Research Article

Prevalence of High Cadmium Levels in Major Metro Cities of India

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ABSTRACT

Aim: High levels of cadmium in the human body may have severe adverse consequences affecting the pulmonary system and the kidney. The purpose of this report was to assess the frequency of high Cd levels in a population of Asian Indians in metro cities in India. **Materials and Methods:** Blood Cd levels from a total of 2,05,637 individuals were included. Technology of Inductively Coupled Plasma Mass Spectromtery was utilized for analysis. **Results:** Cd levels higher than 1.5 µg/L were found at a frequency of 1.9%. The frequency of high Cd levels was significantly different between males and females at $p<0.0001$. Of the top metro cities analysed in this study, the frequency of blood Cd levels above 1.5 µg/L was highest for Mumbai (9.5 %), Bangalore (7.5 %) and Hyderabad (4.4 %). **Conclusion:** Acknowledging the issue of toxicity and addressing the need for testing, monitoring will have to go a long way for charting management plans aligned with development goals.

Key words: Cadmium, India, High levels, Mass Spectrometry, Blood Test.

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INTRODUCTION

Cadmium is a metal belonging to group IIB of the periodic table of elements. Poisoning by Cd has been reported world over by chronic exposure through air, water, or food potentially affecting the pulmonary, urinary, reproductive, cardiovascular and muscular system, even leading to cancer.[1] Exposure to Cd has been documented in historical records wherein lung damage among Cd exposed workers have been recorded in the early 1930s. In the 1960s and 1970s covering the post World War II era, the Japanese were detected to be affected and the Itai-Itai disease caused due to contamination of rice fields affected over 400 people till the year 2007.[2] Environmental Cd contamination and subsequent human exposure has been shown to have dramatically increased during the past 100 years.[3] Absorption of Cd due to ingestion has been shown to be high among individuals affected by deficiency of zinc, iron or calcium.[4] Body burden of Cd has been shown to be negligible at birth but gradually increases until 60 - 70 years of age depending on exposure, as organs like kidney and liver can accumulate up to 50% of the body burden.[5]

Cadmium exposure in humans can be efficiently evaluated by estimating its levels in blood, urine, saliva, hair as well as nail samples. Levels of Cd in blood or urine among humans have been shown to not correlate with the body burden and hence standards to define clinical toxicity remain unknown. However, Cd estimation in biological fluids has been considered to be an effective screening tool to determine acute or chronic exposure, correlating with geography and lifestyle. Analytical technologies widely used for estimation of metals include inductively coupled plasma - mass spectrometry (ICP-MS), inductively coupled plasma - optical emission spectrometry (ICP-OES), flame atomic absorption spectrometry (FAAS) and electro thermal atomic absorption spectrometry (ETAAS). Though FAAS bears the advantage of being simple and effective for Cd estimation, sensitivity continues to be an issue as the processing involves a pre-concentration step prior to detection. Platforms of ICP-MS and ICP-OES

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have been popularly used for elemental analysis including trace, toxic and nutritional elements as it delivers high power of detection, accuracy, sensitivity and precision.[6,7] Our study is aimed at presenting a report on high Cd level (above 1.5 μg/L) estimated from whole blood samples of a pan-India population.

MATERIALS AND METHODS

Study population

Whole blood EDTA samples from a total of 2,05,637 subjected to Cd estimation in our CAP accredited laboratory was included for this study. Estimation of Cd is a routine test in our laboratory, wherein testing for other toxic elements are also done including lead, mercury, arsenic, etc. Since the tests have been carried out in a reference laboratory, informed consent was not deemed a necessity as no client/patient identifiers have been used for this report apart from age, geography, gender and estimated Cd levels. Testing for blood toxic elements is provided as a part of preventive wellness package and hence samples are received from all over the country adding to the diversity in the geography of the samples received for testing.

Data from a total of 2,05,637 was considered for analysis including 1,11,240 males and 94,397 females and the average age in the study population was detected to be 45 +/- 15 years. Average Cd levels in the study population were detected to be 0.5 +/- 0.3 μg/L. The study population characteristics are highlighted in Table 1.

Methodology

Whole blood Cd levels were estimated using ICP-MS (Thermo iCAP Q, Thermo Fisher Scientific, USA) and ^{111}Cd isotope was analyzed. The protocol involved dilution of the blood sample using a 2 mg/L gold solution (Elemental Scientific, USA) in 0.5 % optima grade nitric acid (Fluka-Honeywell Research Chemicals, USA). Calibration of the ICP-MS platform was done using 1.0 mg/L Yttrium working stock solution (Inorganic Ventures, USA), 1.0 mg/L multi-element standard (MES, Elemental Scientific, USA) working stock solution without mercury and with mercury (Elemental Scientific, USA), as well as a blank and a 20 μg/L MES solution without internal standard (yttrium, iridium, rhodium). A successful calibration was indicated by r^2 value of >/= 0.99. Analysis of Cd was done in the standard (STD) mode and the analytical measurement range was 0.1 - 2.5 μg/L.

Sample processing involved addition of 75 μL of internal standard to 120 μL of whole blood and making up the volume to 3 mL using the diluent and vortex to mix. The ICP-MS MassHunter Workstation was used to control analyzer operations throughout the analysis process.

RESULTS

A total of 2,05,637 whole blood samples processed for Cd estimation was included for analysis. The study population included 1,11,240 males and 94,397 females with an average age of 45 +/- 15 years. Cadmium levels of above 1.5 μg/L were considered high for our analysis as per our lab established standards after studying 200 patient samples and as referred to the book of Tietz.

Acceptable values of less than 1.5 μg/L blood Cd levels was detected in 98 % of the study population, while frequency of high levels were detected to be 1.9 %. The frequency among males was detected to be high at 2.5 % compared to females at 1.2 % and the difference in frequency of the acceptable Cd levels and high was detected to be significant at $p<0.0001$. Characteristics of population exhibiting high Cd levels are highlighted in Table 2.

Further analysis involved studying the geography and regions from wherein the high levels of Cd cases were detected. The findings have been highlighted in Tables 3 and 4.

Table 1: Study population.

Study population	Value
Total	205637
Males	111240
Females	94397
Average Age (Males)	45 +/- 15 years
Average Age (Females)	45 +/- 15 years
Average Cd levels	0.5 +/- 0.3 μg/L
Average Cd levels (Males)	0.5 +/- 0.4 μg/L
Average Cd levels (Females)	0.5 +/- 0.3 μg/L

Table 2: High blood Cd levels population characteristics.

Population (> 1.5 μg/L)	Frequency/Value
Total	1.90%
Males	2.50%
Females	1.20%
Average Age (Males)	40 +/- 13 years
Average Age (Females)	45 +/- 15 years
Average Cd levels	2.1 +/- 0.5 μg/L
Average Cd levels (Males)	2.1 +/- 0.6 μg/L
Average Cd levels (Females)	1.9 +/- 0.4 μg/L

Table 3: Top metro cities with high blood Cd levels detected.

City	Frequency (%)	State	Frequency (%)
Mumbai	9.5	Maharashtra	16.0
Bangalore	7.5	Karnataka	8.0
Hyderabad	4.4	Telangana	5.0
Delhi	3.9	New Delhi	3.9
Pune	3	Maharashtra	16.0
Kolkata	2.8	West Bengal	3.9
Chennai	1.8	Tamil Nadu	4.4

Table 4: Top 5 Indian States with high Cd levels detected.

State	Frequency (%)
Rajasthan	25
Maharashtra	16
Karnataka	8
Bihar	7
Telangana	5

DISCUSSION

Existence of Cd in the environment occurs majorly due to human activities like burning of waste, fossil fuels, smoking and leakage of industrial sludge in agricultural soil. Though exposure to Cd has significantly reduced in recent times, its ability to concentrate in the liver and kidney makes it a more damaging environmental pollutant.[6] Studying human exposure to Cd becomes important as it can help understand source of contamination including the food chain and also because of its deleterious impact on human life. It affects cellular proliferation, inhibits cellular respiration, causes DNA breaks and chromosomal aberrations. In toxic levels, it has been shown to cause depletion of glutathione leading to increased production of reactive oxygen species and also to inhibit activity of many antioxidant enzymes like catalase and superoxide dismutase.[7]

Our study report is aimed to present an overview on prevalence of whole blood Cd levels higher than 1.5 μg/L in a pan-India population of over 2 lakh tested in our accredited reference laboratory over a span of one year. A total of 2,05,637 blood samples were tested for whole blood Cd levels using ICP-MS and the isotope ^{111}Cd was measured. Blood Cd levels of over 1.5 μg/L were considered high. Blood Cd levels of less than 1.5 μg/L was detected in 98% of the study population.

Prevalence of high Cd levels was analyzed for and was estimated to be at a frequency of 1.9% and the frequency among males was detected to be higher at 2.5% compared to females at 1.2%. The difference in frequency between males and females was also detected to be significant at $p<0.0001$. Studies have shown even moderate exposure to Cd at levels < 10 μg/L in blood to significantly affect semen quality among men without definitive evidence of impairment in male endocrine function.[8] The aim of the report was also extended to study the geography from wherein maximum high level cases were detected to identify probable causes of exposure.

In our study population major contribution of samples was detected to be from the States of Maharashtra (27%) and Uttar Pradesh (7%) from the North and Southern States including Karnataka (13%), Telangana (8%) and Tamil Nadu (7%). Analysis for high Cd levels detected States of Rajasthan (25%), Maharashtra (16%), Karnataka (8%), Bihar (7%) and Telangana (5%) to be the top 5. Further analysis in each of the top 5 States detected metro cities of Mumbai (9.5%) and Pune (3%) from Maharashtra, Bangalore (7.5%) from Karnataka and Hyderabad (4.4%) from Telangana to be the top 4 Cities.

In case of Maharashtra, the district of Thane is the most industrialized and studies on groundwater and soil samples from this region for metal contamination using inductively coupled plasma - atomic emission spectroscopy (ICP-AES) has detected high concentrations of Cd apart from mercury, arsenic and nickel. This study identified the probable cause to be linked with random dumping of industrial waste. This study also detected levels of Cd to range between 4.1 to 40 μg/L in the water much higher than the WHO permissible limits. High levels have been attributed to use of nickel cadmium batteries and PVC plastics.[9] Groundwater contamination studies from west Uttar Pradesh region in India, detected concentrations of Cd to be well above the WHO recommended concentrations of below 0.003 mg/L for drinking water with the detected average value being 0.06 mg/L.[10] In case of Tamil Nadu, a 2018 online report by the Central Groundwater Board stated detecting high levels of Cd, lead and chromium beyond the permissible limits of the Bureau of Indian Standards (BIS). The causes were linked to toxic effluent being released from tanneries in the region.[11]

In our analysis, the State of Rajasthan was detected to harbor 25 % of high Cd levels and the cities of Jhotwara and Udaipur were detected to have a frequency of 12% each. A study which documented the long-term impact of irrigation with zinc smelter effluent on food crops and soil in Rajasthan detected levels of Cd and lead to be above safe limits of CODEX admission in edible parts of almost all the crops. Studies have shown certain areas of Udaipur to be receiving irrigation through effluents from zinc smelter plants for over five decades.[12] In case of Jhotwara, the high frequency could be attributed to the fact that it is one of the highly industrialized regions of Rajasthan occupied with paper mills, steel rolling mills, cement companies and plastic processors.

CONCLUSION

Cadmium has been widely studied along with lead, arsenic and mercury to be a chief contaminant among geographies near industrial areas making its exposure study crucial in every Country. Further issues in management are complicated by the fact that there exists no consensus regarding treatment of toxicity. Though a few clinical studies indicate use of ethylenediamine tetraaceticacid (EDTA), 2,3-Dimercapto-1-propanesulfonic acid (DMPS) and dimercaptosuccinic acid (DMSA) to increase urinary excretion of Cd, the impact on overall body burden has been shown to not be significant.[13] According to the Third National Health and Nutrition Examination Survey (NHANES), Cd exposure in general population is a worldwide phenomenon and hence screening for burden of toxic elements even in general population is a need. Our report is an attempt to present a pilot aspect on Cd exposure in a pan-India population by estimating levels of the same in whole blood samples using technology of ICP-MS. The authors believe such pilot reports will guide further large scale studies focused at identifying cause of exposure and management of the same.

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CONFLICT OF INTEREST

The authors declare no conflict of interest

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ABBREVIATIONS

BIS: Bureau of Indian Standards; **Cd:** Cadmium; **CAP:** College of American Pathologists; **DMPS:** 2,3-Dimercapto-1-propanesulfonic acid; **DMSA:** Dimercaptosuccinic acid; **EDTA**: Ethylenediaminetetraacetic acid; **ETAAS:** Electro Thermal Atomic Absorption Spectrometry; **FAAS:** Flame Atomic Absorption Spectrometry; **ICP-AES:** Inductively Coupled Plasma - Atomic Emission Spectroscopy; **ICP-MS:** Inductively Coupled Plasma - Mass Spectrometry; **ICP - OES:** Inductively Coupled Plasma - Optical Emission Spectrometry; **NHANES:** National Health and Nutrition Examination Survey; **WHO:** World Health Organization.

SUMMARY

The focus of this study was to assess the frequency of high Cd levels in a pan-India population of over 2 lakh individuals tested over a period of one year. The findings of our study highlight the significance of large scale population-based screening to identify prevalence of elemental toxicities.

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