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Invited critical review

Lead toxicity: An overview of prevalence in Indians

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ABSTRACT

Introduction: Elements form a basic and natural constituent of the Earth's crust and are released into the atmosphere due to many human activities like mining and manufacturing. Of all, the elements, lead toxicity is a prevailing as well as a growing concern the world over because of its ability to affect multiple clinical functions.
Methodology: Blood lead levels have been analyzed in a large pan-India cohort of 222,668 comprising of 121,115 males and 101,553 females respectively. The cohort included all age groups from <2 to >55 years old. The analytical platform of Inductively Coupled Plasma-Mass Spectrometry has been used to assess lead levels.
Result: Blood lead levels of ≥150 μg/L was considered high for analysis. The total frequency of high lead levels detected in our study was 1.16%. The frequency of males affected were higher than females, with the difference being statistically significant..
Conclusion: Lead being ubiquitous in its presence and also serving no biological function, has grown today to become a serious threat to human health. The high frequency of affected detected in our study raises a cause for concern. Determining its presence and the most affected geography in any country will aid in charting guidelines on controlling its release as well as exposure.

Contents

1. Introduction

Elemental pollution has grown to become a major concern in today's world and has been fueled due to many man-made activities like industrialization, mining, and manufacturing. Though most of the elements are naturally found on the Earth's crust, these activities in indiscriminate proportions have led to their release in the environment. Many of the elements enlisted in the periodic table are also micronutrients which aid in multiple cellular functions. However, some are deemed to be extremely toxic, and exposure to these even briefly or presence of these in the human body even in small amounts can cause severe adverse symptoms.

The major drawback associated with these kinds of toxicities in majority are asymptomatic until accumulated to high levels within the body. Also, it becomes difficult to trace the route of exposure in many cases, unless the affected is working or residing in an already known problematic region. A report in the newspaper Times of India, in the year 2013 highlighted the statistics of lead poisoning in 20% of children from Kolkata in India, with studies highlighting every fifth child to be a victim of this poisoning.

Lead (Pb, Plumbum) is the oldest known toxic metal and exposure can majorly occur through drinking water, smoking or even due to various industrial processes like smelting, through battery recycling, and paints. As it does not have any biological function, even in low levels, it can affect multiple clinical functions. Its most prominent effect is on the oxidative stress mechanism, wherein antioxidants like glutathione within

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the cell protect from cellular damage induced by the reactive oxygen species (ROS). High lead levels have been documented to increase amounts of ROS and reduce effect of antioxidants [1]. Lead exerts its toxicity basically by replacing the monovalent and bivalent ions like Na^{+}, Ca^{+}, and Mg^{+2}. This disturbs metabolism and also changes various other processes like cell adhesion, cell signaling, apoptosis, and release of neurotransmitters [2].

Since lead has no biological function, there are no safe levels as its presence can cause multiple irreversible damage. According to guidelines issued by the Centers for Disease Control and Prevention (CDC), blood lead levels of above 10 μg/dL is to be considered a cause for concern and treated [3]. Studies have also shown low lead levels to affect the nervous system causing behavioral changes, affecting concentration and cognitive functions, majorly in children affecting their learning ability and intelligence [4]. Both the central and the peripheral nervous system are affected by lead causing progressive degeneration of certain parts of the brain symptomized by irritability, poor attention span, headache, loss of memory, hallucinations, etc. [5]. Lead has also been documented to cause condition of anemia, both hemolytic as well as Frank's [6]. Acute and chronic nephropathy had also been documented on exposure to both high (>60 μg/dL) and low levels of exposure (~10 μg/dL). Apart from these, it can also cause ischemic heart disease and affect reproductive health.

Most of the body burden of lead is stored in bones and tissues, while blood carries only a minor fraction, though it is the major route for transportation of lead. Its half-life in blood circulation is documented to be between 28 and 36 days [7]. Thus lead has a high bioaccumulative property, and can be stored for ages in the bones, from wherein they leach into circulation with age and bone deterioration, causing long term deleterious effects.

With the ability to affect almost all critical functions in the human body, lead toxicity has become a growing health scare, throughout the globe, with every individual from children to adults being affected. Though popularized as an occupational hazard, the presence of this toxic element has become ubiquitous in today's world. With the discovery of high lead content in one of the popular quick foods of the country having been brought to light this year [8], the need for more awareness and statistics regarding average blood lead levels becomes important. Also, Ayurvedic medicines are widely used in India, many of which have been shown to have a high levels of toxic elements like lead and mercury. The modes available to assess lead levels in the body include biochemical tests to assess blood lead levels, while imaging platforms like K-XRF or K X-ray fluorescence can be utilized to determine lead levels in bone.

The bio-accumulative property has contributed to lead becoming a major environmental pollution burden today the world over, and dealing with the same requires control over all processes which leads to its release. To exactly understand the gravity of the situation, it is necessary to study and document the average blood lead levels across different age-groups throughout the country which will aid in taking measures and charting guidelines to deal with this growing menace of elemental pollution.

Our study was thus undertaken to document the frequency of lead toxicity in a pan-India cohort consisting of residents of the country across all age groups including both genders.

2. Materials and methods

2.1. Cohort

Our study analyzed a total of 222,668 samples from all across the country. The cohort included a total of 121,115 males and 101,553 females including all age-groups from infants to old adults respectively. The exact distribution of the cohort analyzed is highlighted in Table 1.

Table 1
Summary of study group.

Sr. No.	Category	Age-group	Gender	N
1	Infants	<2 years	Boys	67
			Girls	52
2	Children	2–10 years	Boys	405
			Girls	283
3	Adolescents	11–19 years	Boys	1349
			Girls	1209
4	Young adults	20–40 years	Men	52,663
			Women	45,472
5	Adults	41–55 years	Men	37,950
			Women	31,438
6	Old	>55 years	Men	28,681
			Women	23,099
Total				222,668

2.2. Methodology

Whole blood in EDTA Vacuette was used for analysis of blood lead levels post dilution. The diluent used was a 2 ppm gold solution in 0.5% nitric acid. The gold is added to stabilize mercury in the sample, while the acidic medium on the whole stabilizes all the elements present in the sample and prevents their adsorption to the tube. The internal standard used during analysis was 1 ppm Yttrium solution and the same was added to every sample during the dilution stage.

Post sample preparation, analysis was done using the analytical platform of Inductively Coupled Plasma-Mass Spectrometry (ICP-MS; Thermo Fischer Scientific). This is touted to be the gold standard for elemental analysis. Both lead and the internal standard Yttrium were analyzed in the standard (STD) mode. The isotope of lead with an atomic number of 208 was analyzed in all the samples.

Quality control analysis was also performed with each batch of sample analysis. The certified reference material used was NIST certified Seronorm™ Trace elements whole blood controls (SERO), all three levels. The control material was prepared the same way as sample with internal standard and diluent. Also, with every batch calibration multi-element standards were prepared and analyzed from 0.5 to 100 ppb. The linearity regression for all elements was checked to be ≥0.99 before proceeding with sample analysis.

3. Results

The blood lead levels reported were in μg/L units and values ≥150 μg/L of the same were considered to be high for analysis. The blood lead cut-off values were considered taking into account different Indian reports as well as our validation studies. The total frequency of high lead levels (≥150 μg/L) was detected to be 1.16%. Frequency of high lead levels in females and males was detected to be 0.9% and 1.4% respectively. This difference in frequency between both the genders was found to be statistically significant by the Chi-square test with Yates correction ($\chi^2 - 146.8$) and two-tailed P value of less than 0.0001.

The frequency of high lead levels recorded in the study across different age-groups has been highlighted in Table 2.

The data was also analyzed to understand if the difference in the frequency of high lead levels detected across different age groups were statistically significant. The frequency between the young adults group in totality vs adults with the old adults group was found to be statistically significant by the Chi-square test with Yates correction ($\chi^2 - 9.05$) and two-tailed P value equal to 0.0026.

The average blood lead levels detected in the cohort has been summarized in Table 3.

The samples analyzed in this study were from all across the country. Maximum cases of high blood lead levels were detected from the state of Maharashtra at 13.4% and the metro city of Mumbai alone recorded a frequency of 11.9%. A detailed summary on the list of top affected

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