ORIGINAL ARTICLE

The Clinical Spectrum of Plumbism; an Experience from a Tertiary Care Hospital in Karachi, Pakistan

LENA JAFRI[1], NADEEM ULLAH KHAN[2], MUHAMMAD AKBAR BAIG[3], NOMAN ALI[4], HAFSA MAJID[5], AYESHA HABIB KHAN[6]

[1] Assistant Professor at Department of Pathology and Laboratory Medicine, Aga Khan University Hospital, Karachi, Pakistan
[2] Associate Professor and Consultant, Department of Emergency Medicine, Aga Khan University Hospital, Karachi, Pakistan
[3] Senior Instructor at Department of Emergency Medicine, Aga Khan University Hospital, Karachi, Pakistan
[4] Resident year V, Department of Emergency Medicine, Aga Khan University Hospital, Karachi, Pakistan
[5] Senior Instructor at Department of Pathology and Laboratory Medicine, Aga Khan University Hospital, Karachi, Pakistan
[6] Associate Professor and Head at section of Chemical Pathology, Department of Pathology and Laboratory Medicine, Aga Khan University Hospital, Karachi, Pakistan

Abstract

Background: Lead toxicity continues to remain a concerning health problem for developing nations like Pakistan. Due to the lack of studies, we aim to highlight the clinical spectrum of lead poisoning in patients presenting to an urban-based tertiary care hospital in Pakistan.
Method: This is a retrospective review of patients admitted form January 2011 to December 2014 using a structured questionnaire for recording demographics, comorbidities, clinical findings, biochemical abnormalities, clinical findings and treatment provided. Patients were categorized as children (≤18yrs) and adults (>18yrs), further divided into three groups; desired blood lead levels (BLLs) [lead levels <2ug/dl in children and <10ug/dl in adults], high but non-toxic [children 2-10ug/dl, adults 10-70ug/dl] and toxic [children >10ug/dl, adults >70ug/dl].
Results: A total of 86 patients were included in the final analysis, majority (69.6%) of whom were adult males with median age of 35 yrs. Median (IQR) BLL was 6.3 ug/dl (12.8-2.7) in all age groups with BLL in children and adults of 4.2 ug/dl (3.1-5.7) and 6.5 ug/dl (2.6-14.7), respectively. 72% of the children had complaints related to the central nervous system with majority complaining of irritability. The gastrointestinal system was most commonly implicated in adults (93%) with most common complaint of abdominal pain. The commonest risk factor showing a positive correlation with BLLs was battery handling in adults [median (IQR) BLL 18.4ug/dl (8.35-36.1)] and pica eating in children with BLLs in high but non-toxic range [median (IQR) BLL 5.2ug/dl (2.7-5.7)]. The highest BLLs were observed to lie within the high but non-toxic range group in one adult herbal medicine user (54.4 ug/dl) and in children observed in the toxic range group (>10ug/dl) due to occupational battery work exposure and residence in a congested zone.
Conclusion: Lead toxicity continues to be hazardous due to unchecked environmental and occupational exposure. Increasing awareness is tantamount in order to find a solution.

Keywords: Emergency; Lead Toxicity; Pakistan; Plumbism

How to cite this article: Jafri L, Ullah Khan N, Baig MA, Ali N, Majid H, Habib Khan H. The Clinical Spectrum of Plumbism; an Experience from a Tertiary Care Hospital in Karachi, Pakistan. *Asia Pac J Med Toxicol* 2017;6(4):118-22.

INTRODUCTION

Lead is a cumulative toxic metal and is known for its toxicity since time immemorial (1). The major environmental sources of lead exposure include air, dust, soil, drinking water and food contaminated with lead (2). In developing nations like Pakistan, occupations that impose greater risk for lead poisoning include working in industries manufacturing lead-related products such as paints, water pipes, batteries, eye cosmetics, food cans, petroleum (added as an anti-knocking agent), oaring and mining (3-8).

Lead is not an essential element and serves no purpose in the body. The routes of exposure for inorganic lead are primarily through ingestion followed by inhalation (4). Once it is absorbed, lead is found in all tissues, but eventually 90% or more of the body burden is accumulated in the bone with a biological half-life from years to decades. Lead is excreted primarily in the urine (5). It causes pathophysiological effects through the interference of various enzymatic systems by binding to sulfhydryl groups found on enzymes resulting in extensive free radical damage of cell structures including the DNA and cell membranes. Lead can cause a reduction of immune function resulting in excessive inflammation (6, 7).

Blood lead level is the most reliable indicator of lead intoxication. In 1991, the Centers for Disease Control and Prevention (CDC) redefined the reference value of elevated blood lead levels (BLLs) from >25 µg/dl to >10 µg/dl (8). In spite of lead being one of the most prevalent toxins, only few

*Correspondence to: Dr. Muhammad Akbar Baig; Senior Instructor. Department of Emergency Medicine, Aga Khan University Hospital, Stadium Road, P.O. Box 3500, Karachi 74800, Pakistan.
E-mail: dr_akbar2007@hotmail.com , Tel: +92 315 221 87 58
Received 18 October 2017, 23 November 2017

studies have so far been conducted in Pakistan. However, the published data clearly indicate that blood lead levels of both general population as well as the exposed groups are much above the internationally acceptable limits (9-12).

Lead poisoning is a serious public health concern in Pakistan. Although the biochemical and hematological features of acute/sub-acute lead poisoning have been well studied (13), there is paucity of data regarding the clinical spectrum of lead poisoning relevant to our population. Therefore, the objective of this study is to highlight the toxicological syndrome of lead poisoning in patients presenting to an urban-based tertiary care hospital of Pakistan.

METHODS

A retrospective chart review was conducted on all cases admitted at the Aga Khan University Hospital (AKUH) with Blood Lead Levels (BLL) test being performed for suspected or confirmed lead poisoning from period of January 2011 to December 2014. AKUH is a 563-bedded tertiary care teaching hospital in Karachi, Pakistan. It serves more than 80,000 patients annually and has a dedicated drug and poison information center for toxicology-related consultations (14). Whole blood lead levels were performed by graphite tube atomizer, atomic absorption spectrometer 200 series AA (Agilent Technologies, California, US). Three-level quality control materials were run with each batch of samples. The laboratory participated in proficiency testing survey of College of American Pathologist twice a year with >80% performance when compared with the peer group. The study was reviewed by the Ethical Review Committee of AKUH and was granted exemption (3344-Pat-ERC-14).

Medical files of patients registered at AKUH were reviewed using a pre-structured questionnaire by a trained investigator to record the following information about patients;

- Socio demographics,
- Comorbidities (diabetes, hypertension, congestive heart failure, chronic obstructive pulmonary disease, chronic kidney disease),
- Clinical findings (General Physical; pallor, fatigue, muscle/bone/joint pain, weight loss, lead lines on gums, Cardiovascular systems; elevated blood pressure, Central nervous system; developmental delay, learning disabilities, mood disorder/Irritability, seizure, headache, memory loss, hearing loss, foot/wrist drop pain/tingling/numbness of extremities, Gastrointestinal system; anorexia, abdominal pain, constipation, reproductive system; premature delivery, infertility, miscarriage, Renal system; acute Kidney Injury),
- Risk factors (lead battery handlers, pica eating habit, ayurvedic medicine user, aluminum utensils user, petrol pump station worker, resident of a newly painted house, home in polluted zone, home undergoing renovation) and
- Treatment provided (hospitalized for it, Chelation therapy provided).

The data were transferred into an Excel database (Microsoft Corporation, Redmond, WA), cleaned, and analyzed with SPSS version 20. Patients were categorized as children (≤18yrs) and adults (>18yrs); they were further divided into 3 groups; desired BLLs (lead levels <2ug/dl in children and <10ug/dl in adults), high but non-toxic (children 2-10ug/dl, adults 10-70ug/dl) and toxic (children >10ug/dl, adults >70ug/dl).

Normality of data was assessed using Shapiro-Wilk test. Test of normality showed significant results, so median (IQR) was reported. Continuous variables were summarized as medians and interquartile ranges (IQR), while categorical variables are summarized as frequency and percentages. Mann–Whitney U test was done to assess the relationship between systems involved, risk factors and BLLs. A cutoff p-value of < 0.05 was accepted as the cutoff for statistical significance.

RESULTS

Out of 103 patients presented for clinical suspicion of lead toxicity, medical records of 86 patients were reviewed. While twenty-nine patients (33.7%) belong to pediatric age group aged ≤18yrs [median (IQR) age of 5yrs (3-8.5)], a majority of fifty-nine patients (69.6%) belonged to the adult age group aged >18 years [median (IQR) age of 35yrs (25-49)]. The commonest comorbid conditions identified were of hypertension (11.5%; n=10) followed by diabetes (7%; n=6). Twenty (23%) patients were admitted while only one patient was treated with chelation therapy. The median (IQR) BLL was in high but not toxic range of 6.3 ug/dl(2.7-12.8). The median BLL values in adults and pediatric groups are shown in further detail in Figure 1. Amongst the systems involved, signs and symptoms related to gastrointestinal (GIT) system (p value <0.01) and central nervous system (CNS) (p value <0.05) were significant and their respective association with the different BLL groups are shown in further detail in Table 1 and Figure 2.

Table 1. Systems involved associated with desired, high & non-toxic and toxic blood lead levels (BLLs). (N/A=Not available)

System	n (%)	Desired BLLs n (%)	High and non-toxic BLLs n (%)	Toxic BLLs n (%)	P Value (<0.05)
General Physical	30	14	14	2	0.43
Central Nervous System	25	9	14	2	0.05
Gastrointestinal System	42	28	12	2	0.01
Cardiovascular System	10	6	4	N/A	0.5
Reproductive System	3	1	2	N/A	0.59

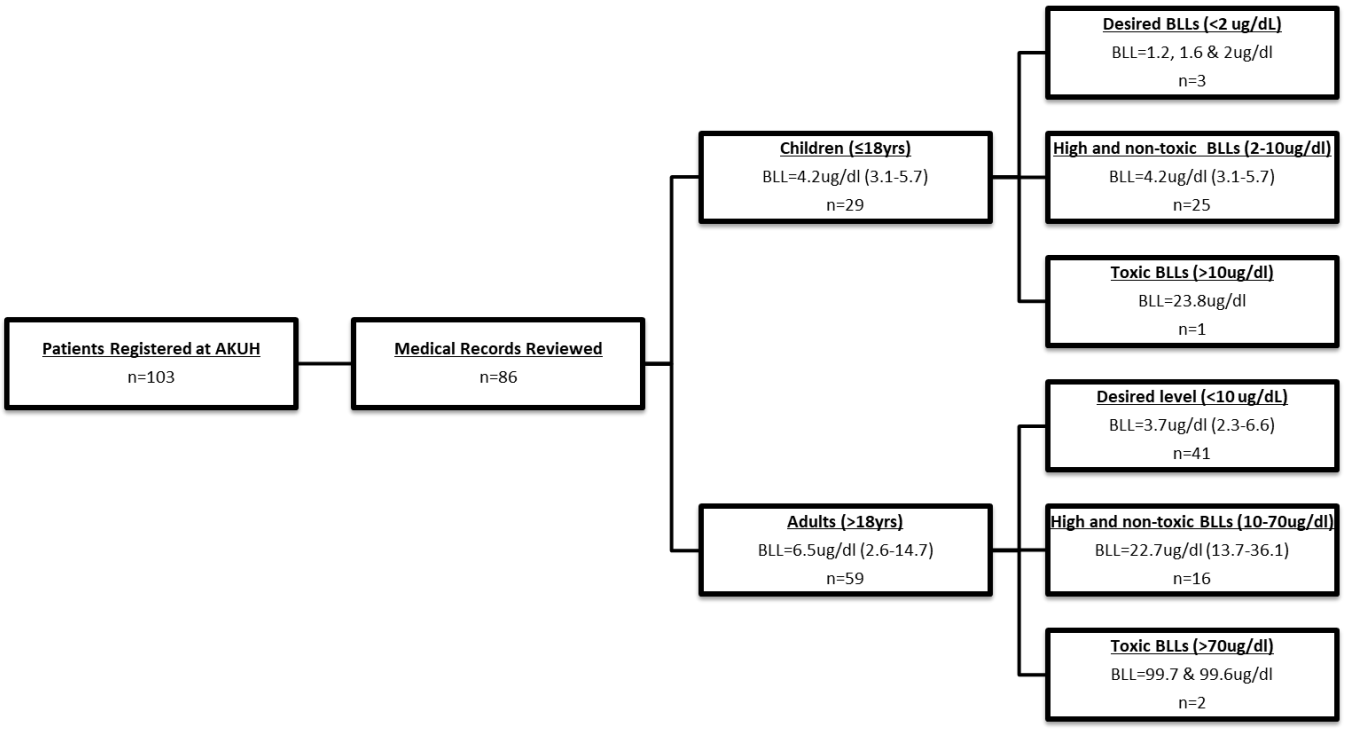

Figure 1. Consort diagram showing distribution of patients tested for blood lead levels (BLLs) for clinical suspicion of lead toxicity at Aga Khan University Hospital (AKUH) from Jan 2011 – Dec 2014.

In the pediatric age group (aged ≤18yrs), we established 89% (n=26) of children to have BLLs that exceeds the desired range, i.e. > or equal to 2 ug/dl. Only one child had a toxic value exceeding > 10 ug/dl. The most common risk factor identified in 80% of the pediatric age group was that of pica eating with a median (IQR) BLL in high but not toxic range of 5.3 ug/dl (2.7-5.7) followed by occupational battery work exposure and indwelling within a congested area noted in one pediatric case only with BLL lying in toxic range of > 10 ug/dl (Table 2 & Figure 3). Risk factors were not identified in 19 pediatric cases (65%) due to absent information. The most common symptoms noted in 72% of children were related to the CNS with majority complaints of irritability [Median (IQR) BLL 4.6 ug/dl (2.7-5.8)] followed by learning difficulty [Median (IQR) BLL 3.4 ug/dl (1.8-6.1)], seizures and developmental delay each with a median BLL >2 ug/dl (Figure 2). 20% of pediatric patients (6 of total) were found to be anemic on physical examination with median (IQR) BLL 4.1 ug/dl (3-6.3). However, the corresponding median (IQR) blood hemoglobin value was equal to 12.5 gm/dl (10.8-14.4).

In the adult age group (aged>18yrs), we observed 30% of patients to have BLLs exceeding desired range > 50% of these patients having BLLs in high but not toxic range group [Median (IQR) BLL 27.2 ug/dl (13.7-36.1)]. BLL amongst various risk factors resided in high but not toxic range group and the most common risk factor observed in 89% of adult patients was occupational related to handling of lead batteries [Median (IQR) BLL 18.4 ug/dl(8.3-36.1)]. This was followed by residence in a polluted zone and usage of herbal

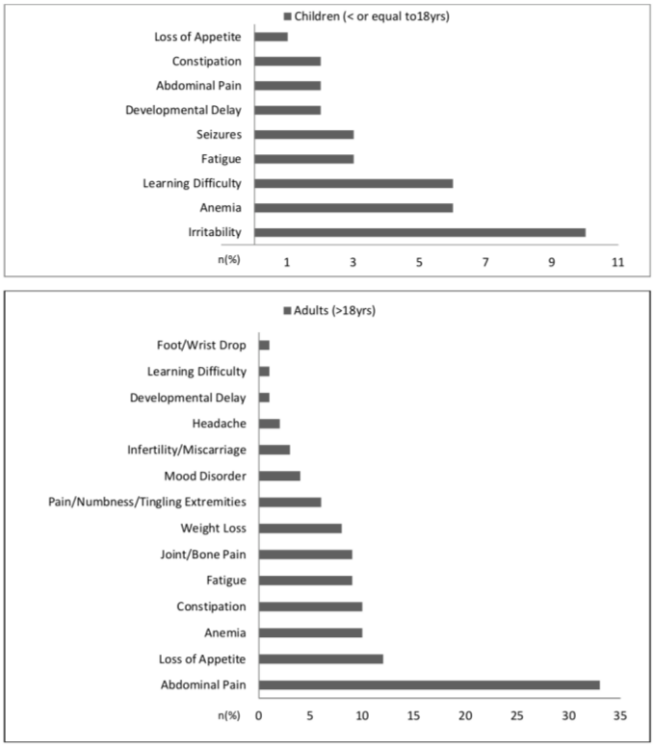

Figure 2. Clinical spectrum in patients with lead poisoning.

medications in one patient only each with the highest recorded BLL of 54.4 ug/dl in herbal medicine user in

Table 2. Risk factors associated with desired, high & non-toxic and toxic blood lead levels (BLLs). (N/A=Not available)

Risk Factors	Desired BLLs (ug/dl) n (%)	High and non-toxic BLLs (ug/dl) n (%)	Toxic BLLs (ug/dl) n (%)	P value(<0.05)	Lead Levels (ug/dl)	Age (yrs.)
Lead Battery Handlers	4	11	2	0.005	18.4 (8.35-36.1)	29 (24-43)
Pica Eating Habit	N/A	8	N/A	0.005	5.2 (5.7-2.75)	2.5 (2-7)
Ayurvedic/Herbal Medicine User	N/A	1	N/A	N/A	54.4	49
Home in Polluted Zone	N/A	2	N/A	N/A	23.8, 37.3	10, 24
Smoking	5	N/A	N/A	N/A	2.9 (2.5-4)	38 (30-50)

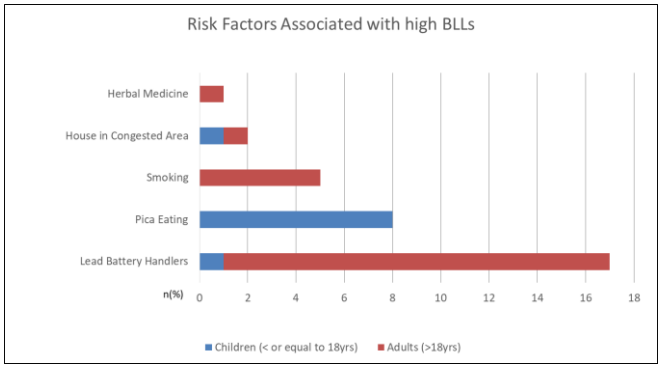

Figure 3. Risk factors in patients with lead poisoning.

comparison to rest of the cases with other risk factors (Table 2 & Figure 3). Missing information for risk factors was noted in 69% (41 of total) of adult patients. The most common symptoms observed in 93% of adults were related to the GIT with abdominal pain being the highest with a median (IQR) BLL in the desired range group of 4.4 ug/dl(2.5-10.6). Higher but non-toxic range BLLs were seen in patients complaining of loss of appetite [Median (IQR) BLL 5.9 ug/dl (2.3-54.1)] and constipation [Median (IQR) BLL 7.3 ug/dl (3.3-41.2)]. A toxic range BLL of 99.7ug/dl was noted in only one adult patient with a complaint of headache (Figure 2).

DISCUSSION

This study is the first of its kind to evaluate the different characteristics of lead poisoning in patients presenting to an urban tertiary hospital of Karachi which is considered to be one of the most heavily polluted city with lead amongst other toxic minerals (15). Most of the present study's patients were adults with a male to female ratio of 3:1.

High level of lead exposure particularly of occupational exposure has been reported to cause hypertension, endothelial dysfunction, arteriosclerosis, and cardiovascular disease (16, 17). Certain studies have shown that prolonged environmental and occupational exposure even to low levels of lead can be associated with the occurrence of elevated blood pressure (18). The commonest comorbid condition observed in our study was that of hypertension. Majority of adult patients had gastrointestinal symptoms on presentation and abdominal pain was the most frequent complaint reported separately in both adults and children (19). This could be because of the primary mode of toxicity being oral ingestion (4). The next frequent toxicity noted in children was of the central nervous system which is most sensitive to effects of lead intoxication (20). Most of the pediatric patients complained of irritability and mood disturbances (21). The developmental effects of lead exposure occur during a critical time frame especially in ages < 2 years. This subsequently enables greater penetration of lead within the CNS and eventual neurotoxicity (22). Findings of anemia were insignificant in this study; however, lead is proven to cause impairment of heme synthesis and red cell destruction (23).

Lead intoxication has long been long associated with occupational exposure (24). Petrol pump station workers showed decreased lead exposure which is probably due to lead-free petrol now being dispensed in Pakistan (25). The most readily occurring occupational intoxication reported was in lead battery repair workers which has been similarly observed in prior studies (26, 27). This suggests the need for preventive measures in battery repair workers and improvements in work safety measures in order to ensure their protection from lead toxicity. Studies conducted in Pakistan have established greater than desired range of BLLs in children with history of pica eating (25, 28), similar to the findings observed in our study. Houses painted with lead-based paint and urban residential areas where there is mobilization of heavy automobile traffic are likely to contain high lead concentrations in environment (29). Although our data analysis did not indicate a significant number of patients residing in a polluted zone, it was still associated with BLLs beyond the desired range. One adult herbal medicine user with high but non-toxic range of BLLs was also brought to attention in our study pointing out the presence of heavy metals in ayurvedic herbal preparations that are marketed without proper regulatory control (30). Smokers are at increased risk to lead exposure as well (26).

23% of patients in our study were admitted to the hospital; however, only one case was offered chelation therapy as we naturally expected majority of cases to be the result of chronic intoxication where chelation therapy is of no significant benefit in light of its numerous side effects (31).

LIMITATIONS

Our study has provided us strong insight into the existing status of symptomology and risk factors associated with BLL exposure in the Pakistani population. However, the study is limited as complete clinical information could not be accumulated due to retrospective nature of the study. Therefore, it would be significantly beneficial to conduct a prospective multicenter study of looking into the toxicity of lead in relation to various socio demographic factors and clinical presentations along with benefits of available treatment options in context to various industrial cities of Pakistan.

CONCLUSION

Lead continues to remain a potentially toxic substance for developing nations like Pakistan. If not handled with care, it may cause dangerous health effects leading to morbidity and mortality at significantly increased levels. At present, our country continues to struggle with routine screening for lead levels. Therefore, increasing awareness to its related hazards would be extremely beneficial in reducing exposure. Another lethal association is that of carcinogenesis with the environmental exposure to lead (32) which will require further and much needed larger scale studies for better elucidation in our population.

Conflict of Interest: None to be declared.
Funding and Support: None.

REFERENCES

1. Klassen CD. Toxicology. 8th ed. New York: Maxwell McMillan Int; 1991.
2. Centre of Disease Control and Prevention (CDC). Sources of Lead. 2015. Available from: https://www.cdc.gov/nceh/lead/tips/sources.htm
3. Centre of Disease Control and Prevention (CDC). Jobs that may have lead exposure. 2017. Available from: https://www.cdc.gov/niosh/topics/lead/jobs.html
4. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for lead. 2007. Available from: https://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=96&tid=22
5. The Association of Occupational and Environmental Clinics (AOEC). Medical Management Guidelines for Lead-Exposed Adults. 2007. Available from: http://www.aoec.org/documents/positions/MMG_FINAL.pdf
6. Flora SJ, Mittal M, Mehta A. Heavy metal induced oxidative stress & its possible reversal by chelation therapy. *Indian J Med Res* 2008;128:501-23.
7. Robert AG, Thomas WC. Toxic effects of metals. 7th ed. United States: McGraw-Hill Professional; 2007.
8. Kazmi T, Omair A. Control of Lead Poisoning in Pakistan. *J Pak Med Assoc* 2005;55:409–10.
9. Rahman A, Maqbool E, Zuberi HS. Lead-associated deficits in stature, mental ability and behaviour in children in Karachi. *Ann Trop Paediatr* 2002;22:301–11.
10. Rahbar MH, White F, Agboatwalla M, Hobhabri S, Luby S. Factors associated with elevated blood lead concentrations in children in Karachi, Pakistan. *Bull World Health Organ* 2002;80:769–75.
11. Hozhabri S, White F, Rahbar MH, Agboatwalla M, Luby S. Elevated blood lead levels among children living in a fishing community, Karachi, Pakistan. *Arch Environ Health* 2004;59:37–41.
12. Agha F, Sadaruddin A, Khatoon N. Effect of environmental lead pollution on blood Lead levels in Traffic Police Constables in Islamabad, Pakistan. *J Pak Med Assoc* 2005;55:410-3.
13. Gordon JN, Taylor A, Bennett PN. Lead poisoning: case studies. *Br J Clin Pharmacol* 2002;53:451-8.
14. Fazal O, Madraswala M, Bangash SSM, Karim M. An assessment of toxicology telephone calls received by the drug and poison information centre at Aga Khan University Hospital, Karachi, Pakistan. *Southern Med Review* 2010;2:24-6.
15. DAWN. Karachi exposed to acute lead pollution. 2009. Available from: https://www.dawn.com/news/879770
16. Mbarouk GS, Sawe HR, Mfinanga JA, Stein J, Levin S, Mwafongo V, et al. Patients with acute poisoning presenting to an urban emergency department of a tertiary hospital in Tanzania. *BMC Res Notes* 2017;10:482.
17. Flora G, Gupta D, Tiwari A. Toxicity of lead: A review with recent updates. *Interdiscip Toxicol* 2012;5:47-58.
18. Vaziri ND. Mechanisms of lead-induced hypertension and cardiovascular disease. *Am J Physiol Heart Circ Physiol* 2008;295:H454-65.
19. D'souza HS, Dsouza SA, Menezes G, Venkatesh T. Diagnosis, Evaluation, and Treatment of Lead Poisoning in General Population. *Indian J Clin Biochem* 2011;26:197-201.
20. Cory-Slechta DA. Legacy of lead exposure: consequences for the central nervous system. *Otolaryngol Head Neck Surg* 1996;114:224-6.
21. Flora SJS, Flora G, Saxena G. Environmental occurrence, health effects and management of lead poisoning. 1st ed. Netherlands: Elsevier Publication; 2006.
22. Sanders T, Liu Y, Buchner V, Tchounwou PB. Neurotoxic effects and biomarkers of lead exposure: A Review. *Rev Environ Health* 2009;24:15-45.
23. Vaziri ND. Mechanisms of lead-induced hypertension and cardiovascular disease. *Am J Physiol* 2008;295:H454–H65.
24. Ji JS, Schwartz J, Sparrow D, Hu H, Weisskopf MG. Occupational Determinants of Cumulative Lead Exposure: Analysis of Bone Lead Among Men in the VA Normative Aging Study. *J Occup Environ Med* 2014;56:435-40.
25. Kadir MM, Janjua NZ, Kristensen S, Fatmi Z, Sathiakumar N. Status of children's blood lead levels in Pakistan: implications for research and policy. *Public health* 2008;122:708-15.
26. Basit S, Karim N, Munshi AB. Occupational lead toxicity in battery workers. *Pak J Med Sci* 2015;31:775-780.
27. Ahmad ASK, Khan MH, Khandkar S, Sarwar AFM, Yasmin N, Faruquee MH, et al. Blood Lead Levels and Health Problems of Lead Acid Battery Workers in Bangladesh. *Sci World J* 2014;2014:7.
28. Khalil M, Rashid J, Khan MMN, Iqbal MS. Determination of serum lead levels in children aged 1–6 years with or without history of pica. *Pakistan Ped J* 2004;28:26–30.
29. Clark CS, Thuppil V, Clark R, Sinha S, Menezes G, D'Souza H, et al. Lead in paint and soil in Karnataka and Gujarat (India). *J Occup Environ Hyg* 2005;2:38–44.
30. Gunturu KS, Nagarajan P, McPhedran P, Goodman TR, Hodsdon ME, Strout MP. Ayurvedic herbal medicine and lead poisoning. *J Hematol Oncol* 2011;4:51.
31. Flora SJ, Pachauri V. Chelation in metal intoxication. *Int J Environ Res Public Health* 2010;7:2745–88.
32. Gwini S, MacFarlane E, Del Monaco A, McLean D, Pisaniello D, Benke GP, et al. Cancer incidence, mortality, and blood lead levels among workers exposed to inorganic lead. *Ann Epidemiol* 2012;22:270-6.