International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 7; Issue 4(B); April 2018; Page No. 11393-11396
DOI: http://dx.doi.org/10.24327/ijcar.2018.11396.1970

Research Article

A COMPARATIVE STUDY OF BLOOD LEAD LEVELS IN CHILDREN AGED 3-12 YEARS WITH DEVELOPMENTAL DELAY, INTELLECTUAL DISABILITY, COGNITIVE AND/OR BEHAVIORAL PROBLEMS WITH NORMAL CHILDREN

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A R T I C L E I N F O

Article History:

Received 25th January, 2018
Received in revised form 13th February, 2018 Accepted 10th March, 2018
Published online 28th April, 2018

Key words:

Lead, Developmental Delay, Intellectual Disability, Cognition problems, Behaviour problems, Comparative study

A B S T R A C T

Lead is a poisonous metal with devastating consequences especially in young children; no biological role in the body has been ascribed to lead so far. Chronic lead exposure leads to so many problems related to the neurological, hematological, gastrointestinal, cardiovascular and renal systems especially in children. The purpose of this comparative study was to determine and compare the blood lead levels in children aged 3-12 years with Developmental Delay, Intellectual Disability, Cognitive and/or Behavioral Problems with normal children of same age and to find the correlation, if any, between the developmental delay, Intellectual Disability, Cognitive and/or behavioral problems and lead.The study wasa hospital based comparative study of both admitted and outdoor patients/children aged 3-12 years. Blood lead concentration was determined by Atomic absorption spectrometry in 71 subjects with 24 cases of developmental delay, intellectual disability, cognitive and/or behavioral problems and 47 controls like acute gastritis, febrile illness, respiratory tract infections etc. The mean blood lead level was higher in children with developmental delay, intellectual disability, cognitive and/or behavioral problems than in controls (8.55 µg/dl with standard deviation of 2.20 µg/dl in Cases and 1.93 µg/dl with standard deviation of 1.50 µg/dl in Controls; $p < 0.001$). An elevation of blood lead level in children may be associated with developmental, neurological and psychiatric problems. A blood lead level could be included in the diagnostic evaluation of children with such problems. It also warrants an exhaustive study of lead levels in pediatric age group and to point out the environmental pollutants containing lead.

INTRODUCTION

Lead is ranked among one of the most serious environmental pollutants worldwide resulting in health hazards to children (and adults) especially due to lack of awareness.[1] It has no known physiological relevant role in the body[2]. Lead is known to bio-accumulate in most organisms, whereas it is generally not biomagnified up the food web. Lead is a known potent neurotoxin and has been found to effect the cognition and development of young children, and there appears to be no threshold below which these effects do not occur.[3,4,5] It is a cumulative toxicant that affects multiple body systems, including the neurological, hematological, gastrointestinal, cardiovascular, renal systems, endocrine and immune systems.[6] Acute severe exposures may even lead to fatal encephalopathy.

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Chronic high level exposure has been shown to reduce fertility in males. Loss of hearing and decaying of teeth has been also linked to lead exposure.[7] Children are particularly vulnerable to the neurotoxic effects of lead primarily because of immaturity of the system(s).[8] The main tool in diagnosing the severity of lead poisoning is laboratory analysis of blood lead level (BLL).[9] Although as of yet no threshold for lead toxicity/safety has been established, a point of concern for level at or above 10µg/dl was established in 1991 by CDC USA.[10,11] The CDC recently states that a BLL of 5µg/dl or above is a cause for concern in children and can impair development even at BLLs below 5µg/dl especially in children below 5 years. In 2012 the United States Centers for Disease Control and Prevention (CDC) recommended reducing the reference value from 10µg/dL to 5 µg/dl.[12]

MATERIALS AND METHODS

The study wasconducted at GB Pant Hospital Srinagar, an associated hospital of GMC Srinagar which is a tertiary care

hospital. It was duly approved by the Ethical Committee (Institutional Review board) of the college (No. Acad/642-62/MC dated 19-02-2014). The study wasa hospital based comparative study of both admitted and outdoor patients/children conducted over a period of 18 months. Children included were 3-12 years of both genders with Developmental delay, Intellectual Disability, Cognitive and/or Behavioral problems fulfilling the diagnostic criteria were taken. Children with normal development, Cognition and/or behavior admitted for diseases other than Developmental delay, Cognitive and/or Behavioral problems of same age/gender were taken as controls. The children who were excluded from the study included children <3years and >12years, children with any neonatal event suggestive of Hypoxic Ischemic Encephalopathy, Intracranial bleed, Bronchopulmonary dysplasia, Bilirubin encephalopathy, Neonatal meningitis imaging suggestive of any structural abnormality of brain, Neurodegenerative disease (excluded by relevant investigations), recent or past accidental ingestion of lead containing compound(s), children with dysmorphic features.After obtaining proper consent(written and informed) from the parents/guardians of all children, a 1-2 ml venous blood sample was collected from each child from the antecubital vein after carefully washing the puncture site with 100% isopropanol in a nonmetal-adhering, lead free tube using 22 gauge sterile syringes. It was frozen and sent for lead estimation.Quantitative measurement of Lead was performed in whole blood sample using Atomic Absorption Spectroscopy (Model: AAS4141). The digestion of blood samples was done using microwave Oven (Model: MG-396 WA). A volume of 0.5 ml each of whole blood samples was taken into Pyrex conical flask separately. 3 ml of freshly prepared mixture of concentrated nitric acid and hydrogen peroxide (HNO_3 - H_2O_2; 2:1, v/v) were added into the sample and kept for 10 minutes at room temperature. Thereafter, the samples were transferred in microwave oven with heating at 800W for 3 minutes. The digestion flasks were cooled at room temperature. The samples were separately diluted with 0.1M nitric acid up to mark in 25 volumetric flasks. The lead was then measured by AAS.For developmental delay, DDST (DENVER II) chart/table was used. Developmental delays may occur in any or all of the major areas of child development.[13] At times, there can be significant variations in attainment of milestone in individual fields, this is called dissociation.[14] Global developmental delay is defined as "a significant delay in two or more of the major areas of child development.[15] For Intellectual Disability, children with IQ less than 70% were diagnosed as cases with Intellectual Disability which was categorized further as mild, moderate or severe depending on the IQ. It is said to be Mild Intellectual Disability, when IQ level is 50–70, Moderate Intellectual Disability when IQ level 35-50), Severe Intellectual Disability when IQ level is 25-35 and Profound Intellectual Disability (IQ level below 25). Severe Intellectual Disability accounts for less than 5% of the population of affected children. For cognitive and/or behavioral problems, CBCL was used for screening and consultant psychiatrist confirmed the diagnosis using DSM IV diagnostic criteria.[16]

The data was entered in Microsoft excel. Continuous variables are presented as mean ± SD. Categorical variables are presented as absolute numbers and percentages. Bar charts were used for graphical representation of data. Unpaired t-test and Chi-square test were used for testing difference between the experimental and control groups. A p-value less than 0.05 was considered statistically significant. Analysis was done using SPSS version 20.0.

RESULTS

Tables 1 and 2 represent the distribution of population of both groups in different age groups and mean age of cases and controls. The age distribution was similar in the two groups as majority of candidates were less than 6 years in both cases (45.8%) and controls (46.8%) and the mean age of cases and controls was nearly similar in the two groups.

Table 1 Age distribution of cases and controls

Age(Months)	Cases		Controls		p-value
	N(24)	%	N(47)	%	
36-72	11	45.8	22	46.8	
73-108	8	33.3	17	36.2	0.0921
109-144	5	20.8	8	17	

Table 2 Mean age of cases and controls

Group	N	Mean age (Months)	Sd. Deviation	p-Value
Cases	24	85.9	31.642	0.464
Controls	47	79.8	33.916	

Table 3 represents the gender distribution of cases and controls and shows that males (75% in cases and 53.2% in controls) outnumbered the females in both groups. However, this was statistically not significant (p-Value 0.075).

Table 3 Sex distribution of the Cases and Controls

Sex	Cases		Controls		p-value
	No.	%	No.	%	
Male	18	75	25	53.2	0.075
Female	6	25	22	46.8	

Table 4 and 5 represent the DQ/IQ in cases and controls with different age groups and shows that the DQ/IQ was significantly higher in controls (Mean98.57) than cases (Mean 77.33) which was statistically significant.

Table 4 Comparison of mean DQ/IQ among children in Cases and Controls

Subjects	N	Mean DQ/IQ	S.D	P-Value
Cases	24	77.33	19.748	0.001
Controls	47	98.57	6.567	

Table 5 Comparison of mean DQ/IQ among children in different age groups in Cases and Controls

Age (Months)	Mean DQ/IQ		
	Cases	Controls	p-value
36-72	74	95.64	0.007
73-108	79.75	102.06	<0.001
109-144	80.80	99.25	0.031

Tables 6 and 7 represent the lead levels in the two groups (of cases and controls along with different age groups) and shows that the lead level was significantly higher in cases (Mean 8.556 µg/dl) than controls (Mean 1.937 µg/dl) which was statistically significant (p-Value <0.001).

Table 6 Comparison of mean blood Lead levels in Cases and Controls

Variables	Blood Lead levels (µg/dl)	Standard deviation	p-Value
Cases	8.556	2.202	<0.001
Controls	1.937	1.504	

Table 7 Comparison of mean blood Lead level among children in different age group in Cases and Controls

Age (Months)	Mean Blood Lead level (µg/dl)		
	Cases	Controls	p-Value
36-72	8.747	1.623	<0.001
73-108	8.735	2.312	<0.001
109-144	7.675	2.002	<0.001

DISCUSSION

Lead, a known neurotoxin, has no known physiological relevant role in the body; and has been shown to affect the cognition and development of young children.[2,4] There appears to be no threshold below which these effects do not occur.[5] Although as of yet no threshold for lead toxicity/safety has been established, a point of concern for level at or above 10µg/dl was established in 1991 by CDC USA and was adopted by most countries in the world.[10,11] The Centre for Disease Control and Prevention recently states that a BLL of 5µg/dl or above is a cause for concern in children and can impair development even at BLLs below 5µg/dl especially in children below 5 years. The evidence of an inverse association between low level lead exposure and IQ is unequivocal, although the evidence of a similar association between behaviour and moderately raised lead concentrations is less clear, but has been demonstrated in a number of studies. Hence there should be complete absence of lead in the blood ideally.[17,18,19]

This hospital based comparative study comprised of 71 children with 24 cases and 47 controls. Cases were selected after ruling out any exclusion criteria and controls were selected randomly from both admitted and outdoor patients at department of Paediatrics, GMC Srinagar over a period of eighteen months.

The present study had a case control ratio of almost 1:2; as was there in the study previously conducted (1:1.96 and 1:1.97 respectively).[8] Males outnumbered females in our study with a male female ratio of 1.535. Male female ratio varied in different studies with 2.214 in one study.[19]

We included the age group of 3-12 years (36-144 months) in the present study. The mean age of cases and controls in our study was comparable {85.92 months (7.16years) and 79.79 (6.65 years; p-value =0.464) months respectively}. The age group has been different in different studies as 4-12 years, 6 to 60 months, 3-7 years.[19,20,21]

We encountered in majority of our cases behavioural problems followed by developmental delay and intellectual disability, (19, 7 and 6 respectively). Some had combination of abnormalities (11). The controls included gastrointestinal cases (9), UTI and enteric fever (3 each), Pneumonia (2), Meningitis (2), acute febrile illness (2). The total number of children from urban areas was 27 and nonurban areas were 44 with a ratio of approximately 1.63. Difference in BLLs in two groups was not statistically significant (5.08+/-3.37 µg/dl and 3.6+/-3.6 µg/dl respectively; p-value 0.09. The distance from the main road had a little effect on BLLs of children. The DQ/IQ in cases with higher lead levels was significantly lower as compared to the controls in our study (77.33+/-19.748 vs 98.57+/-6.567; p-value 0.001) which was consistent with previous studies demonstrating a lower IQ with elevated BLL.[7,20] The mean BLL (µg /dl) in cases was significantly higher than controls (8.556+/-2.202µg/dl and 1.937+/-1.504µg/dlrespectively; p-valve <0.001) which was consistent with other previous studies with mean BLLs in cases of 8.77+/-3.89 µg/dl and that in controls of 5.76+/-3.3 µg/dl (p-value<0.01).[19] Similar results were seen in other studies. Mean blood lead levels in a studywas11.4 (± 5.3) µg/dl in children with behavior problems aged 3-7 years.[21]In this study, the maximum BLL in the cases was 13.26µg/dl and minimum was 4.22µg/dl respectively; and in controls maximum BLL was 5.0 and minimum was 0.0 microgram/dl respectively.

One of the important things was the association of risk factor (s) with elevated blood lead levels. More the number of risk factors present in child, more was the child exposed to lead (or lead containing compounds) and more was the blood lead level.

Hence from this study, elevated BLLs were observed to be present in the children with developmental delay, intellectual disability, and behavioral problems as compared to the normal children; and DQ/IQ was comparatively lower in cases than in controls.

CONCLUSION

Hence it can be concluded that DQ/IQ is significantly lower in cases that havebehavioural problems, developmental delay and intellectual disability, than in controls. Also these patients are associated with elevated BLLs as compared to the controls; and hence lead seems to have an association in the aetiology of these disorders. However, a larger study is recommended to analyse this association and if proven, the routine screening of BLLs in children with these problems is recommended.

Acknowledgements

The authors thank the parents/guardians who consented for the participation of their children in the study. Without their participation the study would not be possible.

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How to cite this article:

Rais Ahmad Lone *et al* (2018) 'A Comparative Study of Blood Lead Levels in Children Aged 3-12 Years with Developmental Delay, Intellectual Disability, Cognitive And/Or Behavioral Problems with Normal Children', *International Journal of Current Advanced Research,* 07(4), pp. 11393-11396. DOI: http://dx.doi.org/10.24327/ijcar.2018.11396.1970

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