat (2004) found that lead has an effect on the mean hemoglobin of the cell and the results of his study were similar to those indicated by both (Mohamed etal., 1998; Wright etal., 2003). The results of the MCHC were significantly higher in males(32.87 ± 0.77 g / dl) than in females(31.74 ± 1.39 g / dl), while for the total group it was (32.31 ± 1.25 g / dl) (Table 3). The results of the RDW-CV were significantly higher in females (15.06 ±

2.85%) compared to males(13.74 ± 0.85%), while for the total sample it was (14.39 ± 2.20%) (Table 3). The results of the RDW-SD were significantly higher in the male group (45.62 ± 3.72 fL) compared to the female group(45.61 ± 4.57 fL), while for the total sample it was (45.61 ± 4.15 fL) (Table 3). The effect of lead and cadmium on the total count of red blood cells, hematocrite and hemoglobin is automatically reflected on the rest of the blood components. The concentration of hemoglobin – RDW-CV and RDW-SD so there is a significant difference according gender in MVH and RDW-CV while the result of RWD-SD was significantly higher.

Table (3): Shows the mean and standard deviation of red blood cells and their indices according to gender.

Gender		Hb (0.00)**	RBC (0.00)**	HCT (0.00)**	MCV (0.00)**	MCH (0.00)**	MCHC (0.00)**	RDW-CV (0.00)**	RDW-SD (0.98)ns
Male	Mean	15.61	5.29	47.42	89.85	29.50	32.87	13.74	45.62
	SD	1.12	0.39	3.22	5.54	2.01	0.77	0.85	3.72
	SR	0.14	0.05	0.42	0.71	0.26	0.09	0.11	0.48
Female	Mean	12.27	4.57	38.48	84.69	26.93	31.74	15.06	45.61
	SD	1.84	0.49	4.77	10.21	3.96	1.39	2.85	4.57
	SR	0.24	0.064	0.62	1.32	0.51	0.18	0.37	0.59
Total	Mean	13.94	4.93	42.95	87.27	28.22	32.31	14.39	45.61
	SD	2.26	0.58	6.05	8.58	3.39	1.25	2.20	4.15
	SR	0.21	0.05	0.55	0.78	0.31	0.11	0.20	0.38

CONCLUSIONS

During the current study, there was a significant increase in both the lead and cadmium elements affected by this increase in gender. Lead and cadmium had an effective effect on the physiological parameters and complete blood count. This effect ranges from the significant increase in some indicators to the significant decline of others, while another group of these indicators were not affected by these minerals. The effect of both lead and cadmium on the studied immunological indicators showed that they caused a significant decrease in (IgG, IgM and IgA) levels.

REFERENCES

1. Ibrahim, Mahmoud (2009). Professional poisoning caused by lead and compounds. Publications of the Arab Institute for Health and Occupational Safety. Damascus.
2. Zubaidi, Ahmed Ali, Abdel Moneim Hamad and Fadel Mohsen Abd (2016). Estimation of lead, cadmium and mercury in the serum of coal industry workers and its effect on some biochemical variables. Tikrit College of Pure Sciences. (2): 1662 – 1813.

3. Al-omar, Muthanna Abdul Razzaq (2000). Environmental Pollution, First Edition, Dar Wael Printing and Publishing Press, Amman / Jordan.
4. Al-Mansour, Nahla Makki Ahmad (2016). Measurement of some heavy metals in umbilical cord blood for newborns and their mothers. A comparative study between Riyadh and Al-Qatif, Master of Science, King Saud University.
5. Hussein, Huda Jaber (2016). A survey study to show the percentage of blood pollution in the operation of generators in the city of Baghdad with some heavy metals. Ibn al-Haytham Journal of Pure and Applied Sciences, (29).
6. Jafat, Haydar Saleh (2004). Effect of Different Concentrations of Acetate Acetate in Some Physiological and Chemical Blood Calibrations and Histopathological Changes in Male White Rabbits, Master Thesis. University of Kufa.
7. Fadhil, Saddam Hussein, Khalid Farouk Abdul Ghafoor and Ali Fadhim Al-Mohammadi (2013). Determination of the concentration of some heavy metals and the study of blood variables in the blood of workers in diesel generators in the city of Ramadi. Journal of Anbar University of Pure Sciences Volume 7. First Issue.
8. Abdel Moneim, Issam Mohammed and Ahmed bin Ibrahim Al-Turki (2012). Heavy elements sources and damage to the environment. Center for promising research in the fight against vital and agricultural information. Al Qussaim university. Kingdom of Saudi Arabia.
9. Shuh, M.P.(2017). Environmental pollution Journal of Applied Biotechnology and Bioengineering, 2(2).
10. Abdullah, k.J.(2017). Using phragmites australis and ceratophyllum demersum for remove some of heavy metals from polluted water. Baghdad.
11. Nakagawa, K. (1989). Hepatic glutathione metabolism in mice acutely treated with lead acetate. JPn – J – pharmacol. 51(2): 173-9.
12. Shoeb, E.(2006). Genetic Basis of heavy metal Tolerance in Bacteria. A thesis the Degree of doctor of philosophy. university of Karachi, palistan.
13. Recasens, M.; Lopez-Bermejo, A. and Ricart, W. (2005). An inflammation score isbetter associated with basal than stimulated surrogate indexes of insulin resistance. J. Clin. Endocrinol. Metab., 90: 112-116.
14. Mindray (BC-3000)plus.(2012). Operators manual. Shenzhen mindray Bio-medical electronics Co., Ltd.

15. Al-jumaily, M.A, Alfhady, N.H., Hassan, M.K., (2011). Serum heavy metals in patients with fragments and shells of improvied explosive devices. Ann. coll. Med. Mosul; 37(1&2): 8-13.
16. Al-gafari, R.N., Ramadhan. R.S., Jeboury, G.H.(2011). Effect of lead, cadmium and continuous exposure to heat as an occupation hazards on fertility in male workers. Journal of Al-Nahrain univer., 14(4): 132-136.
17. Hassani, H.F., Mohamed, W.M., Hasan, H.R., Majeed, B.J. (2016). Heavy metals pollution and men infertility in AL-fallujam city. Baghdad science Journal, 13(4).
18. Pasquier, LD.(2006). Germline and somatic diversification of immune recognition elements in Metazoa Immunol Lett; 104: 2-17.
19. Kimber, I., Jackson, JA., Sonard, MD.,Gidlow, DA., Niewola, Z.(1986). Influence of chronic low- level exposure to lead on plasma immunoglobulin concentration and cellular immune function in man. Int Arch Occup Environ Health, 57: 117-125.
20. Gastillo-Mendez A, Rodriguez –Diaz T, Leon –Lobeck A, Gravalosa – Cruz AJ.(1991) . Influence of occupational lead expposure on the concentration of immunoglobins and immune cellular function in human. Rev Alerg Mex, 38(2): 69-72.
21. Horiguchi, S., Kiyota, I., Endo, G., Teramoto, K., Shinagawa, K., Wakitani, F., Konishi, Y., (1992). Serum immunoglobulin and complement C3 levels in workers exposed to lead. Osaka city Med J, 38: 149-153.
22. Bruce A., Alexander J,. Julian L., Peter W., Martin R., Keith R., (2002). Moleculer Biology of the cell. 4th ed. Routledge. ISBN 978-0-8153-3288-6.
23. Ewers, U. Stiller-Winkler, R.Idel, H. (1982). Serum immunoglobulin, complement C3, salivary IgA level in lead workers. Environ Res., 29: 351-357.
24. Kerr, MA,.(1990). The structure and function of human IgA. Biochem T; 271: 285-96.
25. Nima, S.R, Al-shamri, A.M, Al-kadim, A.M, AL-shahin, H.(2009). Determination of heavy elements levels in blood of children with anemia living at Al-Najaf city. QMJ.vol.5 No.7.
26. Tandon, S.K.; Singh, S.; Prasas, S.; Srivastava, S.; Siddiqui, M.K. (2002). Reversal of lead – in duced oxidative stress by chelating agent, antioxidant or their combination in the rat. Environ – Res., 90(1): 61-6.
27. Mohamed, F.; Mervat, E.; Viola.; Fayez. (1991). Biochemical changes in Rat liver, Brain and Blood in Response to treatment with lead. J. Egypt. Ger. 2001; (004): 233-250.

28. Monamed, W.S.; Hamam, A.M. and Tohamy, M.M. (1998). Some Reprodutive and Blood Perameters of femal Rebbit givein different dose lead acetate. J. Union Arab Biol., Cairo, (A): 385-399.
29. Wright, R.O.; Tsain, S.W., Schwartz, J.; Wright, R.J. (2003). Association between iron deficiency and blood lead level in a longitudinal analysis of children followed in a Uran primary care clinic. J – Pediatr, 142(1): 9–14.
30. Royce, S.E. and Needleman, H.L.(1992). Case studies in environmental medicine lead toxicity. Public Health Service., 1: 1-24.
31. Bours J., Reitz C,. Strobel J., Breipohi W,. (2005). Detection of secretory IgM in tears during rhino – conjunctivitis. Graefes Arch clin Exp. Ophthalmol. 243(5): 456-63.PMID 15931543.doi:10.1007/s00417-004-1048-y.
32. International Agency for Research on Cancer (IARC)(2012). Cadmium and cadmium compounds. In: Review of Human Carcinogens IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Vol. 100C IARC; p.121-45.
33. Weaver Vm, lee bk, Ahn kd, lee gs, Todd ac, Stewart wf, wen j, Simon dj, pArsons pj, schwartz. (2017). association of lead biomarkers with reanal function in korean lead workers. occup environ med, 2003; 60: 551-562.
34. Young, R.A.(2005). Toxicity profiles: Toxicity summary for cadmium, Risk assessment Information system, RAIS univercity of Tennessee, Available from: http://rais.ornl. gov/tox/profiles/cadmium.shtm, Accessed on 20-06-2016.