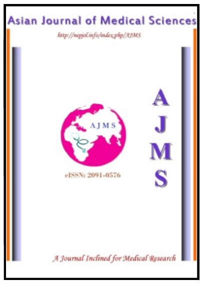
Asian Journal of Medical Sciences 1 (2010) 32-36

ASIAN JOURNAL OF MEDICAL SCIENCES



Placental Lead and its Interaction with Some Essential Metals among Women from Lucknow, India

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Abstract

Objective: The placenta connects and separates two genetically distinct individuals: the mother and the fetus. There is no placental-fetal barrier blocking lead transport, placing the fetus at high risk from lead exposure. The placenta has been investigated as a possible indicator of environmental exposures. Recent studies have been focused on the interaction between toxic and essential metals in placenta as there is little information on the levels of lead and essential metals in human placental tissue in Indian scenario.

Material & Methods: The present study was designed to determine the status of lead and some essential metals in placental tissue of women residing in and around, Lucknow, India. Sixty pregnant women attending the local maternity home in the city were recruited to determine the concentrations of lead (toxic metal) and zinc, copper, iron & calcium (essential metals) using atomic absorption spectrophotometry.

Results: The mean±SD levels of placental lead was 0.35 ± 0.30µg/g which is lower than those reported in Australia (0.56µg/g) & Poland (0.50µg/g), and slightly higher than Spain (0.11µg/g). The mean ± SD (range) of placental zinc, copper, iron & calcium was found to be 7.67± 2.99 µg/g (0.47-13.75), 1.03 ± 0.55 µg/g (0.49-3.41), 76.42 ± 20.13 µg/g (17.67-135.25), 90.46 ± 112.47 µg/g (1.77-420.5) respectively. On the basis of parity, placental lead level was significantly higher ($p<0.05$), while copper and zinc were significantly lower ($p<0.05$, $p<0.01$ respectively) in multiparous cases as compared to nulliparous. Placental lead levels had significant negative correlation with zinc levels ($r= -0.35$, $p<0.05$).

Conclusion: The results suggested that increased lead level affect the essential metal level and its level increased with parity whereas, there was a depletion of maternal stores of essential elements (Zn, Cu, Fe and Ca) with increasing parity.

Key Words: Placenta; Lead; Essential metals; parity; Atomic Absorption Spectrometer

1. Introduction

Human placenta serves as a model to monitor the internal environment of the fetus and also that of the external environment of the mother. It functions as the means by which all necessary nutrients are delivered to the fetus, as well as a barrier to prevent passage to toxic substances, including metals.[1] If the later is accomplished by binding of the metals to the placenta, it may interfere with placental function, in particular the transport of essential trace elements required for fetal growth and development.[2,3] In case of toxic metals, placental tissue can be regarded as a dual biomarker to assess maternal and fetal health. There is no placental-fetal barrier blocking lead transport, maternal and fetal blood lead levels are almost identical, placing the fetus at high risk from lead exposure.[4] Environmental pollution is generally considered to be the main contributor to the body burden of heavy metals.[5-7] Heavy metal pollution of an environment, particularly with lead results in the accumulation of this element in human

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tissues.[7] Silbergeld et al. (2000) pointed to the particular relevance of transplacental exposure to lead and the increase risk of cancer in later life.[8] Major sources of environmental lead exposure are leaded gasoline, leaded pipes for water supply, lead based paints, use of lead ceramics, and lead in cosmetics and folk remedies.[9] The accumulation of lead in pregnant women depends on the women's exposure to lead from industrial and environment pollution. It is clear that a biomarker of prenatal lead exposure to this important environmental toxicant is required for assessing the risks of adverse health effects and for identifying potentially vulnerable groups. Different authors have proposed the placenta as a biomarker that could be taken as an alternative to repeated to maternal blood sampling for assessing lead exposure in utero.[10,11] Based on this information, present study, the first of its kind from India was designed to determine the status of placental lead (Pb) and essential metals (Zn, Cu, Fe and Ca) and also the interaction of lead with essential metals in placental tissue of women from Lucknow, India.

2. Material and Methods

2.1. Selection of subjects

The present study is based on the results from 60 women whose placentas were analyzed for metal concentrations. Pregnant women enrolled in the study, were drawn from Lucknow, the capital of most populous state, Uttar Pradesh in India and nearby areas attending the local maternity homes in the city. All the placentas were from healthy pregnant women who gave birth to single healthy babies. All the pregnant women had given informed consent and were interviewed before delivery, to ascertain maternal age, education, occupation, residential area (rural/urban), socioeconomic status, dietary habit, parity, gestational age, reproductive history, and past diseases. Information from their obstetrical medical records was also available. All the placentas from healthy pregnant women aged between 20-40yrs were included in the study and women suffering from chronic diseases were excluded from this study. Both the nutritional status of the mothers and their eating habit were judged as normal. Neonatal birth weight and gender were also recorded. None of the women lived close to an industrial source of lead emission or reported accidental /occupational exposure to lead. Lead detected in placental tissue was from contamination of food chain and /or environmental pollution. The Institutional Human Ethics committee of Industrial Toxicology Research Centre, Lucknow (India), approved the study.

2.2. Collection of placental samples and processing

Placental tissue was collected during parturition. We selected mainly trophoblastic placental tissue with no signs of calcification, avoiding the decidua basalis and chorionic plate in accordance with other recent studies.[1, 12]. Falcon et al. (2003) found no significant differences in the metal concentration of different trophoblastic zones analyzed from the same placenta.[13] Approximately 25g of placental tissue taken from each subjects were collected in wide-mouthed contamination free containers as coded samples. They were transported to Department of Analytical Toxicology, Industrial Toxicology Research Centre (ITRC), Lucknow immediately after collection for metal analysis. Person analyzing the metals was totally blind as to the case history of the subjects.

2.3. Analysis of metals

Lead , copper, zinc, calcium and iron in trophoblastic placental tissue were analyzed by Flame atomic absorption spectrometer (Varian SpectraAA 250+) using hollow cathode lamps (283.3nm ,324.7nm, 213.9nm, 422.7nm, and 248.3nm for lead, copper, zinc, calcium and iron, respectively). The instrument was calibrated using aqueous standards of 1.0, 3.0, 5.0, and 7.0 mg/ml for lead , 0.5, 1.0, 1.5, and 2.0mg/ml for copper, 0.2, 0.4, 0.8, and 1.2 mg/ml for zinc, 1.0, 3.0, 5.0, and 10.0mg/ml for calcium, 2.0, 4.0, 6.0, 8.0, and 10.0mg/ml for iron. Detection limits were 0.01mg/ml for lead, 0.05mg/ml for copper, 0.01mg/ml for zinc, 0.08mg/ml for calcium and 0.09mg/ml for iron. One gram of placental tissue in a 50 ml Erlenmeyer flask was digested at 120 ºC-150 ºC with conc. nitric acid till a clear solution was obtained, approximately 2h, quantitatively transferred to a 10 ml volumetric flask and made up to volume with deionized water. A blank sample was also prepared with each set of samples in order to control possible metal contamination by external sources.

The accuracy of the method for metal estimation was further controlled by participation in an inter laboratory quality-assurance programme (ITRC, Lucknow) wherein coded samples were analyzed regularly and results scrutinized by the quality manager. Further, a quality check sample was always run with each set of samples for lead analysis to maintain accuracy.

2.4. Statistical evaluation

Two groups of pregnant women (nulliparous and multiparous) were compared by using student's t-test (Table-3). Linear regression analysis was performed to determine the strength of relationship between placental lead levels and essential metal levels (Figure-1).

3. Results

The demographic data of the subjects are presented in Table.1.The mean age of participating mothers was 26.2±3.27 years. There were 62% multiparous and 38% nulliparous women (no previous children) in this study. Sixty eight percent (68%) cases were drawn from urban areas in and around Lucknow. None of the women lived closed to an industrial source of lead emission or reported accidental or occupational exposure to heavy metals.

Table-1: Characteristics of the pregnant women

Variables	No. (%)
Age in year (Range)	26.2 ± 3.27 (20-35)
Parity	
Nulliparous	23(38. 33)
Multiparous	37(61.66)
Dietary habit	
Vegetarian	8(13. 4)
Non-vegetarian	52 (86.6)
***Abode**	
Rural	20(33.3)
Urban	40(66.4)
Socioeconomic status	
High	2(3.3)
Middle	42(70.0)
Low	16(26.7)
Child gender	
Male	40(66.6)
Female	20(33.4)
Child weight (Kg)	2.77±0.31

*Abode: It was decided as rural or urban depending on the majority of time of stay in the past 30 years.
Values represented Mean ± SD or No. of subjects (%)

The concentrations of lead and essential metals in placentas are summarized in Table 2.

Table-2: Levels of lead and some essential metals in placenta of women

Metals	Mean	Median	SD	Range
Pb	0.35	0.3	0.30	0-1.2
Cu	1.03	1.06	0.55	0.49-3.41
Zn	7.67	7.55	2.99	0.47-13.75
Fe	76.42	75.25	20.13	17.67-135.25
Ca	90.46	23.9	112.47	1.77-420.5

Results are in µg/g, wet weight basis

Placental lead was found (mean,0.35 mg/g; S.D. 0.30;median 0.30;range 0-1.2) whereas in case of essential metals zinc (mean,7.67 mg/g; S.D. 2.99; median 7.55;range 0.47-13.75) copper (mean,1.03 mg/g; S.D. 0.55;median 1.06; range 0.49-3.41), iron (mean,76.42 mg/g; S.D. 20.13; median 75.25; range 17.67-135.25) and calcium (mean,90.46 mg/g; S.D. 112.47; median 23.9; range 1.77-420.5) was found in the placental tissue of the women. Placental lead was significantly higher in multiparous women when compared with nulliparous women (0.40 ± 0.30 vs. 0.27 ± 0.28) ($p<0.05$), whereas copper and zinc levels were significantly higher in nulliparous group as compared to multiparous group (1.24 ± 0.64 vs. 0.91 ± 0.45 and 9.04 ± 2.95 vs. 6.82 ± 2.72 respectively) ($p<0.01$ each) (Table 3).

Table 3: Comparison of lead and some essential metals between the nulliparous and multiparous women

Metals	Nulliparous n=23	Multiparous n=37	p-value
Pb	0.27 ± 0.28	0.40 ± 0.30	< 0.05
Cu	1.24 ± 0.64	0.91 ± 0.45	< 0.01
Zn	9.04 ± 2.95	6.82 ± 2.72	< 0.01
Fe	80.14 ± 20.56	74.10 ± 19.79	NS
Ca	102.98 ± 131.23	82.69± 100.22	NS

*Results are in µg/g, wet weight basis

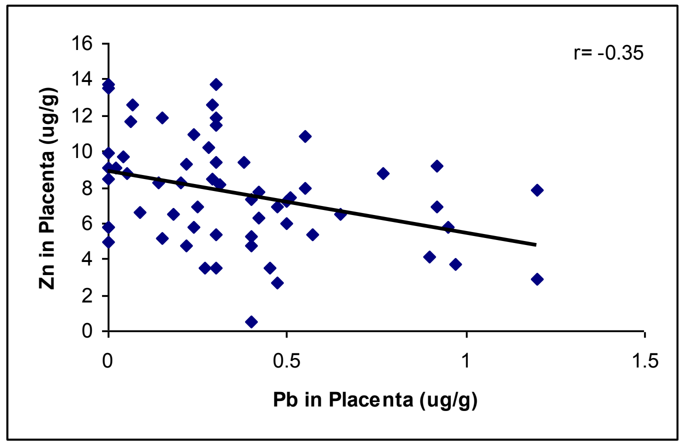

Figure-1: Correlation between the concentration of Pb and Zn in Placental tissue of the women

Placental lead had significant negative correlation with zinc (r= -0.35, $p<0.05$) (Figure 1). However, this was not in case of copper, iron and calcium.

4. Discussion

The placenta is an organ formed by the fusion of maternally and embryonically derived tissue inside the uterus facilitating contact with the maternal compartment.[14] Toxic and/or foreign compounds may interfere with placental function at many levels, e.g. signaling, production and release of hormones and enzymes, transport of nutrients and waste products, implantation, cellular growth and maturation, and finally, at the terminal phase of placental life, i.e. delivery. Therefore, any deviation from normal development may constitute a potential threat to placental function, resulting in preterm delivery, congenital malformation, or abortion. Iyengar (2001) suggested that, if the toxic metal concentrations in placental tissue are high, this information could be used to diminish postnatal exposure of the fetus or maternal exposure during subsequent pregnancies.[11,14] However, it is well-known that the placenta does have a substantial reserve capacity which may modulate some of these toxic effects.

The influence of environmental pollution on pregnant women is of special interest and much attention has been paid to investigation of heavy metals such as lead that is transferred from mother to developing fetus, and to their influence on pregnancy outcome and fetal development.[15,16] Baranowska (1995) suggests that passage of lead through the placenta may be the main cause of fetal intoxication.[7] In the present study, mean level of placental lead was 0.35±0.30μg/g, which was slightly lower than those reported in Australia (0.56μg/g) 17 & Poland (0.50μg/g) 7and higher than Spain (0.11μg/g).[13] The placental lead levels reported in these countries were on dry tissue weight basis while in the present study lead level was estimated on wet tissue weight basis.

It is well established that maternal exposure to heavy metals may cause placental damage and change the transportation of essential trace metals to the fetus.[18, 19] A low status of essential elements may increase the risk of toxic effects of such as lead.[20] Recent studies have focused on the distribution of some toxic metals such as lead and its interaction with essential elements in animals and humans as such interactions might have adaptive implications to environmental pollution.[21] In the present study, inverse correlation was found between lead and zinc that is in accordance with previous observations.[22, 23] During pregnancy, trace elements are indispensable for life maintenance not only for the mother but also for the developing fetus.[24] The placenta has a storage function, during the first few months of pregnancy it accumulates calcium and iron to be used in the later months for fetal growth.[11,14] Zinc and copper are transferred more readily through the placenta to the fetus.[25] Zinc may act as a positive marker or even an enzymatic enhancement for the human placental vital functions. Placental zinc and calcium decreased with parity, indicating that the amount of those elements is not restored before the next pregnancy.[1] According to Kantola et al. (2000) parity affects the zinc and copper contents in placenta.[26] Osman et al. (2000) suggested that there is depletion of maternal stores of essential elements with increasing parity.[1] Akesson et al. (1998) also reported decreasing iron status with parity.[27] Similarly, in the present study there was significant depletion of copper and zinc levels with increasing the parity and supporting the findings of previous studies. Furthermore, in the present study, higher level of placental lead was also found in the multiparous women. Therefore, it may be anticipated that with increasing parity elevated lead levels and concomitant depletion of maternal stores of essential elements, implying a risk for inadequate fulfillment of the requirements of fetus.

Acknowledgements

Authors express their sincere thanks to Mrs. Poonam Saxena for her help in metal estimation. One of the authors (Jyoti) gratefully acknowledges the financial support provided by the University Grants Commission, Government of India.

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