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ASSOCIATION OF MATERNAL AND CORD BLOOD LEAD LEVEL WITH THE FETO-MATERNAL OUTCOME.

Gynaecology

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ABSTRACT

Prenatal lead exposure has known adverse effects on maternal health and infant outcomes across a wide range of maternal blood lead levels. In 2010, the Centers for Disease Control and Prevention issued the first guidelines regarding the screening and management of pregnant and lactating women who have been exposed to lead. In humans, the lead is absorbed into the blood plasma where it equilibrates with the extra-cellular fluid and crosses the membranes like the placenta and the blood brain barrier. Therefore the fetus is exposed to maternal blood lead levels from the 12th week of gestation which is associated with preterm delivery, abortions etc.The present study was conducted to find the effect of maternal exposure to lead and neonatal birth weight among women living in the urban slums of Lucknow. Our study hypothesis was that lead exposure would reduce birth weight.

KEYWORDS

Cord blood, Lead (Pb), Feto-maternal, ICP-MS, Heavy Metal

Introduction:

Lead is an eminent human reproductive toxin. Some other toxic metals are also known such as mercury (Hg) and cadmium (Cd) [1]. The toxic metal lead (Pb) is mainly stored in the bone, and it can be released during times of physiological stress such as pregnancy, lactation, and menopause [2]. Most of toxic heavy metals are fat soluble, non-ionizing chemicals which can quickly cross the placental barrier, with blood flow, metabolism, thickness, surface area, lipid and protein content of the membranes and the carrier systems of the placenta, which are variable during pregnancy [3]. Lead early exposure occurs either before conception via parental exposure, during pregnancy via the placental barrier or after birth via breast milk or directly from the environment [2-4]. In many countries, lead exposure has been linked to unfavorable outcomes in pregnant women and newborns [5]. Pb concentrations can vary, not only because of mobilisation of Pb from bones during pregnancy, but also because of changes in haematocrit values [5]. Fetal development affected by lead exposure such as impediment in the embryonic development of various organ systems, including retardation of cognitive development in early childhood [3,5]. Lead provided by maternal transfer during pregnancy is an important contribution to the infant's lead load [5,6]. First it's absorbed from the gastrointestinal tract or the respiratory system, after that it is transported bound to erythrocytes and then further accumulates in bone. Half-life of lead is approximately 30 years [6,7]. Even if the blood lead level (BLL) is between 5-10 mg/dl behavior and academic performance of children can be adversely affected [7]. Pregnancy is a most critical time for revelation to lead for both the mother as well as fetus [6]. Most countries have reduced exposure to lead in recent years by using the removal of lead from water pipes, paint, and food cans, and lead-free petrol [8]. Exposure of lead is directly associated with an increased incidence of premature rupture of the membranes and pre-term delivery [9]. Some of minor congenital anomalies have been reported to be positively correlated with umbilical cord blood lead concentration [4,10]. Heme synthetase is one of an enzyme in the heme biosynthetic pathway, which is responsible for the incorporation of iron into the protoporphyrin ring is inhibited by lead can result in anemia [6,11]. World Health Organization (WHO) states low birth weight (LBW) defined as a weight <2,500 g has become a global disease burden [12]. The prevalence of LBW infants has shown distinct geographic pattern, with 25% in India, 7.6% in the United States, and between 5.9-11.8% in China [13,14]. This is also a leading cause of morbidity and mortality in the neonatal period, both in developing and developed countries [15]. Over the past few years has led to increasing concern related to the health effects of environmental pollution due to the rise in industrialization and urbanization throughout the world.

Materials and Methods

This cross-sectional study was performed between June 2013 to July 2014 King George's Medical University, Lucknow Uttar Padesh, India. Subject were fully informed with previous informed consent was taken at the time of delivery or prior to giving birth. Inclusion criteria for study group were age between 20 to 40 years, exposure to lead (Pb) more than five years, BMI less 25 and subject having not any systemic disease. Subject who did not met the definitive inclusion criteria were excluded from the study. Recruited subject were explained about the study protocol. Umbilical cord blood and maternal blood samples were obtained from 110 subjects. Detailed history of occupational exposure to Pb, hypertensive disorders and other socioeconomic status were taken during pregnancy.

Questionnaire

The subjects were interviewed at the time of enrollment and the questionnaire was used to collect detailed history on socioeconomic status as well as demographic parameters. Health status like (drugs using during pregnancy, anemic, any other chronic disease and mode of Pb exposure, lead ceramics, lead pipes heating system in home, the battery exposure, paints used by women, near factory cities.

Estimation of Lead (Pb) in Maternal and Cord blood:

Blood samples for Pb estimation were analyzed via inductively coupled plasma mass spectrometry (ICP-MS) based on atomic

absorption furnace in both the groups (maternal blood as well as in cord blood), in the department of Biochemistry, King George's Medical University, Lucknow. The lowest limit of quantitative (LLOQ) in umbilical cord blood was 0.03ul. Umbilical Cord blood with the maternal blood (5-10 ml) were obtained at the time of delivery. Both the blood samples for Pb measurement were collected in EDTA (ethylene diamine tetra acetic acid) tube as the anti-coagulant & stored at (-200C) until analyzed.

Statistical analysis:

Data has been presented as the mean ± SD and values were represented in number (%) of all the observations. All the analyses were performed on SPSS (version 15.0) statistical analysis software. The values from the two groups of subjects were compared by independent students "t" test. Non-parametric alternative Mann-Whitney U test was also applied where the data was not normal or heterogeneous.

Result:

Total 110 pregnant women had lead measurement. The age distribution of the 110 subjects with their socio-demographic parameters is presented in Table 1. All characteristics such as Age, BMI, Gastric age SBP, DBP, Blood lead level Hb, shows no significant correlation were found as P>0.05 in all parameter. Lead (Pb) levels of pregnant women presentation are summarized in Table 2. The mean lead Pb level in pregnant women was found significantly (p<0.001) different and exceptionally higher as compared to cord blood lead (Pb) level of subjects. Table2 also demonstrate correlation between maternal blood lead and cord blood lead with their feto-maternal outcome. Subjects with hypertensive disorder (Preeclampsia) the mean Pb level 3.979±1.335higher in maternal blood as compared to cord blood mean 3.634±0.941& found to be significant P<0.05 similarly cord blood lead levels of subjects with hypertensive disorders was significantly higher than normotensives p<0.05. Same as subject with pretermed delivery defined as birth before the 37th week of pregnancy mean 2.899± 1.168 in maternal blood lead level was slightly higher as compared to cord blood 2.411±1.044. Subject with preterm delivery had lower maternal BLL as compared to those who delivered at full term and not found to be statistically significant p<0.05 .Cord blood lead levels of subjects who delivered preterm babies was found to be lower than those who delivered at full term and this difference was found to be statistically significant p<0.05. Only 11(10%) mothers were found to be IUGR. In IUGR, maternal and cord BLL was lower than Non-IUGR mother and these were statistically significant. Maternal BLL of subjects delivering low birth weight babies (less than 2.5 Kg) was found to be lower as compared to healthy babies and these difference was not found to be statistically significant p>0.05. In contrast to this Cord blood lead levels of subjects with low birth weight (less than 2.5 Kg) was found to be higher than healthy born subjects and this difference were not found statistically significant p>0.05. The maternal BLL of subjects with APGAR score ≤7at birth was found to be higher than those with APGAR ≥7but these difference was not found to be statistically significant p>0.05, whereas cord blood lead levels of subjects with APGAR Score ≤7 at birth was found to be higher than those with APGAR Score ≥ 7and difference between these two was not statistically significant p>0.05.

Table 1: Demographic and biochemical parameters (Mean ± SD) of two groups

Characteristics	Maternal Subjects with blood lead (Pb) levels	Maternal Subjects with Cord blood lead (Pb) levels	p –Value
Age (yrs)	38.16 ± 6.82	38.34 ± 7.98	0.887
Height (cm)	163.56 ± 5.20	163.94 ± 6.31	0.701
Weight (kg)	65.26 ± 6.18	63.15 ± 8.09	0.091
BMI (kg/m^2)	24.82 ± 2.34	24.41 ± 2.26	0.306
Gestation age ≤34 weeks	3.104± 1.114	2.637±0.921	0.628
SBP (mmHg)	122± 1.29	120±2.13	0.231
DBP (mmHg)	83±3.17	80± 2.14	0.134
Blood lead level (mg/dl)	3.172±1.219	2.684±0.995	0.705
Hemoglobin (%)	11±2.10	12±101	0.217

Data are represented as mean, ±SD. SD=Standard deviation

Table 2: Correlation between maternal and Cord blood lead levels with fetomaternal outcome

Parameters	No. of Subjects	Maternal blood lead (Pb) levels (3.172±1.219)	p-value	Cord Blood lead (Pb) levels (2.684±0.995)	p-value
Hypertensive Disorders (Preeclampsia Eclampsia)	19	3.979±1.335	0.038*	3.634±0.941	0.002*
Preterm delivery	35	2.899±1.168	0.108	2.411±1.044	0.048*
IUGR	11	3.373±1.340	0.567	2.955±1.149	0.345
Baby Sex Male	11	3.373±1.340	0.567	2.955±1.149	0.345
Female	99	3.150±1.210		2.654±0.979	
Low Birth weight(≤2.5Kg)	37	3.126±1.174	0.779	2.744±1.074	0.655
APGAR at birth ≤7(n=105)	50	3.417±1.350	0.079	2.853±1.111	0.139

*= Significant (p= <0.05), Data are represented as mean, ± SD (Standard deviation)

Discussion:

Foetus depends on mother for its requirement and developments. The transfer of the nutrients takes place through the placenta [16]. Apart from these nutrients and oxygen, foetus is also exposed to toxic substances and other unwanted substances present in the maternal blood [17,18]. Lead (Pb) crosses the placenta as early as 12th weeks of gestation and total lead contents in foetal tissues increase throughout pregnancy suggesting that infants are exposed in utero to blood levels in proportion to those of mother [18,19]. The aim of this study to find out the maternal and cord blood lead levels and its correlation with fetomaternal outcome [19]. The main diseases end points considered in this analysis are low birth weight and preterm vaginal deliveries in foetus and hypertensive disorders, anemia and other complication during delivery [19, 20]. There were significant correlation between maternal blood and cord blood lead level (CBLL).The umbilical cord blood lead levels correlated significantly with maternal blood lead levels (MBLL) and lower gestation age [19, 21, 22]. Maternal blood lead level were found to be higher among ≥30 years age group subjects while cord blood lead levels came to be higher among 26-30 years age group subjects, this relation did not came out to be statistically significant. The blood lead levels in pregnant women in urban slums of Lucknow were found to be higher. The means of BLL was 2.2 µg/dl among women living in inner city of neighborhood near heavy vehicular traffic, than those who are living in other neighborhood [23]. The cadmium content in maternal and newborn hair and association with parity, birth weight and hypertension was studied then found higher lead level in mothers with parity three or greater [24]. A significant association between low level lead exposure and elevation in maternal blood pressure during labour and delivery can be observed at umbilical cord blood levels ≤ 2µg/dl [25]. The prevalence of gestational hypertension has been shown to be increased even at blood lead levels lower than 5µg/dl [26]. The women with BLL ≥ 102µg/dl were at fourfold increased risk for having a small for date (SGA) infant [27]. The evidences for lead (Pb) effect on critical period of development and latency of the manifestation of the effect [28]. In the study of body lead burden and pregnancy outcome, there was strong positive association between higher blood lead levels and preterm vaginal deliveries [29]. The impact of elevated prenatal blood leads on trace elementsin occupational non exposed women were found hypertension, malaria and low birth weight were significantly higher in women with elevated blood lead (p<0.05) than in those with low blood levels [30]. Thus the impact of CBLLs on the birth weight of baby demands further research to determine the magnitude of effect.

Conclusion:

To our knowledge in this study the base line lead (Pb) levels in maternal blood lies below 5µg/dl.The 7.2% of mothers and 1.7% babies are having lead levels ≥5µg/ dl, which were crossing the CDC intervention level for lead concentration. The Pb level is higher in rural areas and among vegetarian, lower socioeconomic status, pipe water as source of drinking water, primiparous female, of age group ≥ 21- 30

years. Higher maternal and cord blood Pb level was also significantly associated with among babies with weight ≤2 kg as well as in female with gestation of age group ≤ 34 weeks. Higher lead concentration was found associated with adverse pregnancy outcomes like preterm deliveries, hypertension and low birth weight but the association was not statistically significant. The impact of lead exposure on feto-maternal outcome demands further research to determine the magnitude of the effect.

Conflict of interest:
The authors have no conflict of interests in this article.

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