SindhUniv. Res. Jour. (Sci. Ser.) Vol. 53 (02)159-164 (2021)

SINDH UNIVERSITY RESEARCH JOURNAL (SCIENCE SERIES)

Hepato-renal toxicity and hypertension induction by lead toxicity in battery smelter from district Hyderabad

F. G. MEMON, Z. N. MUGHAL, J. A. ZAI[++], N. GILL[*], A. A. KHAND

Department of Physiology, University of Sindh Jamshoro Pakistan

Received 10th December 2020 and Revised 19th April 2021

Abstract: Background: The present study was undertaken to evaluate the long term toxic effect of lead on blood pressure, hepatic and renal functions in battery smelter from district Hyderabad.

Methods: A case-control study was conducted from August 2016-January 2017 at the Department of physiology University of Sindh, Jamshoro**.** We recruited 195 current battery smelter male workers and 200 healthy male as a control from different urban areas of District Hyderabad for this study. The physical parameter of each subjects (age, weight, height BMI and blood pressure) were assessed by standard protocols after taken written consent and their blood sample were taken for analysis of blood Lead, Cystatin C, AST, and ALT using atomic absorption, and standard diagnostic kits protocols respectively. The data were measure using SPSS as mean and SD.

Results: The study resulted in mean age of the subjects as 30.16±4.26 years, mean blood lead concentration 21.87±9.66 µg/dl, systolic and diastolic blood pressure 125.27±7.19, 104.36±7.97 mmHg respectively, Cystatin C 0.8552±0.1163 mg/L, ALT 28.28±10.89 IU/L and AST 26.57±11.63 IU/L. At low blood lead levels no correlation ship was found between blood lead blood and any of the biochemical markers but they sharply increased at concentration higher than 40 µg /dl.

Conclusion: A sharp rise in Cystatin C and drop in eGFR blood level at or above 40 µg /dl are suggestive of a renal damage and worst consequences associated with it. Therefore in occupational workers, blood lead levels must not cross the limit of 40 µg /dl and warrants clinical intervention. The efforts should also focus on monitoring blood lead levels of unexposed general population by introducing regular monitoring and control programs. Safer limits should be reinvestigated and clinical intervention done wherever necessary.

Keywords: Cystatin, Lead Poisoning, Occupational Workers, ALT, AST.

1. INTRODUCTION

Lead has been used by mankind since centuries. Its versatility and toxicity are also well documented. It has been used in domestic water pipes, plastics, paints, inks, power storage devices additive in fuel and other applications (Tong, *et al.*, 2000). (Silbergeld, and Weaver, 2007).. The toxic waste from its uses may enter human beings though ingestion, respiration and cutaneous absorption causing disorders of renal, hematologic, nervous, digestive, reproductive, and cardiovascular systems (Nawrot, *et al.*,2002). (Ekong, *et al.*, 2006).. Primary and secondary smelting of metal are two important activities to which occupational workers are directly exposed resulting in accumulation of metal in blood. It is therefore recommended that concentration of metal in blood of humans should not exceed 10.00 µg/dl (Abdul and. Usmani, 2015). (Binns, *et al.*,2007). The both kidneysare the main targeted organ of lead toxicity and many studies reported the impaired kidney function in occupational workers exposure to lead metal which followed by the hypertension and increase risk of liver, heart and cardiovascular disorders (Harari, *et al.*,2018).. It is estimated that about 90% total lead body burdenstored in bones as the half-life of lead in bone is about years to decade while in blood its half-life is approximately 1 month (Barry, *et al.*, 2019).

Cystatin C is the 122 amino acid chain encompassing small protein belongs to a lysosomalcysteine protease inhibitors group, synthesized by nucleated cells at constants rate and expressed ubiquitously (Zhang, *et al.*, 2019). Now a day for early evaluation of impaired renal function or glomerular filtration rate (GFR) the cystatin C has been used as well-known marker instead of serum creatininebecause of the lower molecular weight the Cystatin C freely filtered neither secreted in the proximal renal tubules of kidney unlike creatinine.

[++]Corresponding Author: Jawaid Ahmed Zai, email: jawaidzai@yahoo.com, Contact No: +923213027513;
fahmida.gv@gmail.com , zaibunisamughal@yahoo.com, nazia.gill@usindh.edu.pk, aftab.khand@usindh.edu.pk
[*] Department of Statistics, University of Sindh Jamshoro Pakistan

Moreover, Serum cystatin C concentration is not affected by body mass, gender, age,muscle mass and protein consumption (Poręba, *et al.,* 2011).

The present study was conducted to observe the changes in blood pressure, Cystatin C. AST, and ALT of battery smelterdue to changes in blood lead concentration.

2. METHODOLOGY

The case control study conducted from August 2016- January 2017 at the Department of physiology University of Sindh, Jamshoro. This study included total 395 male subjects ages range between 18-40 years.195 occupational workers involved in battery recycling activity, andresiding near recycling smelters and worked 8 hours per day along with 200 age and sex matched healthy controlswho did not have exposure to metal were randomly selected from different region of Hyderabad for sampling. Written inform consents were obtained from all participant and experimentations was performed accordance to the recommendation of World Medical Association Declaration of Helsink. 10 ml venous blood samples were collected using standard blood sampling protocol and weight height was measured to calculate the BMI. Lead in blood was analysed by graphite Furnace atomic absorption spectrometer (GFAAS) while ALT, AST, and Cystatin C were analysed by Human diagnostic standard kit methods. For blood pressure the subjects were monitored for one week continuously before declaring them hypo or hypertensive individuals. The data was collected and analysed for T test and Chi-square using SPSSv20.

3. RESULT

The total 395 male subjects were included in the study with mean age of 27.96±5.6 years in smelter worker while 27.34±4.5 years in control. The significantly elevated blood lead level 19.94±8.06 was observed in battery smelter in comparison with control subjects 10.20±5.06. We also found the remarkably increase blood Cystatin C level 1.09±0.35 in smelter however it was within normal range 0.69±0.25 in control participants. The liver damage marker ALT 34.52±9.14 and AST 27.33±7.93 were also increased in smelter as compare to control. Meanwhile the systolic 126.03±6.82.66 and diastolic blood pressure 107.4±7.45 were higher in smelter and it's directly proportional to blood lead, cystatin C, ALT and AST level found in battery smelter.

Individuals from controls and smelters were grouped according to the blood lead levels observed (Table 1). A large fraction of controls (63%) were having blood lead levels <10mg/L while a large fraction of smelters (46.16%), occupationally exposed to lead were having blood lead levels ≥ 20mg/L.

Table 1:

	Controls (%)	**Smelters (%)**
Lead < 10 mg/L	63	10.26
Lead ≥ 10 - <15 mg/L	19	16.93
Lead ≥ 15 - <20 mg/L	11	26.67
Lead ≥ 20 mg/L	7	46.16

Table 2 showing various parameters recorded for smelters with occupational exposure to the lead and controls. Controls of similar age group were selected and no significant difference was observed between controls and smelters group. Occupationally exposed smelters group was having significantly higher level of circulating blood lead level in comparison to the control population. A slightly raised level of cystatin C, a renal damage marker was observed in the smelter group, the difference with the control group was also significant (0.001). The values for the liver damage markers ALT and AST were within their normal range, however a significant higher level of these enzymes was observed in smelter group when compared with the control group. A similar significant (0.001) higher level of systolic and diastolic blood pressure was recorded in the smelter group.

Table 2:

	Age years	Lead mg/L	CystatinC mg/L	ALT U/L	AST U/L	SBP mmHg	DBP mmHg
Controls (n=200)	27.34±4.57	10.21±5.23	0.95±0.26	23.85±9.96	15.95±6.09	119.09±5.22	97.88±6.24
Battery Workers (n=195)	27.96±5.69	19.95±8.07	1.3±0.34	34.53±9.15	27.34±7.94	126.04±6.83	107.43±7.46
Anova	n.s.	***	***	***	***	***	***

Individuals with occupational exposure and controls were divided into four groups based on the blood lead level to observe the effects of occupational and passive exposure to the lead. The results presented in Table No.3. The difference for the age was found to be significant only in group I (Lead < 10mg/L). The mean lead level was similar in all three groups; the difference was only significant (0.05) in the group IV

(Lead ≥ 20mg/L). comparatively small differences were observed for the cystatin C level between smelter and control individual in different groups, the difference was significant (0.01) in group II (Lead ≥ 10 - <15mg/L) and group III (Lead ≥ 15 - <20mg/L). A significant difference between smelter and controls was observed for the ALT and AST enzymes when compared in different groups. The difference was non-significant for ALT only in group 4 and for AST in only in group II. Small difference was observed for the systolic and diastolic blood pressure in different groups, which was non-significant, with the exception of group IV where a significant difference was observed for both of the systolic (0.01) and diastolic (0.001) blood pressure. The difference was also significant (0.001) for systolic blood pressure for group III.

Table 3

		Age years	Lead mg/L	Cystatin C mg/L	ALT U/L	AST U/L	SBP mmHg	DBP mmHg
Lead < 10								
	Controls (n=126)	26.7±4.85	6.96±1.47	0.8±0.15	17.67±6.42	12.36±4.21	116.19±3.9	94.35±4.34
	Battery workers (n=20)	23.05±4.62	7.09±1.51	0.81±0.11	21.17±5.54	15.87±4.38	115.12±3.29	93.82±4.38
	Anova	**	n.s.	n.s.	*	***	n.s.	n.s.
Lead ≥ 10 - <15								
	Controls (n=38)	27.72±4.11	12.17±1.49	1.05±0.09	31.3±3.32	19.8±0.96	122.33±1.75	102.04±3.48
	Battery workers (n=33)	26.55±4.59	12.77±1.41	1.01±0.07	25.75±5.32	20.3±6.15	119.97±3.3	101.18±4.15
	Anova	n.s.	n.s.	**	***	n.s.	***	n.s.
Lead ≥ 15 - <20								
	Controls (n=22)	29.32±3.02	17.17±1.27	1.22±0.09	36.09±2.25	22.52±1.6	124.5±1.6	104.69±3.68
	Battery workers (n=52)	26.95±5.49	17.52±1.5	1.14±0.06	33.36±5.04	26.75±3.95	124.51±1.82	106.4±2.48
	Anova	n.s.	n.s.	**	*	***	n.s.	n.s.
Lead ≥ 20								
	Controls (n=14)	29.08±4.09	23.26±2.88	1.54±0.13	40.07±3.64	27.47±2.47	127.99±3.25	107.62±2.51
	Battery workers (n=90)	30.16±5.42	26.85±5.62	1.6±0.23	41.4±5.83	32.82±5.67	131.57±4.54	113.34±3.9
	Anova	n.s.	*	n.s.	n.s.	***	**	***

To observe the effects of lead on various parameters regardless of the mode of exposure (occupational or passive) the total individuals (smelters and controls) were divided into four groups based on the level of circulating blood lead levels. A highly significant (0.001) difference for all of the parameters was observed between different groups.

Table 4:

	Age years	Lead mg/L	CystatinC mg/L	ALT U/L	AST U/L	SBP mmHg	DBP mmHg
Lead < 10 (n=146)	26.2±4.96	6.97±1.47	0.8±0.14	18.15±6.4	12.84±4.39	116.04±3.83	94.28±4.33
Lead ≥ 10 - <15 (n=71)	27.17±4.35	12.45±1.48	1.03±0.08	28.72±5.15	20.03±4.22	121.23±2.83	101.64±3.8
Lead ≥ 15 - <20 (n=74)	27.65±4.99	17.42±1.44	1.17±0.08	34.17±4.56	25.49±3.93	124.51±1.75	105.89±2.97
Lead ≥ 20 (n=104)	30.01±5.26	26.37±5.46	1.59±0.22	41.22±5.59	32.1±5.65	131.09±4.55	112.57±4.22
Anova	***	***	***	***	***	***	***

4. DISCUSSION

Although human were aware of the toxic effects of lead as early as the 2nd century. The early rising empire of Roam remained ignorant of this, as the effects were mostly affecting the artisan workers of low social orders. While the toxicity creped in nobles and decided their predecessors with its effects on productivity and collapse of many of these empires with the induction of dementia among emperors (12). With the passage of centuries, humanity has become less ignorant and with a better understanding of the lead toxic effects, several effective controls were instrumented to decrease human exposure to lead toxic effects. Despite these efforts, the lead toxicity resulted in around 1million death and was casual of disability in around a 24million peoples in the year 2017 (13). However, the craftsman and peoples working in the lead-related industry are still exposed and suffering the lead toxic effects like the artisan workers of earlier history.

Present study results are indicative of a higher burden of BLL (blood lead level) in smelters in comparison to the control group. In the year 1991, the CDC has recommended the elevated blood level to ≥10mg/dl and consideration of treatment for the lead levels of ≥15mg/dl (14). It is observed that 72.82% of subjects with occupational exposure to lead were having a BLL level of ≥15mg/dl and out of these 46.15% were having a BLL level of ≥20mg/dl, the BLL level that was recommended as treatable. A 1976-1980 spawned survey followed mortality rate in US adults in correlation to BLL found a 46% increase in overall mortality, circulatory mortality increase by 39% and cancer mortality increase by 68% in adults having BLL 20-29mg/dl in contrast to those having BLL <10mg/dl (15). Only 10% of the smelter found to have BLL <10mg/dl in contrast to the control population where 63% were falling in this group. It is interesting to note that even 11% of the control population found having BLL ≥15mg/dl, an additional 7% having BLL ≥20mg/dl. Literature related to lead toxicity reveal that no level of blood lead can be considered safe, even lower BLL (≥2mg/dl) was found to be associated with mortality due to myocardial infarction (16).

Toxicity induced by lead may result in damage to multiple organs including the liver, kidney, brain and cardiovascular system. AST and ALT in circulation serve as a marker for hepatic cellular damage. The mean values for serum AST and ALT observed in both groups were within the normal reference range, the mean values for AST were significantly (0.05) higher in the occupationally lead-exposed smelters group than subjects in the control group. ALT level was also found to be higher in the smelter group, but the increase was non-significant. It was also observed that similarly rising levels of both of these enzymes were observed in both the group in relation to the BLL regardless of the exposure mode i.e. occupational as in smelters and passive in the control group. S Can et al., (17) also have reported a comparatively higher level of AST and ALT in battery workers in comparison to the control group. A positive correlation of BLL with AST and ALT was reported (18, 19).

Kidneys are considered as the prime target for heavy metals toxic effects, because of their tendency for reabsorption and accumulation due to apical membrane and bicollateral membrane transportation difference; this may lead to the build-up of heavy metals in renal tissue.

The duration of exposure and dosage determine the extent of the damage. Several workers have reported the association of chronic exposure to lead and higher BLL levels with various degrees of nephropathy and increased renal damage markers (20, 21). Cystatin C is an antiprotease and is the product of housekeeping gene activity of the cells, passaged freely across glomeruli, and is not reabsorbed to blood. Serum cystatin C is inversely proportional to the GFR and is considered a better marker to assess renal function than serum creatinine (L9, 1347). The comparison of the mean for cystatin C among two groups reveals a significant (0.01) higher level in the smelter groups, however the values were at the borderline of the reference range for serum cystatin C for males (0.60 – 1.03mg/L).

Lead toxicity induced glomerulo-tubular nephropathy with its effects on GFR was found to be associated with hypertension (1347). Comparatively higher values for both of the systolic and diastolic pressure were recorded in the smelter group in comparison to the control group. The difference was found to be significant (0.01) for the systolic blood pressure and was not significant for the diastolic blood pressure. Our results are in confirmation with Rahman et al., who reported the association of BLL with hypertension in the Pakistani adult population with non-occupational exposure to lead (JZUSB07).

Significant differences were observed in all the studied parameters (except age) when the individual were grouped based on the BLL levels. This indicates that the toxic effects of lead are independent of mode of exposure in the population studied. This also indicates that monitoring lead in general population is as important as in the industrial workers exposed to lead.

REFERENCE:

Abdul L. W., J. A. Usmani, (2015). Lead toxicity: a review. Interdisciplinary toxicology, 8(2), 55.

Binns, H. J., C. Campbell, M. J. Brown, (2007). Interpreting and managing blood lead levels of less than 10 µg/dL in children and reducing childhood exposure to lead: Recommendations of the Centers for Disease Control and Prevention Advisory Committee on Childhood Lead Poisoning Prevention. Pediatrics, 120(5), e1285-e1298.

Barry, V., A.C Todd, K. Steenland, (2019). Bone lead associations with blood lead, kidney function and blood pressure among US, lead-exposed workers in a surveillance programme. Occupational and environmental medicine, 76(5), 349-354.

Can, S., C. Bağci, M. Ozaslan, (2008). Occupational lead exposure effect on liver functions and biochemical parameters. Acta Physiologica Hungarica 95(4), 395-403.

Dongre, N. N., A.N. Suryakar, A. J. Patil, D.B. Rathi, (2010). Occupational lead exposure in automobile workers in North Karnataka (India): effect on liver and kidney functions. Al Ameen J Med Sci, 3(4), 284-92.

Harari, F., G. Sallsten, A. Christensson, (2018). Blood lead levels and decreased kidney function in a population-based cohort. American Journal of Kidney Diseases, 72(3), 381-389.

Ekong, E. B., B. G. Jaar, V. M. Weaver, (2006). Lead-related nephrotoxicity: a review of the epidemiologic evidence. Kidney international, 70(12), 2074-2084.

Kazmi, T., A. Omair, (2005). Control of lead poisoning in Pakistan. Journal –Pakistan medical association, 55(10), 409Pp.

Lustberg, M., E Silbergeld, (2002). Blood lead levels and mortality. Archives of internal medicine, 162(21), 2443-2449.

Muntner, P., J.He, S. Vupputuri, J. Coresh, V. Batuman, (2003). Blood lead and chronic kidney disease in the general United States population: results from NHANES III. Kidney international, 63(3), 1044-1050.

Menke, A., P. Muntner, V. , Batuman, (2006). Blood lead below 0.48 mmol/L (10 mg/dL) and mortality among US adults. Circulation, 114(13), 1388-1394.

Murty, M. S. N., U.K. Sharma, V.B. Pandey, S.B. Kankare, (2013). Serum cystatin C as a marker of renal function in detection of early acute kidney injury. Indian journal of Nephrology, 23(3), 180.

Murty, M. S. N., U.K. Sharma, 2013). Serum cystatin C as a marker of renal function in detection of early acute kidney injury. Indian journal of Nephrology, 23(3), 180.

Nawrot, T. S., L. Thijs, E. M., Den Hond, H. A., Roels, J. A. Staessen, (2002). An epidemiological re-appraisal of the association between blood pressure and blood lead: a meta-analysis. Journal of human hypertension, 16(2), 123-131.

Nawrot, T. S.,Staessen, J. A, (2006). Low-level environmental exposure to lead unmasked as silent killer. Circulation, 114:1347-1349.

O'Connor, D., D. Hou, J. Ye, (2018). Lead-based paint remains a major public health concern: A critical review of global production, trade, use, exposure, health risk, and implications. Environment international, 121, 85-101.

Patil, A. J., V.R. Bhagwat, J.A. Patil, (2007). Occupational lead exposure in Battery Manufacturing workers, Silver Jewellery workers and spray painters of Western Maharashtra (India): Effect of liver and kidney functions. J Basic Clin Physiol Pharmacol, 18(2), 63-80.

Poręba, R., P. Gać, M. Poręba, Antonowicz-Juchniewicz,. (2011). Relation between occupational exposure to lead, cadmium, arsenic and concentration of cystatin C. Toxicology, 283(2-3), 88-95.

Rahman, S., Khalid, N., Zaidi, J. H., Ahmad, S., & Iqbal, M. Z. (2006). Non-occupational lead exposure and hypertension in Pakistani adults. Journal of Zhejiang University Science B, 7(9), 732-737.

Riva, M. A., A. Lafranconi, M.I. D'orso, G. Cesana, G. (2012). Lead poisoning: historical aspects of a paradigmatic "occupational and environmental disease". Safety and health at work, 3(1), 11-16.

Silbergeld, E. K., V. M. Weaver, (2007). Exposure to metals: are we protecting the workers?141-142.

Tong, S., A. J., McMichael, P. A. Baghurst, (2000). Interactions between environmental lead exposure and sociodemographic factors on cognitive development. Archives of Environmental Health: An International Journal, 55(5), 330-335.

Weaver, V. M., B. Lee, K., Ahn, (2003). Associations of lead biomarkers with renal function in Korean lead workers. Occupational and environmental medicine, 60(8), 551-562.

Zhang, W., M. Zi, L Sun, F, Wang, S, Chen,. (2019). Cystatin C regulates major histocompatibility complex-II–peptide presentation and extracellular signal-regulated kinase-dependent polarizing cytokine production by bone marrow-derived dendritic cells. Immunology and cell biology, 97(10), 916-930.