Effects of Elevated Blood Lead Levels in Preschool Children in Urban Vellore

VENKATA RAGHAVA MOHAN, [#]SRUJAN SHARMA, [$]KARTHIKEYAN RAMANUJAM, [$]SUDHIR BABJI, [^]BEENA KOSHY, [**]JOSEPH DIAN BONDU, [*]SUSHIL MATHEW JOHN, AND [$]GAGANDEEP KANG

From Departments of Community Health, [#] Surgery, [$] Gastrointestinal Sciences, [^]Developmental Pediatrics, [**] Clinical Biochemistry and [*]Low Cost Effective Care Unit, Christian Medical College, Vellore. Tamil Nadu.

Correspondence to: Dr Venkata Raghava Mohan, Department of Community Health, Christian Medical College, Vellore 632 002, Tamil Nadu, India. venkat@cmcvellore.ac.in

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Objectives: To study the burden and associated risk factors for elevated blood lead levels among pre-school children (15-24 months) in urban Vellore, and to study its effects on child cognition and anemia.

Design: An investigative study through Mal-ED cohort.

Setting: Eight adjacent urban slums in Vellore, Tamil Nadu.

Participants: 251 babies recruited through Mal-ED Network.

Outcome measures: Blood lead levels using Graphite Furnace Atomic Absorption Spectrophotometry method at 15 and 24 mo; hemoglobin estimation by azidemethemoglobin method; cognitive levels using Bayley Scales of Infant Development III.

Results: Around 45% of children at 15 months and 46.4% at 24 months had elevated blood lead levels (>10 µg/dL). Among children who had elevated blood lead levels at 15 months, 69.2% (45/65) continued to have elevated levels at 24 months. After adjusting for potential confounders, children from houses having a piped drinking water supply and houses with mud or clay floors were at significantly higher risk of having elevated blood lead levels at 15 months. Thirty one percent (21/67) of the children with elevated blood lead levels had poor cognitive scores. Children with elevated blood lead levels at 15 months had higher risk (Adjusted OR 1.80; 95% CI 0.80 - 3.99) of having poorer cognitive scores at 24 months. More than half of the children (57%) were anemic at 15 months of age, and elevated blood lead levels were not significantly associated with anemia.

Conclusions: Elevated blood lead levels are common among preschool children living in urban slums of Vellore. Poorer conditions of the living environment are associated with elevated lead levels.

Keywords: *Anemia, Cognition, Lead poisoning.*

Lead exposure during childhood contributes to intellectual disability among children. Absorption of ingested lead is higher in children with nutritional deficiencies, and pica further enhances the absorption rate [1-3]. Children are more vulnerable to the toxic effects of lead even with low levels of exposure potentially causing serious and possible irreversible neurological damage. Lead exposure is also known to adversely affect the behavior and cognitive development among children [3-5]. Younger age and pre-existing iron deficiency pose increased risk of developing lead-induced anemia. The prevalence and severity of lead induced anemia is known to correlate well with blood lead levels (BLL) [6-8].

This study aimed to investigate the proportion of children with elevated BLLs and associated risk factors for elevated BLLs at 15 and 24 months among the Mal-ED cohort in Vellore, India. The effects of elevated blood lead levels on child cognition and anemia among pre-school children were also assessed.

METHODS

Vellore is a large town in Southern India located 120 km from the Tamilnadu State capital Chennai. As part of a multi-country study on malnutrition, a birth cohort (called the Mal-ED) was recruited from an urban slum of 8 neighbourhoods with an approximate population of 12,000 to be followed up at home, and at a clinic in the study area by a team of trained field workers, nutritionists, psychologists and medical staff.

Pregnant women residing in an urban slum were identified through a house-to-house survey, and information on the expected date of delivery was obtained. Mothers were visited soon after birth and invited to participate in the study. Exclusion criteria were: multiple pregnancies, another sibling in the study or family planning to migrate outside study area.

Socio-economic status (SES) of the families was assessed at 6 monthly intervals after recruitment using the following components: access to improved water and sanitation, assets owned by the family, maternal education and income (the WAMI index). The households were further classified as belonging to low, middle or high SES based on tertiles of the total score.

The risk factors tested included sex of the child, low birth weight, duration of exclusive breastfeeding, maternal anthropometry two months after childbirth, maternal mental status, and (as collected by a SRQ-20 questionnaire), number of living children in the family, any previous child death in the family, socioeconomic status, and housing indicators, including the type of floor, walls and drinking water. The association between socio-demographics, associated risk factors and elevated BLLs was tested using a multivariate backward conditional logistic regression analysis to adjust for confounding factors; adjusted ORs were estimated.

Blood lead levels: A maximum of 5 mL of venous blood was collected from the children at 7, 15 and 24 months for various biochemical tests, of which around 1 mL of whole blood was preserved with Dipotassium Ethylenediamine-tetraacetic acid (K2 EDTA) for determination of lead levels. The samples were refrigerated immediately, and were transported to the laboratory within a few hours using cold packs. Lead levels in whole blood were estimated by Graphite Furnace Atomic Absorption Spectroscopy (GFAAS) method using an M Series Atomic Absorption Spectro-photometer. A value of 10 µg/dL was considered as the cut-off level to identify elevated BLLs.

Cognition, motor, language, social-emotional and adaptive behaviours were assessed using the Bayley Scales of Infant Development III (BSID III) [9,10] at 6, 15 and 24 months. BLLs at 15 months were correlated with cognition scores at 24 months, as recorded by the BSID-III.

Hemoglobin (Hb) estimation by azidemethemoglobin method was done at 7, 15 and 24 months using a Hemocue at the study clinic. The severity of anemia was graded using the World Health Organisation's Hb cut-offs of mild (10 to 10.9 g/dL), moderate (8 to 9.9 g/dL) and severe anaemia (less than 8 g/dL) [11,12]. Associations between anemia at 15 months, child's cognition at 24 months and elevated 15-month BLLs were tested using Chi-squared test.

RESULTS

A total of 301 mothers were visited soon after child birth and invited to participate in the study, thereby enrolling 251 children between March 2010 and February 2012. Ten mothers were unwilling to participate and 40 babies were excluded. Of the enrolled 251 children, 25 were lost to follow-up due to non-participation (8), migration (15), and death (2). The mean (SD) birth weight of the cohort was 2.82 (0.44) kg; 124 (56%) were girls.

Seventeen percent of babies were low birth weight and majority (62%) were exclusively breastfed for less than 4 months. Over a third (82/226) of mothers were either uneducated or studied till 5th grade. The mean (SD)

TABLE I RISK FACTORS FOR ELEVATED BLOOD LEAD LEVELS AT 15 MONTHS AMONG THE STUDY CHILDREN

Risk factor	*Blood Lead Level*		*Unadjusted OR*	*Adjusted OR*
	Elevated, No. (%) (n = 102)	*Normal, No. (%) (n = 124)*		*(95% CI)*
Males	47 (46.1)	55 (44.4)	1.07	1.09 (0.61 - 1.94)
Low birth weight (<2500 g)	16 (16.2)	21 (17.2)	0.93	1.36 (0.60 - 3.07)
Exclusive breastfeeding <4 mo	60 (59.4)	79 (64.2)	0.81	0.92 (0.50 - 1.70)
Maternal age <24 y	50 (49.5)	57 (46.3)	1.13	1.62 (0.87 - 3.03)
SRQ score of >10 at 6 mo	15 (14.7)	25 (20.2)	0.68	0.68 (0.30 - 1.53)
Overweight or obese mothers (BMI ≥25)	28 (28.3)	21 (18.3)	1.76	1.84 (0.91 - 3.73)
>2 living children in the family	67 (66.3)	71 (57.7)	1.34	1.58 (0.88 - 2.86)
Any child death in the family	09 (8.9)	07 (5.7)	1.62	1.02 (0.29 - 3.64)
Low SES (WAMI <33rd centile)	33 (32.4)	36 (29.0)	1.28	1.14 (0.56 - 2.33)
Piped water supply	11 (10.8)	06 (4.8)	2.38	3.68† (1.10 - 12.40)
Mud/clay floor of the house	11 (10.8)*	03 (2.4)	4.87#	5.14† (1.30 - 20.17)
Mud walls in the house	17 (16.7)	19 (15.3)	1.1	0.77 (0.33 - 1.81)

**P<0.05, Chi-square test; #P<0.05, Bivariate analysis; †P<0.05, Multivariate logistic regression.*

TABLE II MULTIVARIATE LOGISTIC REGRESSION MODEL OF EFFECT OF ELEVATED 15 MONTH BLOOD LEAD LEVELS ON COGNITION AT 24 MONTHS

Risk factor	*Poor cognitive scores (< 33rd centile) (n=36)*	*Better cognitive scores (≥33rd centile) (n=107)*	*Adjusted OR (95% CI)*
Elevated (>10µg/dL) BLL at 15 mo	21 (58.3)	46 (43.0)	1.84 (0.83-4.08)
Males	16 (44.4)	56 (49.5)	0.76 (0.35-1.68)
Low birth weight (<2500 g)	8 (22.2)	21 (20.2)	1.15 (0.44-2.98)
Maternal education (up to 5th grade)	12 (33.3)	35 (32.7)	1.11 (0.40-3.08)
Any child death in the family	5 (13.9)	5 (4.8)	3.00 (0.75-11.92)
Low SES (< 33rd centile; based on WAMI index)	10 (27.8)	30 (28.0)	0.89 (0..2-2.53)

maternal body mass index (BMI) was 22 (3.98) kg/m^2 and 41% of the mothers were either underweight, overweight or obese (***Table* I**). Less than one-third (69/226) of the children were from lower socio-economic strata.

Water supplied through public taps by the local municipality was commonly (85.5%) used for drinking and less than 10% of the houses had piped water supply into their yards or dwellings. Around 16% of the houses had mud walls and 6% of them had floors made of mud, clay or sand.

A total of 226 blood samples were tested for lead levels at 15 months, and 138 blood samples at 24 months. The mean (SD) BLLs were 10.3 (5.0) and 11.8 µg/dL (8.6) at 15 and 24 months, respectively. The BLLs (µg/dL) ranged between 2.4 to 29.7 at 15 months, and between 1.5 and 66.8 at 24 months. Around 45% of children at 15 months and 46.4% at 24 months had BLLs over 10 µg/dL. Nearly 15% of children at 15 months and 24 months had BLL >15 µg/dL. The 24 months BLLs had a significant positive correlation with the 15 month BLLs (Spearman's rho of 0.37;P<0.01). Among children who had elevated BLLs at 15 months, 69.2% (45/65) continued to have elevated BLLs at 24 months, while 26% (19/73) of children without elevated 15 month BLLs subsequently had elevated levels at 24 months.

After adjusting for selected variables from the univariate analysis, children from houses having a piped drinking water supply, and houses with mud or clay floors were at significantly higher risk of having elevated BLLs at 15 months (***Table* I)**.

Cognitive function was assessed using the Bayley's scale on 143 children at 24 months. The mean (SD) cognitive score was 60.6 (3.2). Cognitive scores at 24 months were negatively correlated with the BLLs at 15 months; however, this was not statistically significant (P=0.23). After adjusting for sex of the child, birth weight, SES, maternal education and sibling death in the family, children with elevated BLLs at 15 months did not have significantly higher risk (OR 1.80; 95% CI 0.80 - 3.99) of having poorer cognitive scores at 24 months (***Table* II**).

The mean (SD) hemoglobin level among the study children was 10.6 (1.3) g/dL at 15 months. More than half of the children (57%) were anemic at 15 months of age. Hemoglobin levels and BLLs at 15 months were not significantly correlated (P>0.05). Children with low BLLs had higher proportions of anaemia across all categories (***Table* III**).

DISCUSSION

In this prospective observational study from urban Vellore, nearly half of the children had elevated BLLs at 15 and 24 months of age. Having a piped water supply and mud or clay floors in the house were significantly associated with elevated BLLs. Proportion of children with poor cognitive performance was higher among the group with elevated BLLs but there was no significant association between elevated BLLs and childhood anaemia.

Lack of detailed information on child rearing practices and behaviors, and exposures pertaining to outdoor environment were potential limitations. The Centers for Disease Control (CDC) had earlier defined an

TABLE III ANEMIA AND BLOOD LEAD LEVELS AT 15 MONTHS OF AGE

Category	*BLL <10 µg/dL No.(%)*	*BLL ≥10µg/dL No.(%)*	*Overall*
No anemia	51 (52.6)	46 (47.4)	97 (43.5)
Mild anemia	39 (55.7)	31 (44.3)	70 (31.4)
Moderate anemia	24 (51.1)	23 (48.9)	47 (21)
Severe anemia	08 (89)	01 (11)	9 (4)
Overall	122 (54.7)	101 (45.3)	223

WHAT IS ALREADY KNOWN?

- The burden of lead poisoning is highest in the developing countries with children being the most vulnerable group.

WHAT THIS STUDY ADDS?

- Nearly half of the pre-school children living in urban slums of Vellore have elevated blood lead levels and their living environment plays a role in the exposure pathway.

elevated BLL as ≥10 μg/dL for children under 6 years of age [4]. Recently, the CDC has updated the 'level of concern' for BLL among children to >5 μg/dL. This cut-off is based on the upper reference interval value of the 97.5th percentile of the distribution of the combined 2007-2008 and 2009-2010 cycles of the National Health and Nutrition Examination Survey (NHANES) in the United States. Since most of the available information is based on the the earlier cut-off value, this study used a value of >10 μg/dL to identify elevated BLLs.

Proportion of preschool children with elevated BLLs in this region is higher than the values reported earlier from most parts of India (12 to 38%) [13,14]. A study done among older children from urban areas of Chennai has reported even higher prevalence of 52.5% [15]. Only a few studies are available from India looking at family demographics and environmental factors that might correlate with BLLs among children. Educational status of the parents, age and sex of the children, lower SES, total number of children born to the mother and weight/height ≤95th percentile are established risk factors in the developing countries. Age of the house, materials used for flooring inside the house, piped water supply, duration of occupancy or painting a residence are some of the important environmental predictors associated with elevated BLLs [8,16,17].

An association between early childhood lead levels and cognitive impairment at a later age is well documented [18-20]. Evidence from a systematic review indicates that doubling of BLL is associated with a mean deficit in the full scale IQ by 1 to 2 points [21]. A study among urban children aged 3 to 7 years from Chennai, India, found that high BLLs were associated with reduced visual-motor abilities [15]. In our study, children with elevated BLLs at 15 months had excess risk of having poorer cognitive scores at 24 months although this finding was not statistically significant. Future prospective assessments of cognition and school performances are needed to better understand the effect of lead exposure on neurodevelopment of children. Younger age and pre-existing iron deficiency pose increased risk of developing lead induced clinical anemia. Anemia has been reported to be more common among children below 3 years of age with high BLLs (75.3 % *vs*. 67.4 %) [17]. In our study, more than half of the study children were anemic at 15 months of age but significant association between BLLs and hemoglobin levels at 15 months was found. Findings from this study could be limited in terms of not adjusting for other risk factors for anemia, including nutritional deficiencies.

Elevated BLLs are clearly a public health concern among preschool children living in urban slums of Vellore. Poorer conditions of the living environment seem to be associated with higher lead levels. More research focusing on the built environment and behavioral characteristics of children and parents is needed to understand the exposure pathways in greater detail, and to investigate causality.

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