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Blood Lead Levels And Its Effects On Different Domains Of Development In Children With Global Developmental Delay. Effects of Blood Lead Level in Children with Global Developmental Delay

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Abstract

Early development of a child results from a unique interplay between internal constitutional factors and external environmental exposures. Lead is a potential neurotoxin that can affect child development in various domains. Objectives: To estimate the blood lead levels (BLL) and its effects on different domains of development in children with global developmental delay. Methods: Cross-sectional study conducted in Paediatric OPD and DEIC of a tertiary care hospital among children with GDD aged 6-60 months. The developmental assessment between 6 to 42 months of age was done by using the Bayley-III Screening Test. For children above 42 months, development quotient (DQ) was derived in various domains Results: More than half (53%) of children had elevated BLL. Regular application of kohl and use of folk/herbal medicine were identified as significant risk factors. Around 82% of children had development in the risk category for cognitive, communication, gross motor and fine motor domains. Increase in severity of developmental delay in all domains was associated with an increase in BLL and these negative correlations reached statistically significant levels in receptive communication (ρ=-0.24, P=0.03) and expressive communication domains (ρ=-0.21, P=0.05). Conclusions: Lead is a potential neurotoxin and its effects are more on the developing nervous system of children. A positive association between BLL and various domains of childhood development particularly in receptive and expressive communication domains was noted. For countries like ours which are rapidly undergoing industrialisation, the potential sources of lead exposure need to be identified promptly and swift action to tackle this is strongly needed.

Introduction

Lead is a highly prevalent environmental toxin that is associated with numerous adverse effects on hematological, gastrointestinal and nervous systems. Major sources of lead exposure include building paints, vividly colored edibles and toys, cosmetics, folk remedies, glazed ceramics, etc. Lead, being non-biodegradable in nature may persist in air, food, water, and soil for a long time and pose constant threat of exposure. No level of lead is shown to be

safe for the human body (Bellinger, 2008). After gaining entry, lead gradually accumulates in the body and is regarded as one of the most harmful environmental toxins for children. Lead poisoning is mostly asymptomatic initially and once symptoms do appear, they are often confused with other illnesses. Early development of a child results from a unique interplay between internal constitutional factors and external environmental exposures (Gupta et al., 2016). Lead wreaks havoc so silently and insidiously that its effects often go unrecognized and young children are at the greatest risk of suffering lifelong neurological, cognitive and physical damage. Lead irreversibly damages children's developing brains and the consequences can be devastating including developmental delay. Studies exploring the effects of lead exposure on neurological dysfunctions in children have reported that these adverse effects are persistent (Chen et al., 2005; Min et al., 2007). The children with developmental delay are feared to have compromised rearing conditions and persisting hand-to-mouth behavior which make them potentially more at risk of lead exposure.A series of studies have shown that lead toxicity affects the cognitive and behavioral development of children (Delgado et al., 2018; Hou et al., 2013; Hsueh et al., 2017; Kumar et al., 1998). Aligarh and surrounding areas in the state of Uttar Pradesh, India, being the hub of various industries like lock making, metal polishing, battery repair etc., are feared to be homes to children at risk of exposure to lead. Thus, the present study was designed to estimate the BLL in children with GDD and its relation to different domains of development.

Objective

To estimate the BLL in children with GDD and its correlation with different domains of development.

Materials and methods

Type of Study: Cross sectional study.

Setting and Duration: This hospital-based cross -sectional study was conducted between October 2019 and October 21 in Paediatric Out Patient Department, District Early Intervention Centre and Nutritional Rehabilitation Centre of Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh, UP, India in collaboration with the Department of Biochemistry, Era Medical College, Lucknow.

Sample size: The following formula was used to calculate the sample size

$$n = Z^2P(1-P)/d^2$$

where, n: required sample size, Z: Statistic corresponding to the level of significance (1.96 for 95% CI), P: Expected prevalence Elevated Blood Lead Level (EBLL), d: Absolute error or precision. Considering the prevalence of EBLL of 9% (Ghosh et al., 2014) and precision of 5%, the sample size obtained was 130. However, due to situations arising out of the COVID-19 pandemic during the study duration, the required sample size could not be achieved and the study was performed with 94 participants.

Inclusion criteria: Children from 6 months to 60 months of age with developmental delay in at least 2 domains.

Exclusion criteria: Children with any of the following characteristics were excluded from the study

1. Sick children requiring admission.
2. Children on various supplements like calcium, zinc, and iron.

Procedure: Children with Global Developmental Delay aged 6 months to 5 years along with their mothers were enrolled in the study after due consideration of inclusion and exclusion criteria. The parent or legal guardian were asked to answer certain questions which included a detailed history regarding the child's potential exposure to lead. Data regarding clinical and sociodemographic characteristics as well as parental attributes was documented in a predesigned semi-structured proforma. Details about the symptoms suggestive of lead poisoning were enquired and the responses were noted. The details of general and systemic examination were noted in the proforma. Blood sample was collected from children and their mothers

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for estimation of blood lead and hemoglobin levels. The developmental assessment between 6 months to 42 months of age was performed by Bayley Scales of Infant and Toddler Development Screening Test - Third Edition (Bayley-III Screening Test). Children were categorised into 3 groups - risk, emerging and competent according to the scores obtained in different domains. The scoring was done based on the number of items passed in the given range as described in the manual (Bayley-III Screening Test). For children above 42 months, development quotient (DQ) was derived for various domains of development: gross motor, fine motor, language and social and adaptive. A DQ below 70% was considered as delayed development.

Ethical committee approval and consent

The study was approved by the Institutional Ethics Committee (D No 117/FM/IEC dated 28.10.2020), Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh. Written informed consent for participation in the study was obtained and consent for blood sampling was also obtained from parents/legal guardians of the children. Data Management and Analysis. Statistical analysis was done using the Statistical Package for Social Science (IBM SPSS version. 20.0) Software for Windows. For categorical data, frequencies and percentages with 95% CI were used. For normally distributed continuous data, description was done using the mean and standard deviation (SD), while Student's t-test and One way ANOVA were used to compare the mean between two groups and more than two groups, respectively. For continuous data that were not normally distributed, Mann–Whitney test or Kruskal Wallis test was used as applicable.

Results

The mean age of study subjects was 27 ± 12 months. Most of the study subjects belonged to 13 to 24 months age group (38%) followed by 25 to 36 months age group (28%). The prevalence of Elevated Blood Lead level (EBLL) defined as blood lead level >5µg/dl in children with GDD was found to be 53%. Higher mean BLL was seen among children showing non-specific features of lead toxicity in the form of neurobehavioral and gastrointestinal symptoms, as compared to children who did not have such symptoms. However, these differences in the level of lead were not statistically significant (Table 1).

Table 1: Relationship of Symptomatology with mean Blood Lead Level in children

S. No.	Symptoms	Mean BLL (mcg/dl) ± SD	P value
1	Lethargy		0.159
	Present	10.6±5.54	
	Absent	6.59±5.49	
2	Hyperactivity / Irritability		0.934
	Present	6.64±5.26	
	Absent	6.74±6.72	
3	Sleep disturbances		0.097
	Present	7.97±3.99	
	Absent	6.52±5.70	
4	Convulsion		0.176
	Present	7.72±5.59	
	Absent	6.29±5.46	

Table 1: Relationship of Symptomatology with mean Blood Lead Level in children

S. No.	Symptoms	Mean BLL (mcg/dl) ± SD	P value
5	Constipation		0.067
	Present	7.88±5.53	
	Absent	6.00±5.41	
7	Underweight		0.778
	Present	6.83±5.48	
	Absent	6.15±5.76	
8	Stunting		0.104
	Present	6.80±5.15	
	Absent	6.42±6.80	
9	Wasting		0.851
	Present	7.06±5.59	
	Absent	6.21±5.41	

Developmental status of children aged 6-42 months and Blood Lead Level Mean BLL of children in different categories is shown in Table 2. While evaluating the cognitive domain, 81% children were found to be in the risk category. Median BLL in risk, emerging and competent category was 5.31, 3.43 and 2.72 µg/dl respectively (P =0.080). Receptive communication development in the risk category was seen in 83% of children. Mean BLL in risk, competent and emerging categories were found to be 7.17, 5.63 and 1.89µg/dl respectively while median BLL were 5.64, 2.98 and 1.66µg/dl respectively (P=0.070). In expressive communication domain, 82% of children were found to have development in risk category. Mean BLL in risk, competent and emerging categories were found to be 7.16, 5.99 and 1.46 µg/dl respectively while Median BLL were 5.64, 3.45 and 1.66 µg/dl respectively (P value =0.073). Across different categories of gross and fine motor development, mean BLL was found to be similar (Table 2).

Table 2: Relationship of Developmental status with mean BLL in children (6-42)

Domains of development	Frequency (%)	Mean ± sd	95% ci	Significance
Cognitive				0.080
Risk	70(81.4)	6.88± 5.44	5.62-8.11	
Emerging	11(12.8)	5.75 ±6.09	2.52-9.89	
competent	5(5.8)	7.48 ±9.26	1.23-16.2	
Receptive communication				0.070
Risk	71(82.6)	7.17±5.47	5.88-8.40	
Emerging	12(14.0)	5.63±7.32	2.24-9.92	
competent	3(3.6)	1.89±0.73	1.31-2.72	
Expressive communication				0.073
Risk	71(82.6)	7.16±5.52	6.03-8.46	
Emerging	15(17.4)	5.99±6.77	2.85-10.00	
competent	3(10.0)	1.46±1.37	0.00-2.72	

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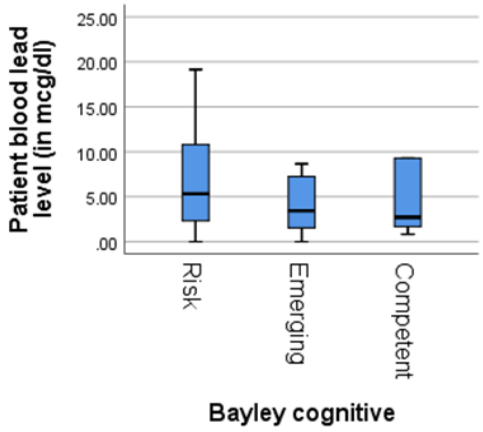
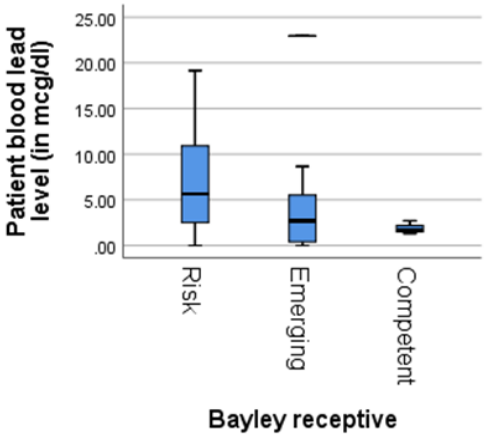
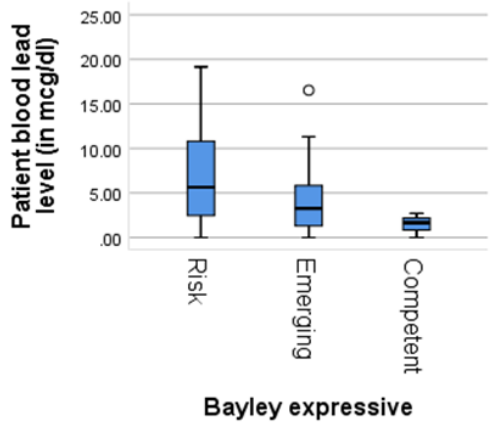
Domains of development	Frequency (%)	Mean ± sd	95% ci	Significance
Gross motor				
Risk	71(82.6)	6.79 ±5.79	5.59-8.27	0.923
Emerging	15(17.4)	6.65 ±5.48	4.25-9.45	
competent	-	-	-	
Fine motor				
Risk	70(81.4)	6.59 ±5.47	5.38-7.90	0.910
Emerging	15(17.4)	7.72 ±7.00	4.6-11.64	
competent	1(1.2)	5.18	-	

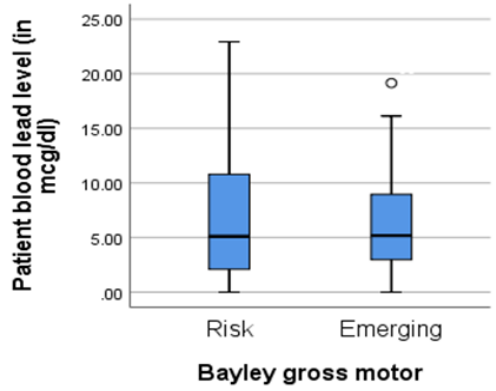
Correlation between BLL and various domains of development

Increased levels of blood lead were associated with an increase in severity of delay in cognitive, receptive communication and expressive communication domains. In addition, these negative correlations reached statistically significant levels in receptive communication (ρ = -0.236 and P =0.029) and expressive communication domains (ρ = - 0.211 and p value =0.05).









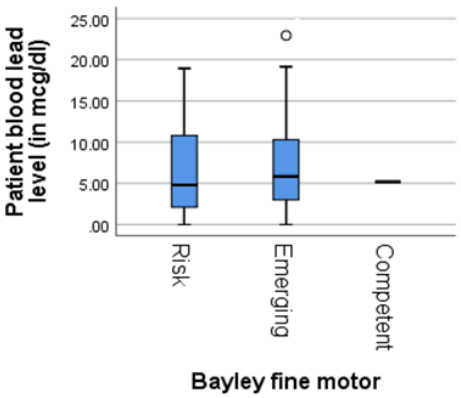


Figure 1: (a-e): BLL distribution in various domains of development

In children above 42 months of age, gross motor domain was most severely affected. All 4 developmental domains were negatively correlated with BLL. (Table 3).

Table 3: Relationship of Developmental status with BLL in children (> 42 months of age)

Domains of development	Development quotient in % (Mean±SD)	Mean blood lead level (mcg/dl)±SD	Spearman Correlation coefficient "rho/ρ"
Gross motor	11.5±7.98	6.72±5.50	-0.651P=0.081)
Fine motor	23.5±24.79		-0.374P=0.362)
Social and adaptive	19±19.57		-0.700P=0.053)
Language	17±18.01		-0.609P=0.109)

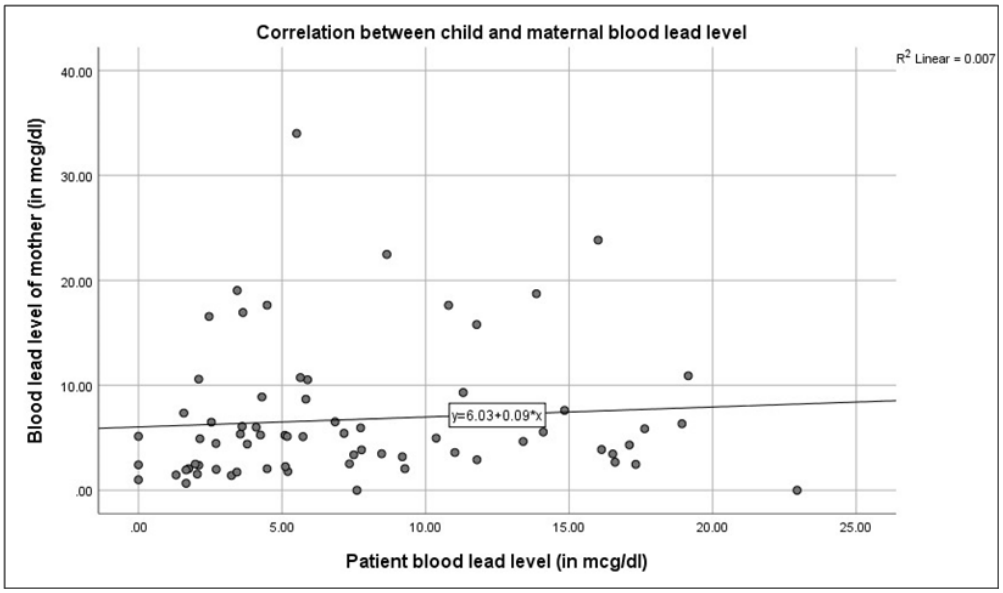


Figure 2: Correlation of maternal BLL and children's BLL

Maternal BLL showed weak positive linear correlation with their children's BLL (Spearman coefficient/ rho =+0.218, p value= 0.072, figure 2).

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Discussion

There is mounting scientific evidence that no level of lead is safe (Canfield et al., 2003; Lanphear et al., 2005; Nigg et al., 2010). This prompted Centers for Disease Control and Prevention to lower the reference value of BLL to 5 µg/dL from the earlier cutoff of 10 µg/Dl (Centers for Disease Control and Prevention, 2012; for Disease Control, n.d.). Applying the same cut-off, we found that more than half (53%) of our study population had elevated BLL with a mean BLL of 6.72 µg/dl. While analyzing various developmental domains by using Bayley Scale of Infant and Toddler, approximately 82% of children with GDD below 42 months of age were found to have significant delay (risk category) in cognitive, receptive communication, expressive communication, gross motor and fine motor domains. Increasing levels of blood lead were associated with an increase in severity of developmental delay in cognitive, receptive communication and expressive communication domains. In children above 42 months age, all 4 major domains of development were affected and they showed weakly negative linear correlation with BLL. Higher BLL was also found among children with underlying neurological disorders as compared to age matched healthy controls in the study by Kumar A et al (Kumar et al., 1998). Another recent study involving apparently healthy children found elevated BLL (>5 mcg/dl) in around 19% of school going children (Sharma et al., 2021). Out of these, 16% had Developmental Delays while13% had GDD. Various other investigators from other parts of the world have also demonstrated an increased risk of developmental delays among children with a high blood lead concentration (Delgado et al., 2018; Hsueh et al., 2017). In addition, abnormal behaviors such as social withdrawal, depression, typical body movements and aggression were also seen. Similar to our findings, a significantly negative correlation with the developmental quotients of various domains has also been reported (Hou et al., 2013).

A study exploring the neurochemical basis of effect of BLL found that serum serotonin and dopamine levels showed a negative and positive correlation with BLL respectively. Serotonin and dopamine regulate behavior, cognition, memory and reward centre of the brain and an alteration in their levels by lead may affect early development as well as behavior of children (L et al., 2021). Children in low- and middle-income countries continue to have dangerously high BLL. Lead is a cumulative toxicant that affects multiple body systems and is particularly harmful to young children. There is no known safe level of lead exposure and even low levels of lead exposure have been shown to damage children's health and impair their cognitive development. Childhood lead poisoning commands an urgent response.

Conclusions

Lead is undoubtedly a potential neurological toxin and its effects are plausibly more on the developing nervous system of children. A positive association between BLL and various domains of childhood development particularly in receptive and expressive communication domains was noted. For countries like India which is rapidly undergoing industrialisation, the potential sources of lead exposure need to be identified promptly and swift action to tackle this toxin is strongly needed. Prevention of lead exposure, capacity building for BLL testing, public awareness and behaviour changes, policy making and legislation as well as regional and global action are highly desirable to curb this menace

Recommendation

We recommend that future studies in children with developmental delay be carried out with a control group, and be directed at exploring putative environmental risk factors. Further, BLL is likely to depend on demographic factors like air, food, water and soil and hence, estimation of lead content of soil and water along with lead level in blood could unravel the other potential sources of lead exposure for children.

Limitations

The limitation of the present study is that we did not have a matched control group of normally developing children in our study, hence our finding of a relationship between lead level and delays in development is only suggestive and not deterministic. Due to the impact of the COVID-19 pandemic on delivery of health care services, the required sample size of 130 children could not be attained and a total of 94 children were studied instead.

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