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**Research Article**

# BLOOD-LEAD LEVEL AS A BIOMARKER OF HUMAN EXPOSURE TO ENVIRONMENTAL POLLUTION AND HEALTH RISK

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**ABSTRACT**

Blood, a specialized liquid tissue is not only a primary clinical sample for diagnosis of diseases, but also biological sample for assessing human exposure to environmental elements and for relating its higher status with environmental and occupational health risk. Lead among other trace elements, is best indicated by blood sample in comparison to other samples namely urine, teeth, hair, nail etc. Hence, blood lead levels have been widely assessed throughout world. The mean concentration of blood lead, lesser that 5 µg/dL is considered as the reference value useful for comparison between subjects of different places to recognize whether the subject is exposed to a particular source of lead pollution. Among other groups (adults, women and workers), pregnant mothers and children are studied generally for their exposure status, because they are most susceptible to toxic effects of lead. Blood lead levels of subjects from a region are compared with lead levels of environmental samples (air, water, soil, food) to find source and with their metabolic parameters and characters of several diseases to predict health hazards.



## INTRODUCTION

Environmental monitoring is a systematic method practiced throughout the world for assessing human exposures to chemical substance of natural and man-made sources, based on sampling and analysis of substances of environmental origin and tissues and fluids of the subjects . This technique takes advantage of the knowledge that chemicals that have entered the human body leave markers reflecting the exposure. The marker may be the chemical itself or breakdown product of the chemical or some change in the body that is a result of the action of the chemical on the individual and habitat of the subjects. For example alterations in the levels of certain enzymes or other proteins, modifications of normal body process and the environment may serve as markers of exposure. In the case of elements, the fluctuating levels are considered as the biomarkers of human exposure.

In the modern world, synthetic chemicals are a part of every aspect of human life; they are critical to preventing and treating disease, the transportation, to agricultural production and to the many consumer products used for supporting the standard of living that we enjoy. Therefore, it is not surprising that many of these find their way into the soil, air, water and food and thus ultimately into the fluids and tissues of individuals. So, biomonitoring of lead (Pb) may be used to assess its levels, effects and sources whether natural or man-made means of reaching the environment. For example, lead being available as naturally existing forms or pollution products that are part of the food that we eat, water that we drink and the air that we breathe can be determined in the blood of subjects from different habitats to serve as a valuable tool in various public health activities aimed at avoiding the deleterious effects associated with exposure to toxic substances.

Lead contamination is widespread throughout the world and all the groups of subjects from fetus in womb, children and adults in home, outside and working places are exposed to lead from various sources. From a risk assessment of blood lead level (BLL) and risk-management perspectives, the present review targets to

- ✓ Establish baseline and reference levels for environmental chemicals.
- ✓ Apply in clinical evaluations to assess individual risk of exposure.
- ✓ Identify highly exposed sub populations and health endpoints of concern.

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- ✓ Assess the effectiveness of steps taken to reduce exposures and help physicians to diagnose and treat the patients who may have had unusually high BLL.

***Sources***

***Water***

When consuming drinking water with worst quality (>99%ile) in England, up to 46% of children aged 0-7 years old may had elevated blood lead levels (BLLs) (>5 µg/dL) (Jarvis *et al*. 2018). Therefore, the elevated BLL indicates that drinking water being distribution through lead pipes, may be contaminated and become the major source of lead (Pb) to the children. It is further predicted that the small proportion of children between 0 and 7 years old might have been subjected to toxic effects of Pb.

***Dust and air***

In 173 students aged 7-12 years from three schools with varying distance from the ferro-manganese alloy plant, blood lead levels median (range) were 1.2 µg/dL (0.2-15.6). Among them, 97.8% had <5 µg/dL. Pb levels in settled dust of the school premises varied between 18 and 81 µg/m2/30 days with no association with distance from the plant (Rodrigues *et al*. 2018).

A positive association was found between lead in ambient air and in the blood of the 1000 children at school beginner age living in the vicinity of industrial sources of three different hot spots (Duisburg North, Duisburg South and Dortmund Hörde) and in a rural area of North Rhine Westphalia (NRW), Germany (Wilhelm *et al* 2007). The higher BLL in the children of both the cases is ascribed to the direct exposure to Pb from the dust and ambient air of industrial regions.

***Traffic***

Blood lead toxicity has been prominently related to vehicular emissions. Rashid *et al*. (2019) showed that the highest blood lead levels were observed in the age group of 4-8 years children residing in poor residential conditions than those living in better conditions. High proximity of school to highway distance seemed to play a vital role in the concentration of lead in children while the traffic flow density was observed to have proportionality effect on the blood lead levels.

***Indirect exposure***

123 children aged 1-6 years living close to the lead smelters/battery recycle plant at Wah/Gujranwala, Pakistan (lead-exposed group) had significantly higher BLLs median (range) 8.1 µg/dL and range 1-20.9 µg/dL than the control group (N=123) living 30 km away from the industrial area (mean 6.7 µg/dL and range 1-13.3 µg/dL (p <or= 0.01) (Khan *et al*. 2010). The children of industrial workers had elevated BLL (>10 µg/dL) in 38 (31%) as compared with 14 (11%) in controls. Hematopoietic, renal, and hepatic functions were significantly impaired in the lead-exposed children. In conclusion, the children of lead-related occupational workers had significantly increased frequency (31%) of lead poisoning. The potential source of lead overexposure in these children may be indirect through father's clothes and contaminated environment at home. There is a probability of affecting health of these children due to Increased lead accumulation.

***Exposure of Different groups***

***Workers***

There was a significant correlation between the concentrations of lead in air and the level of lead in blood ($p = 0.012$, $r = 0.31$) of female electrical parts solderers (N=40) working in two electrical parts manufacturing factories in Neyshabur city (Mohammadyan *et al*. 2019). Mean occupational exposure to lead was 0.09 ± 0.01 mg/m3, and the mean level of lead in the blood of solderers was 10.59 ± 3.25 µg/dL. The level of lead in the workers' respiratory region ($\beta = 0.36$, $p = 0.033$), body mass index ($\beta = 0.25$, $p = 0.028$), and the season of the year ($\beta = 0.21$, $p = 0.019$) were the strongest factors affecting blood lead levels. There was a significant relation between lead in workers' air and their blood, although all blood indices were in normal range. Using lead-free alloys and local ventilation systems, and reducing exposure times are recommended to decrease exposure to lead among solderers.

The Blood Lead Levels (BLLs) was significantly ($P<0.001$) increased in the workers of Pb-battery plant from Tamil Nadu as compared to control (Kalahasthi and Tapu 2018). The BLL of battery workers from Tunisia (715 µg/ L-1) was significantly higher compared to the controls (93.6 µg/ L-1) exceeding the Occupational Safety Health Administration (USA) cutoff values ($p < 0.01$) (Nouioui *et al*. 2019). Victory *et al* (2019) reported that out of 15 123 Missouri residents with a BLL in 2013 (median: 1.5 µg/dL, range: 0-151 µg/dL), 3145 (21%) had BLLs ≥10 µg/dL. Occupational exposures accounted for the majority of residents (n = 3099, 98%) with elevated BLLs, mostly in battery manufacturing (n = 1373, 44%) and lead mining (n = 821, 26%) industries that may be considered the high-risk industries, and have to further reduce overexposures to lead.

***Children***

579 children (boy and girl with 11 yr of age) from Dunedin, New Zealand, had mean (SD) BLL, 11.08 (4.96) µg/dL and each 5 µg/dL increase in childhood blood lead level was associated with a 1.34-point increase in general psychopathology and thought disorder symptoms (Reuben *et al*. 2019).

Cai *et al*. (2019) indicated that median blood lead level of children from (e-waste) recycling town named Guiyu was 4.88 µg/dL, higher than the 3.47 µg/dL blood lead level of children ($P < 0.001$) from Haojiang, a nearby town with no e-waste recycling activity. 47.2% of Guiyu children had blood lead levels exceeding 5 µg/dL. They suggested that lead exposure in e-waste recycling areas may result in a decrease in serum cortisol levels and an increase in child sensory integration difficulties, since cortisol may be involved in touch-related sensory integration difficulties.

Rashid *et al*. (2019) reported that the greater BLL were observed in the age group of 4-8 years (5.46 µg/dl) with mother's education having an inverse proportionality with the blood lead levels of children. Furthermore, children belonging to families with income (> 100,000) exhibited the highest blood lead levels (5.52 µg/dl) than the rest of the categories.. From the study, it is concluded that 28% of the children in the sample population were having lead levels above the permissible limits as per Centre for Disease Control and Prevention. Their study reflects the alarming toxicity of lead in children residing in a non-industrial region which further gives rise to concerns about the health of the children residing in industrialized regions of the world with high lead levels in the environment.

In a sample of 221 children from Syracuse, New York, aged 9-11 years with a mean BLL of 1.06 µg/dL (SD = 0.68), Castro *et al* (2019) showed increase in spatial density of vacant properties and predicted increase in median blood-PB levels, b = 0.14 (0.06-0.21), $p < .001$. The reason is that as vacant properties deteriorated, lead-contaminated dust likely dispersed into the surrounding environment. High-density areas have an accumulation of lead hazards in environmental media, namely soil and dust, putting more children at risk of exposure.

***Women and Mothers***

The mean blood lead level was 2.38 ± 2.43 µg/dL in controls and 3.42 ± 2.18 µg/dL in preeclamptic women which was significantly higher ($p = 0.0132$) and strong correlation of BLL was observed with blood pressure in pre-eclamptic women (Disha *et al*. 2019). Pre-eclamptic patients were observed to be at increased risk of being lead exposed in terms of occupation and living conditions.

Bede-Ojimadu *et al*. (2018) reported that mean blood lead levels of women ranged from 0.83 to 99 µg/dl. The overall weighted mean of blood lead levels was 24.73 µg/dl. The weighted mean from analyses of data on blood lead levels of pregnant women alone was 26.24 µg/dl. Identified sources of lead exposure included lead mine, informal lead-acid battery recycling, leaded gasoline and piped water (Bede-Ojimadu *et al*. 2018). Elevated BLLs were associated with incidence of preeclampsia, hypertension, and malaria and important contributing factors for elevated blood lead levels (BLL) in these women include poverty, high environmental lead burden, low awareness on lead exposure hazards and lack of regulation for lead in consumer products. BLLs of women of childbearing age in SSA are unacceptably high (Bede-Ojimadu *et al*. 2018).
Soomro *et al*. (2016) reported that Cd was statistically related to gestational diabetes mellitus (GDM) or impaired glucose tolerance (IGT) and Pb to GDM. They further concluded that the growing evidences support the role of maternal exposure to heavy toxic metals that persist longtime in the environment as a risk factor for GDM.

***Maternal and Umbilical cord blood Pb***

Ladele *et al*. (2019) reported that the median maternal and umbilical BLL was 64.3µg/dl and 39.2µg/dl respectively. The levels were above 5µg/dl in 75.6% and 66.8% of mothers and umbilical cord respectively. There was a strong positive correlation between the maternal and umbilical cord blood lead levels. Use of calcium supplements during pregnancy was significantly associated with a lower maternal blood lead level ($p = 0.010$) while recent painting and renovation of residential accommodation were associated with a higher umbilical cord blood lead level ($p = 0.025$). There were no statistically significant associations between the maternal and umbilical cord blood lead levels and the gestational age and anthropometry of the newborns at birth. The blood lead levels in newborns of women residing in Lagos, Nigeria are high and administration of antenatal calcium is associated with lower blood lead levels.

***Safe level of Exposure and no Effect***

When lead levels were compared between lead apron users (N=46) and nonusers (N=12), hand dust-wipe lead was undetectable (<3 µg/sample) in all cases and blood lead levels of the radiology workers ranged from 0-3 µg/dL and no difference found. Hence no increased risk of lead contamination was reported in the blood of workers who were within the physiologically safe status (Shoag *et al*. 2019).
Average value of 4.26 µg/dL for BLL measured in young American men prior to chronic occupational exposure at lead recycling plants was not associated with, neurocognitive performance in young American men (Yu *et al*. 2019). Thus, depending upon BLL, workers are identified as either highly or less exposed to predict whether control measure of exposure is required.

***Health Hazards***

Lead is broadly used in various industries and causes irreversible damage to human tissues, organs, and systems (Liu *et al*. 2019). There are a number of studies reporting use of BLL in assessing lead toxic status and effects on health.

***Interaction of Pb and Other Elements***

It is reported that widespread pollution of elements is associated with health hazards e.g. higher blood lead levels (BLLs) have been linked to neurologic deficits and impaired growth. Bulka *et al*. (2019) found that lead was linearly associated with increases in systolic blood pressure, but not with diastolic blood pressure or pulse pressure of subjects from Bangladesh. A non-linear association was observed for manganese, such that mid-range concentrations were associated with decreases in systolic, diastolic, and pulse pressure. Baseline selenium concentrations in the highest quartile were also associated with longitudinal decreases in both systolic and diastolic blood pressure, while null associations were observed with pulse pressure. In exploratory analyses, the combination of mid-range manganese and high selenium concentrations completely offset lead-associated increases in blood and pulse pressure. In conclusion they revealed a direct, linear association of Pb exposure with systolic blood pressure and a blood pressure-lowering effect of Mn and Se in this population.

***Sexual Maturity in Boys***

Williams *et al*. (2019) reported that in 481 Russian boys with 8-9 years and to adulthood, 28% had BLL ≥ 5 µg/dL. In adjusted models, boys with BLLs ≥5 µg/dL had later maturity than those with lower levels by 4-5 months depending on pubertal indicator. In mediation analyses, height and body mass index at age 11 accounted for 40-71% of the shift in age at maturity for boys with higher compared to lower BLLs. Higher BLLs were not associated with pace of pubertal progression. Higher lead levels were associated with later attainment of sexual maturity in males, but not with the duration of pubertal progression. A high proportion of the delay in sexual maturity for boys with higher as compared to lower BLL was shown to be attributable to mediating effects of BLL on reduced growth.

### Sexual Maturity in Girls

Liu *et al*. (2019) examined the association of prenatal and early childhood lead exposure with pubertal stages among 264 boys and 283 girls aged 9.8-18.0 years in Mexico City and showed that early childhood blood lead was inversely associated with breast growth (patella OR = 0.72, 95% CI: 0.51-1.00; blood OR = 0.70, 95% CI: 0.53-0.93) in girls. Girls with maternal patella lead in the 3rd tertile and child blood lead in the 2nd tertile had a later age at menarche compared with girls in the 1st tertile (patella HR = 0.60, 95% CI: 0.41-0.88; blood HR = 0.65, 95% CI 0.46-0.91). No associations were found in boys. They suggested that higher prenatal and early childhood exposure to lead may be associated with delayed pubertal development in girls with the reproductive effects of lead for girls but not for boys.

### Children' Behavioural Disorders

Erdenebayar *et al*. (2019) showed that the mean BLL of children (4-7 year) living in two cities of Mongolia was found to be 3.8 ± 2.6 µg/dL (range: < 1.5-17.2 µg/dL) and 27.8% of the children had BLLs ≥5 µg/dL. Average BLL of children in Erdenet (a mining center) was significantly higher than that for children in Darkhan, and there was statistically significant difference between average BLL of children who lived in ger district (4.2 ± 2.8 µg/dL) compared to those of children in housing units within the city (3.2 ± 2.4 µg/dL). In spite of the low values, BLLs was significantly associated with a number of effects on the spectrum of behavioral disorders, specifically with the scores for hyperactivity, conduct disorder and pro-social behavior. Thus, from behavioural disorders it is evident that lead toxicity damages systematically central nervous system.

In two-way interaction analyses, cord blood Pb marginally interacted with gestational age leading to an increase in mtDNA content for pre-term births (Benjamini-Hochberg False Discovery Rate correction; BH-FDR = 0.08). Thus it is concluded that lead exposure in pregnancy alters mtDNA content in cord blood; therefore, alteration of mtDNA content might be a mechanism underlying the toxicity of lead.

### DNA Damage

In 276 children living in eleven communities in four states of Mexico, lead levels in blood ranged from 0.5 to 24 µg/dL with the highest DNA damage level ($p<0.05$) in their blood cells (olive tail moment=7.5±3.5), when compared with DNA damage levels in children living in the other scenarios assessed in the work of Jasso-Pineda *et al*. (2015). Further, it is indicated that children living in high risk areas of contamination showed high levels of Pb exposure that contributes to DNA damage and an increased health risk in the studied sites.

The effect of Pb has been observed at gene level. Liu *et al*. 2019 reported that single nucleotide polymorphisms (SNPs) in TRPV5, a calcium channel-related gene, rs4252424 was significantly associated with lead susceptibility, measured by blood lead level (BLL) (β = -0.069, plinear = 0.029) in Chinese workers The further expression Quantitative Trait Loci displayed that CC genotype of rs4252424 is significantly associated with higher BLL ($p < 0.0001$).

### Lead Effects on Workers

Among 211 Adult men enrolled in a lead surveillance programme residing near New York City, median (IQR) bone, maximum past blood and current blood leads were 13.8 (9.4-19.5) µg lead per bone mineral gram, 29.0 (14.0-38.0) µg/dL and 2.5 (1.5-4.4) µg/dL, respectively (Barry *et al*. 2019). Bone lead was significantly associated with past maximum and current blood lead. The association between bone and current blood lead was possibly driven by bone lead resorption into blood. Bone lead, but not past or current blood lead, was associated with elevated systolic BP and estimated glomerular filtration rate.

**Table 1** The mean BLL reported in the control and exposed children from different places

| SN | Subjects/ children | Place of residence | BLL (µg/dL ) reported in the control and exposed children | | | | Reference |
|---|---|---|---|---|---|---|---|
| | | | Control children | | Exposed children | | |
| | | | Place | BLL µg/dL | Place | BLL µg/dL | |
| 1 | School children | Brazil | Living away from smelter | 1.2 | Living close to smelter | <5 | Rodrigues et al. 2018 |
| 2 | Children living near Pb smelter | Wah/ Gujranwala, Pakistan | Living away from Industries | 6.7 | Living close to smelter | 8.1 | Khan et al. 2010 |
| 3 | School children | Largest e-waste recycling site of China | from Haojiang, a town with no e-waste recycling | 3.5 | from Guiyu a town (e-waste recycling) | 4.88 | Cai et al. (2019) |
| 4 | Children | Kashmir, India | Children from High income family | >5.5 | Children from low income family | 5.52 | Rashid et al. (2019) |
| 5 | Children aged 9-11 years | Syracuse, New York | Children from free from pollution | 1.06 | Children from polluted place of vacant properties | <1.06 | Castro et al (2019) |
| 6 | children (4-7 year) | Mongolia | children in Darkhan | 3.2 | Erdenet (a mining center) | <3.2 | Erdenebayar et al. (2019) |

### Pb and mt DNA

Sanchez-Guerra *et al*. (2019) reported in a prospective birth-cohort with enrollment of 1050 pregnant women from Mexico City that maternal blood Pb measured in the second (mean 3.79 µg/dL, SD 2.63; β = 0.059, 95% CI 0.008, 0.111) and third trimester (mean 3.90 µg/dL; SD 2.84; β = 0.054, 95% CI 0.002, 0.107) during pregnancy and Pb in cord blood (mean 3.50 µg/dL, SD 2.59; β = 0.050, 95% CI 0.004; 0.096) were associated with increased cord blood mtDNA content (mean 1.46, SD 0.44).

***Reference values***

The baseline or reference values are identified for the blood lead used for comparison between values of subjects of different places. Such comparison is essential to recognize whether the BLL estimated in a particular subject group is at higher level that may be harmful enough to cause ill health. In the table 1 are shown the mean BLL for both control and exposed children so that difference in exposure status either low or high could be perceived. The mean BLL lesser than 5 µg/dL is the reference value and above 5 µg/dL is considered as the value of subject exposed to a particular source of lead pollution.

## CONCLUSIONS

Blood lead level of subjects above 5 µg/dL indicates the exposed state and hence, it is a reliable biomarker of lead poisoning. Since children are easily affected by the lead above 5 µg/dL, they are preferable subjects of study about environmental exposure assessment to other subjects. Besides environmental exposure assessment, BLL in the workers of various metal based industries could reveal the occupational exposure and health risk and facilitate for taking appropriate preventive measures for the safety of all sections of population.

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