November 2003

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Abstract

Objective: To evaluate association of blood lead levels with pregnancy outcome in the obstetrics and gynaecology unit.

Methods: Blood lead levels were measured in 73 pregnant women at the time of delivery and assessed its association with pregnancy outcome.

Results: Mean maternal lead level was 9.91+4.44 mg/dL (range 2.28 - 36.35 mg/dL). Mothers of boys had significantly higher (p=0.013, one-tailed t test) blood lead levels (11.05+5.19) when compared to mothers of girls (8.74+3.18 mg/dL.

Conclusion: Maternal lead levels at the time o delivery showed no association with gestational age, birth weight, recumbent length, or head circumference (JPMA 53:529;2003).

Introduction

Due to excessive use of lead in industry and automobile fuel, human beings have been, and are constantly being, exposed to it. Environmental lead exposure is a public health problem on global level[1], as it adversely affects the function of several organ systems including cardiovascular, renal, nervous, hemopoietic, endocrine and skeletal systems.[2,3] Although the exact magnitude of lead poisoning in Pakistan is not known, some sporadic studies have indicated that the levels in population are much above the safety levels (10 mg/dL) recommended by the United States Center for Disease Control and Prevention (CDC). Mean blood lead levels were reported to be 18.8 mg/dL (5.0-38.8 mg/dL) in children in Rawalpindi[4] and 34.4, 31.8, 29.9 and 38.2 mg/dL in males, females, soldiers and children, respectively, from Karachi.[5] Of these, over 90% population had levels above the safety limit. More recently, more than 80% children from Karachi were found to have lead levels above 10 mg/dL.[6]

Lead gets into the body through food, water and air. Environmental pollution, agricultural technology and food processing are the main sources of exposure.[7] Absorption and retention in the body depends on age, chemical environment of the gastrointestinal tract and nutritional status of the individual. Generally, conditions that favor calcium absorption also favor lead absorption and retention. The total body content of lead does not affect its absorption, as there is no feed back mechanism for its absorption.[7] The mean biological life of lead in blood is about 30 days[8], after which majority (70-95%) of it is accumulated within the long-lived compartments of bones, with the elimination half-life of 5-10 years.[9]

The increased nutritional requirements during pregnancy and the pregnancy-induced homeorhesis may result in elevated blood lead levels. During pregnancy stores of lead deposited in bones over lifetime may be mobilized, particularly in those whose calcium intake is low.[10-12] Mobilization from bones depends on maternal age, overall nutritional status, parity, race and gestational age.[11] In addition, absorption from the gut may be increased. Since placenta does not offer any restrictive barrier to the transfer of lead from maternal blood to the fetal blood[10,13-16], the developing fetus may be exposed to the adverse effects of lead.

The effects of high blood lead levels on pregnancy outcome has been thoroughly investigated and reviewed. Children born to women with high lead levels are usually smaller, weaker, slower in development, and have a higher infant mortality.[11] High lead levels during pregnancy are associated consistently with increased spontaneous abortion, still birth, premature birth, and neonatal deaths.[10] Low levels of exposure have shown inconsistent results with birth weight and prematurity.[10,11] The results vary from no effect to mild, statistically non-significant association, to a significant dose dependent effect.[10,11,17,18] The reasons for the inconsistency are differences in the lead levels, stage of gestation in which blood samples were taken, and whether association was determined with maternal or fetal blood lead levels.

Poor pregnancy outcomes like miscarriage, stillbirths, intrauterine growth retardation and low birth weight are fairly common in this country.[19,20] How much of these problems are associated with high lead levels is not known and is worth investigating. The purpose of this study was thus to investigate the association of blood lead levels during pregnancy with pregnancy outcome in a population of women from Karachi, where lead levels are presumably high from heavy industries and heavy traffic using leaded gasoline.

Materials and Methods

Subject Selection

This study was conducted at the Jinnah Postgraduate Medical Center, Obstetrics and Gynecology unit. Women

who were brought to the clinic for labour between 09:00 and 14:00 hours over a period of four weeks were sequentially recruited after obtaining their verbal informed consent. Weight and height of the mothers were recorded to the nearest 0.1 Kg and 0.1 centimeter, respectively, using the standard techniques. 5 ml of the venous blood was drawn in heparinised vaccutainers and was stored at 4°C for lead analysis. After delivery, birth weight of neonate was recorded to the nearest 10 grams and recumbent length (crown-heel length) and head circumference were measured to the nearest 0.1 centimeter, using non-stretchable tape. Gestational age was calculated from the first day of the last menstrual period, if known, or by asking mothers the age of the fetus in months. Term deliveries, reported by some mothers, were considered as 40 weeks of gestation. Data were recorded on a total of 75 mother-fetus pairs.

Analysis of lead

Lead content in whole blood was determined at the Pakistan Council for Scientific and Industrial Research (PCSIR) laboratories, Karachi, Pakistan. The CDC, USA, provided quality control for analyses. Lead was analyzed by Hitachi polarized Zeeman atomic absorption spectrophotometer, (model Z-800, Hitachi, Tokyo, Japan) with a graphite furnace. The instrument was calibrated with lead standards (lead nitrate, 1000 mg/dL, Cat. # 45556, BDH, Dorset, England) by the standard addition method as described by Miller et al.[21] The instrument specification are given in table 1.

Samples and standards were prepared with a matrix modifier solution which contained 0.5% v/v Triton X-100, 0.2% v/v 65% (16 M) extra pure nitric acid and 0.2% dibasic ammonium phosphate[21] all from Sigma Chemical Co. (St. Louis, MO). Water used for reagents preparation was purified to approximately 18 M W/cm with a Milli-Q system (Millipore).

Statistical analyses

The data was analyzed with Statistical Package for Social Sciences (SPSS) software (version 8.0) for windows. Univariate and multivariate regression analyses were carried out to measure the association of maternal blood lead with gestational age, birth weight, birth length and head circumference. In multivariate regression analyses, variables with no significant effect were removed from the full model in a step-wise manner and the data presented is for only the best models. Group comparisons between boys and girls were estimated with the Student's t-test. The level of significance was set at $P < 0.05$.

Results

Of the 75 mother-fetus pairs included in the study, one mother gave birth to twins and was excluded from the study. Lead levels could be measured in 73 women for whom the data is presented. Table 2 shows data on mean

Table 1. Instrument specification for lead analysis.

Instrument conditions			
Lamp current	7.5 mA		
Wavelength	283.3 nm		
Slit	1.3 nm		
Cuvette	Cup		
Carrier gas	200 ml/min		
Interrupted gas	30 ml/min		
Sample volume	20 µl		
Temperature Program			
	Temperature (C)		Time (Second)
Stage	Start	End	
Dry:	80	120	30.0
Ash:	400	400	30.0
Atom:	2000	2000	10.0
Clean:	2400	2400	3.0

Table 2. Demographic and anthropometric information and blood lead levels of pregnant women (n = 74) at the time of delivery.

	Mean ± SD	Range
Age (years)	25.5±4.8	15.0-39.0
Weight (Kg)	57.8±7.0	44.0-81.0
Height (cm)	156.2±8.0	127.5-170.0
Education (number of years)	4.9±4.7	0-12
Number of children before	2.7±1.9	1-9
Blood lead level (mg/dL)*	9.91±4.44	2.28-36.35

* n = 73

Table 3. Birth weight, recumbent length, head circumference and gestational age (Mean ± SD) of male and female infants born to study mothers.

	Male (n=37)	Female (n=37)	Total (n=74)
Gestational age (weeks)	39.7±1.8	39.6±1.7	39.6±1.8
Birth Weight (gm)	2793±547	2650±427	2722±493
Recumbent length (cm)	51.1±4.6	52.0±4.0	51.5±4.3
Head circumference (cm)	32.5±3.0	32.1±2.7	32.3±2.8

Table 4. Univariate regression analyses of the association of maternal variables with infant outcome variables.

Outcome Variable	Maternal Covariates	Coefficient (β)	R^2	p-value
Birth Wieght	Blood lead	19.12	3.0	0.146
	Age	-0.31	0	0.979
	Weight	21.27	9.2	0.009
	Height	33.25	4.7	0.064
	Education	-6.13	0.3	0.619
	Parity	-83.39	10.6	.005
	Gestational Age	11.60	8.2	0.013
Head Circumference	Blood lead	0.054	0.7	0.477
	Age	-0.059	1.0	0.395
	Weight	0.089	5.0	0.056
	Height	0.097	1.2	0.348
	Education	0.096	2.6	0.168
	Parity	-0.373	6.5	0.028
	Gestational Age	0.072	9.8	0.007
Recombent Length	Blood lead	0.03	0.1	0.796
	Age	-0.087	0.9	0.410
	Weight	0.100	2.7	0.165
	Height	0.438	10.7	0.004
	Education	0.042	0.2	0.695
	Parity	-0.329	2.2	0.212
	Gestational Age	0.104	8.7	0.011
Gestational Age	Blood lead	0.291	1.1	0.375
	Age	-0.041	2.6	0.174
	Weight	0.129	0.6	0.527
	Height	0.453	1.4	0.310
	Education	0.271	1.1	0.373
	Parity	-1.424	5.1	0.054

Table 5. Multivariate regression analyses of the association of maternal variables with the infant outcome variables.

Outcome variables	Model used	β	p-value	R^2
Birth weight	Age	31.32	0.024	21.4
	Parity	-116.63	0.001	
	Gestational age	9.43	0.036	
Head circumference	Weight	0.080	0.071	15.6
	Education	0.079	0.236	
	Gestational age	0.066	0.012	
Recombent length	Height	0.397	0.008	17.3
	Gestational age	0.092	0.020	

age, body weight, height, number of previous births (parity), years of education and their blood lead levels. Mean blood lead levels were 9.91±4.44 mg/dL. The mean (±SD) gestational age (weeks), birth weight (grams), recumbent length (cm) and head circumference (cm) of infants born to the study mothers were 39.6±1.8, 2722±493, 51.5±4.3 and 32.3±2.8, respectively (Table 3).

No difference was observed in gestational age, birth weight, recumbent length and head circumference between boys and girls (Table 3). Univariate regression analysis showed no association of maternal lead levels at the time of delivery with any of the growth parameters in new-borns (Table 4). Of the other variables, maternal weight and gestational age were significant positive predictor of birth weight. Head circumference was significantly associated with gestational age, whereas, significant predictors for recombent length were maternal height and gestational age. Number of previous children (parity) had negative association with all the four outcome variables tested, but

the effect was statistically non-signifcant for recombent length. In the multivariate analyses, the effect of gestaional age on birth weight, head circumference and recumbent length remained significant after controlling for confounding variables (Table 5). The negative effect of parity on birth weight, and the positive effect of maternal height also remained significant in the multivariate analyses (Table 5). We compared the growth parameters of infants born to mothers with blood lead levels of <10 mg/dL with those of mothers with lead levels of >10 mg/dl, and did not find any significant difference between the two groups in any of the parameters (data not shown). Mothers of boys had statistically significant higher blood lead levels (11.05±5.19 mg/dL, n=37) when compared to mothers of girls (8.74±3.18 mg/dL, n=36). The one-tailed t-statistic of 2.295 gave a P-value of 0.013.

Discussion

Karachi is a densely populated city with increased lead burden from environmental pollution. This is translated into increased blood lead levels in general population.[5,6] Poor pregnancy outcomes like intrauterine growth retardation, premature births and high maternal mortality rate are common in this part of the world. A positive association has been shown in a number of published reports between high blood lead levels and poor pregnancy outcome[22,23], but such association has not been substantiated by other studies.[17,18,24,25] We, therefore, undertook this study to investigate the association of blood lead with pregnancy outcome in our population.

We selected our study sample from maternity clinic of the Jinnah Postgraduate Medical Centre, as it is a catchment hospital for a much wider population and attracts mostly women from relatively low socio-economic status. These women are more likely to have high blood lead levels because of increased environmental, occupational and dietary lead exposure.

A previous study from Karachi[5] reported very high mean blood lead levels (38 mg/dL) in women. We therefore, expected lead levels to be even higher in our study population because of pregnancy-induced increased absorption from the gut and increased mobilization from bones.[7,11,12] However, mean blood lead level in our study sample was much lower than the previously reported blood lead level from Karachi women.[5] This discrepancy could be explained by two hypotheses: (1) Blood lead level is a reflection of the current exposure, as most of the lead gets accumulated in bones after about 30 days.[8,9] In pregnancy the mobility is decreased which may result in decreased exposure and hence decreased blood lead levels. (2) Blood volume increases in pregnancy, by as much as 30-40%, and the relatively lower blood lead levels in pregnant women that we report here could be due to this dilution effect. These factors should be considered in future such studies.

The outcome variables in our study are gestational age, birth weight, head circumference and crown-heal length of the fetus. Gestational age is not only an outcome variable but also a major confounding factor affecting fetal growth. One major limitation of our study is the recall bias in the gestational age, as majority of the women did not remember the first day of their last menstrual period (LMP), from which the gestational age should be calculated. Those women who did not remember their first day of LMP were asked whether the index baby is a term delivery or preterm. Term deliveries were considered as 40 weeks of gestation.

We did not find any association of blood lead with gestational age, as opposed to findings from several studies showing a shorter gestational age in women with high lead levels.[17,22,26] This could be explained in many ways. Firstly, majority of gestational data in our study is based on the close approximation of gestational age, as explained earlier, and there might have been some over-estimation in reporting gestational age. Secondly, we selected our subjects in specified times of a day and as such we might have missed miscarriages and preterm deliveries that had occurred at other times. Thirdly, our sample may not be large enough to pick up the reported association. Lastly, individual and racial differences in the effect of lead have been reported[27], which could explain partly lack of the association in our study population.

We found no association of blood lead with fetal growth either in terms of birth weight or birth length. Similarly no association has been reported by a number of studies.[17,18,25,28] A threshold level of 15 mg/dL has been suggested by Gonzalez-Cossio et al.[29] in order to show an adverse effect on birth weight. The lower mean blood lead level in our study population (<10 mg/dL) may explain this apparent lack of inverse association of blood lead with fetal growth.

An interesting observation in our study was that mothers of boys were found to have significantly higher mean blood lead levels when compared to mothers of girls. The physiological relavence of this apparent finding remains unclear. Lead is known to disturb the normal profile of reproductive hormones in animals, both at hypothalamic-pituitary and at the gonadal levels.[30-32] Whether lead has similar effects on human reproduction, remains to be investigated.

Acknowledgements

We acknowledge Ms Hina Zuberi for helping with data analysis and Dr. Safiuddin Siddiqui for reviewing the manuscript.

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