Elevated Maternal Blood Lead Level - A Risk Factor for LBW - An Observational Study

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ABSTRACT

Introduction: Lead exposure is common in women. Lead stored in bones is released during pregnancy and can potentially affect foetal growth. We conducted this study to estimate the effect of maternal blood Lead (BPb) status on Low Birth Weight (LBW) in newborns.

Methods: 168 mothers were selected from Special Neonatal Care Unit (SNCU) and Postnatal care (PNC) wards of a tertiary care hospital from Central India and their BPb levels analysed by Graphite Furnace Atomic Absorption Spectrophotometer.

Results: 22 (13.10%) mothers having BPb level ≥ 5µg/dL gave 23 births (one twins); of which 65.22% mothers delivered babies with birth weight < 2500gm (LBW) ($p = 0.0007$). The mean birth weight of newborns of mothers with high BPb levels was significantly lower by 269 gm ($p = 0.0265$). Mothers with BPb ≥ 5µg/dL delivered 39% premature babies as compared to 10 % mothers with BPb < 5 µg/dL ($p < 0.003$). Significantly more mothers exposed to kajal, nail polish, lipstick and paints had BPb levels ≥ 5µg/dL.

Conclusion: Significant association is detected between maternal BPb and both LBW and prematurity in the given population.

Keywords: Blood Lead; Cosmetics; Newborn; Preterm; Toxic

INTRODUCTION

Lead is a toxic environmental contaminant omnipresent in our environment causing several health problems in exposed population.[1] Common sources of lead are colours / paints, cosmetics and batteries. Women and children are particularly vulnerable to cosmetic plumbism described way back in 1973. US FDA has set a limit of 10 ppm for Pb in cosmetics.[2] In Jan 2012, CDC recommended reduction of BPb levels to < 5 µg/dL.[3] The CDC stated that there is no safe limit for lead to cause adverse effects.[4] The Government of India on its National Health Portal has also stated dangers of lead exposure at levels as low as < 5 µg/dL.[5]

Lead is stored in bones predominantly and for prolonged duration. Increased requirement of calcium in pregnancy causes demineralisation of bones, concurrently liberating bone lead previously stored in bones increasing vulnerability to lead toxicity.[6] Lead crosses the placental barrier freely with a fetal-maternal ratio of 0.7 - 0.9.[7] Prenatal lead exposure influences foetal and maternal health.[8] High maternal BPb levels increase risk of prematurity and is associated with reduction in Mean Birth Weight (MBW).[9]

However, studies have also reported conflicting data about birth weight in babies exposed to maternal lead. Taylor et al have reported adverse effect of maternal lead on birth weight but not on incidence of LBW.[9] Gonzalez-Cossio T et al. showed inverse relation between birth weight and bone-lead burden.[10] Whereas Awasthi et al. reported direct relation between birth weight and BPb level levels.[11] Factor-Litwak P et al. have failed to find an association between the two variables.[12] In view of this, we studied the association between maternal lead exposure and LBW. The primary objective was to study whether maternal BPb level ≥ 5 µg/dL is associated with and is a risk factor for LBW. The secondary objectives were to study the environmental factors like (Lead paints, cosmetics etc.) predisposing to maternal BPb level ≥ 5 µg/dL and to compare pregnancy outcomes like prematurity and IUGR in mothers with BPb level ≥ 5 µg/dL and < 5 µg/dL.

METHODS

The study was conducted in a tertiary care hospital in Central India after approval of protocol by the Institutional Ethics Committee. Consecutive, informed, consenting, eligible 168 mothers of varied gestations were enrolled from SNCU and wards. Maternal venous blood sample (6 ml) was collected aseptically within 24 hrs of delivery, in heparinised 15 ml Falcon tube and transported in insulated frozen ice pack carrier and stored at 4°C till processing. Blood lead (BPb) was analysed by graphite furnace atomic absorption spectrophotometer (Perkin Elmer) at 283.3 nm which used longitudinal Zeeman background correction and a transversely-heated furnace.[13] Gestational age of newborn was assessed by New Ballard Score (NBS) and anthropometry (Birth weight, occipito-frontal head circumference, crown to heel length) recorded within 24 hours of birth. Maternal history about exposure to various lead containing chemicals was recorded in structured proforma. (Kajal- a black pasty cosmetic applied to eyelids including kohl, soorma, kajal). Chi-square tests were used to analyse differences in categorical data. Multivariate logistic regression analysis was used to examine the effect of the binary variables high blood pressure, high BPb, maternal pallor, gestational age (GA) score, parity, prematurity and painting as a hobby on birth weight.

RESULTS

Of 168 mothers, 156 were 20 to 30 years old. There were three twin deliveries thereby yielding 171 babies. Mean maternal BPb was 2.044 µg/dL (Range 0.05 – 20.48 µg/dL). BPb level was ≥ 5 µg/dL in 22 (13.10%) out of 168 mothers, of which 14 (63.64%) delivered babies with birth weight < 2500 grams (LBW). Of the 146 mothers with BPb < 5 µg/dL, 43 (29.45%) delivered LBW babies. (p = 0.0007) (Power = 87%) (Table 1)

Of 168 mothers, 109 had BPb < 2 µg/dL giving 110 births, of which 31 (28.18%) were LBW babies; while 59 had BPb ≥ 2 µg/dL giving 61 births, of which 27 (44.26%) were LBW. (P = 0.043) (Table 2).

Babies born to mothers with BPb ≥ 5µg/dL weighed 269 gm less than those born to mothers

Table 1. Distribution of mothers according to birth weight and maternal BPb ≥ or < 5 µg/dL

Maternal lead level	No. of mothers delivering neonates with birthweight		
	< 2500 grams	≥ 2500 grams	Total
≥ 5 µg/dL	14 (63.64%)	8 (36.36%)	22 (13.10%)
< 5 µg/dL	43 (29.45%)	103 (70.55%)	146 (86.90%)
Total	57 (33.93%)	111 (66.07%)	168
p value = ***0.0007			

*p < 0.05 = significant**
*p < 0.01 = very significant***
*p < 0.001 = extremely significant****

with BPb level < 5 µg/dL. (p = 0.0265) (Power = 70%) (Table 3).

Twenty two (13.45%) mothers having BPb ≥ 5 µg/dL delivered 23 babies, of which nine (39.13%) were preterm which was significantly more in comparison to mothers with BPb < 5 µg/dL (Power =88%) (Table no 4). Of 23 births from 22 (13.45%) mothers having BPb ≥ 5 µg/dL, six (26.09%) babies were IUGR. Of 146 mothers with BPb < 5 µg/dL, giving 148 births, 38 (25.08%) were IUGR. (p= 0.9903)

Multivariate logistic regression analysis was done after adjusting high maternal BPb for maternal risk factors for LBW like high blood pressure, BMI, pallor, parity, painting as a hobby and risk factor in newborn viz gestational age score. In this, the maternal BPb was not found to be a risk factor for LBW. Multivariable linear regression showed gestation age score as per NBS as a risk factor for LBW. (Table 5)

Table 3. Comparison of maternal blood lead level and mean birth weight

Maternal blood level	Mean birth weight
≥ 5 µg/dL	2352.27 ± 600.49
< 5 µg/dL	2621.43 ± 404.87
p = *0.0265	

Table 2. Distribution of neonates according to birth weight and maternal BPb ≥ or < 2 µg/dL

Maternal Lead Level	No. of neonates with birthweight		
	< 2500 grams	≥ 2500 grams	Total
≥ 2 µg/dL	27 (44.26%)	34 (55.74%)	61 (35.67%)
< 2 µg/dL	31 (28.18%)	79 (71.82%)	110 (64.33%)
Total	58 (33.33%)	113 (64.91%)	171
p value = 0.043			

Of 168 mothers, 101 (60.12%) used kajal, of which 18 (17.82%) had BPb ≥ 5 µg/dL, while 67 (39.88%) did not use kajal, of which four (5.97%) had BPb ≥ 5 µg/dL(P = 0.0257). One hundred and five mothers (62.5%) used nail polish, of which 20 (19.05%) had BPb ≥ 5 µg/dL while in 63 (37.5%) who did not use nail polish, two (3.17%) had BPb ≥ 5µg/dL (p = 0.0032). Among 78 mothers (46.43%) using lipstick, 15 (23.81%) had BPb ≥ 5 µg/dL while 90 (53.57%) did not use lipstick, of which seven (7.78%) had BPb ≥ 5 µg/dL (p = 0.0282). Of 109 (64.88%) mothers using glazed ceramic pottery, 10 (9.17%) had BPb ≥ 5µg/dL while among 59 (35.12%) not using it, 12 (20.34%) had BPb ≥ 5µg/dL (p = 0.0406). Nine mothers (5.36%) were exposed to paints as a hobby, of which five (55.56%) had BPb ≥ 5 µg/dL; while 159 mothers (94.64%) were not exposed to paints, of which 17 (10.69%) had BPb ≥ 5 µg/dL (p = 0.0007). There was no significant difference in BPb levels between

Table 4. Distribution of neonates according to maternal lead level and prematurity

Maternal lead level	No. of mothers	No. of children		
		Preterm	Term	Total
≥ 5 µg/dL	22	9 (39.13%)	14 (60.86%)	23 (13.45%)
< 5 µg/dL	146	16 (10.18%)	132 (89.19%)	148 (86.54%)
Total	168	25 (14.61%)	146 (85.38%)	171
p = ***0.0003				

Table 5. Multivariable logistic regression for risk factors of LBW

LBW	Odds ratio estimate	Standard error	P-value	Lower 95% CI
Lead level	2.119	0.3625	0.3002	0.512, 8.774
High blood pressure	3.792	0.3724	0.0735	0.881, 16.326
Body Mass Index	0.907	0.0701	0.1621	0.79, 1.04
Maternal pallor	0.283	0.5932	0.2874	0.028, 2.896
GA Score as per NBS	0.722	0.0756	<0.0001	0.622, 0.837
Parity	1.567	0.2263	0.3212	0.645, 3.804
Prematurity	2.67	0.4702	0.2963	0.423, 16.868
Painting as hobby	1.787	0.562	0.6055	0.197, 16.175

mothers exposed to and not exposed to other cosmetics or environmental factors. We could not find a significant difference in LBW in mothers using and not using cosmetics. We could not find a significant difference in LBW in mothers exposed and not exposed to various environmental sources of lead.

DISCUSSION

In our study, mean maternal BPb was 2.044 µg/dL, which is much below the reference level than recommended by CDC and Govt of India. This is comparable to studies by Patel AB et al. in India (2.0 + 2 µg/dL) and Odland et al. in Norway (1.25 µg/dL) and Russia (2.92 µg/dL).[14,15] High levels of mean maternal BPb level (64.3 µg/dL) has been reported by Ladele et al.[16] The level recorded by McMichael et al. was 11.2 µg/dL and by Awasthi S et al. was 14.34 µg/dL which are much higher than our study.[17,11] The differences in mean BPb between studies can be explained by the variable exposure to various environmental sources in the study population, by the variable mobilisation of lead from bones and differences in laboratory test standards. We reported a significant decrement of 269 gm in mean body weight of babies born to mothers with BPb ≥ 5µg/dL. Similar findings are reported by Taylor CM et al.[9], Berkowitz et al. also found reduction in MBW by 71 g in Lead exposed mothers.[18] Contradictory results were found by Awasthi et al. who reported higher mean body weight in babies born to mothers with higher levels of BPb.[11] Factor-Litwak P et al. did not find any association between the two variables.[12]

In our study significantly more i.e. 63% LBW babies were delivered by mothers with BPb ≥ 5µg/dL. Ugwuja et al has reported increase in delivery of babies with LBW with increasing maternal BPb, with mothers in BPb groups 20.0 – 29.9, 30.0 – 39.9, and > 40 µg/dL having significantly higher LBW newborns (13.9%, 17.6% and 22.7%, respectively) when compared with women in the BPb < 10 µg/dL (7.6%) and 10–19.9 µg/dL (11.1%) groups.[19] In Norway, Irgens et al. observed similarly that babies of lead exposed mothers had a higher risk of LBW (RR = 1.34; CI = 1.12-1.60).[20] Taylor et al. however found no correlation between maternal blood lead level and LBW.[9] Ladele J et al. in Lagos found no association between mean maternal BPb and birth weight < 3rd centile.[16]

However, in our study when the birth weight was adjusted with other variables in the multiple regression analysis, factors like high BP, BMI, maternal pallor, GA score as per NBS, parity, prematurity, painting as hobby, the association of high BPb levels and LBW was not statistically significant. In the multiple regression analysis the GA score has been shown to have a statistically significant risk association. This can be easily attributed to the fact that babies with lesser gestation are physiologically liable to have a lower birth weight. Lead mimics calcium and competes with it for foetal bone deposition can impair normal foetal bone growth.[21] Rats exposed to lead have reduced bone calcium content, reduced trabecular bone volume, altered growth plate morphology, and enhanced activities of spontaneous uterine contraction.[20] Lead may also have endocrine-disrupting capabilities by reducing responses to hormones that are necessary for growth, such as insulin-like growth factor and growth hormone, and inhibiting the hypothalamic-pituitary-growth axis.[22] These mechanisms can explain the deranged foetal growth in terms of mean body weight and LBW.

In our study, when high maternal BPb was analysed for association with birth of preterm infant, the association was statistically significant. This is consistent with Jellife-Pawlowski et al., where prenatal PbB >10 µg/dL was associated with significantly less total days of gestation and higher risk of preterm and small-for-gestational age (SGA) birth.[23] This could be possibly due to induction of preterm delivery because of lead-induced reproductive hormone disruption and induction of uterine contractibility.[24,25] In pregnant rodents given lead at moderate doses (BPb: 10 – 40 µg/dL), serum progesterone levels were decreased in dams and hypothalamic levels of gonadotrophin releasing hormone (GnRH) and somatostatin were suppressed in both dams and foetuses.[26] However various studies have observed that frequency of premature births was not influenced by maternal BPb.[16,18,19] When high maternal BPb was analysed for association with IUGR no meaningful conclusions could be drawn because of low power for the variable.

In this study, BPb ≥ 5 µg/dL was significantly more in women using kajal, lipstick and nail polish. Nir A et al. reported elevated BPb levels in children exposed to kohl.[27] Several studies have reported Pb content of cosmetics.[28] Repeated and prolonged exposure to cosmetics may increase the risk of lead poisoning; both through transdermal and enteral routes. In our study, BPb was ≥ 5 µg/dL in those women exposed to paints as a hobby. We did not find an association of maternal BPb with other environmental exposures. Al-Jawadi et al. reported low parity, smoking and Hb level < 11 gm/dl as predictors of high maternal BPb but did not report association with cosmetics or other environmental factors.[29] Farias found that use of ceramic glazed pottery was the main determinant of high BPb level[30], but we paradoxically found that significantly more mothers not using glazed ceramic pottery had higher BPb levels which can be attributed to questionnaire design. The data can be more precise if the duration or frequency of exposure per day, week or month is recorded. Cosmetics need to be lead-safe considering the widespread usage among women in child bearing age group. CDC has stated that there is no safe BPb level. This is emphasised by the results of various studies cited in above discussion. In this context, it is notable that 146 out of 168 mothers in our study had BPb levels <5 µg/dL, of which 109 mothers had BPb < 2 µg/dL. This latter group could be vulnerable to risks of lead exposure even at low levels. The level of reference for BPb has reduced dramatically over the years to a cut-off of 5 µg/dL in 2012. Currently, the CDC is considering a reduction to 3.5 µg/dL based on the 98 percentile of blood lead levels for children in a National survey in United States. In this study, 28% babies born to mothers with BPb < 2 µg/dL had LBW as against 44% babies born to mothers with BPb ≥ 2µg/dL which was significant. These findings can guide policy makers for further changes in level of reference for lead.

Well designed, population based studies with bigger sample size are needed to confirm these findings and to delve deeper into the environmental sources of lead, hazards of exposure to lead at various BPb levels especially in women, developing foetus and children. The policy makers and stakeholders need to be informed of the threats of lead in order to bring about positive changes at national and global levels.

CONCLUSIONS

Mothers with BPb ≥ 5 µg/dL had significantly higher association with LBW, prematurity and mean body weight. On multivariate logistic regression analysis, after adjusting high BPb for other risk factors of LBW, the maternal BPb was not found to be a risk factor for LBW. This study found that BPb ≥ 5 µg/dL was significantly more in women using cosmetics like kajal, lipstick and nail polish and those with exposure to paints.

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