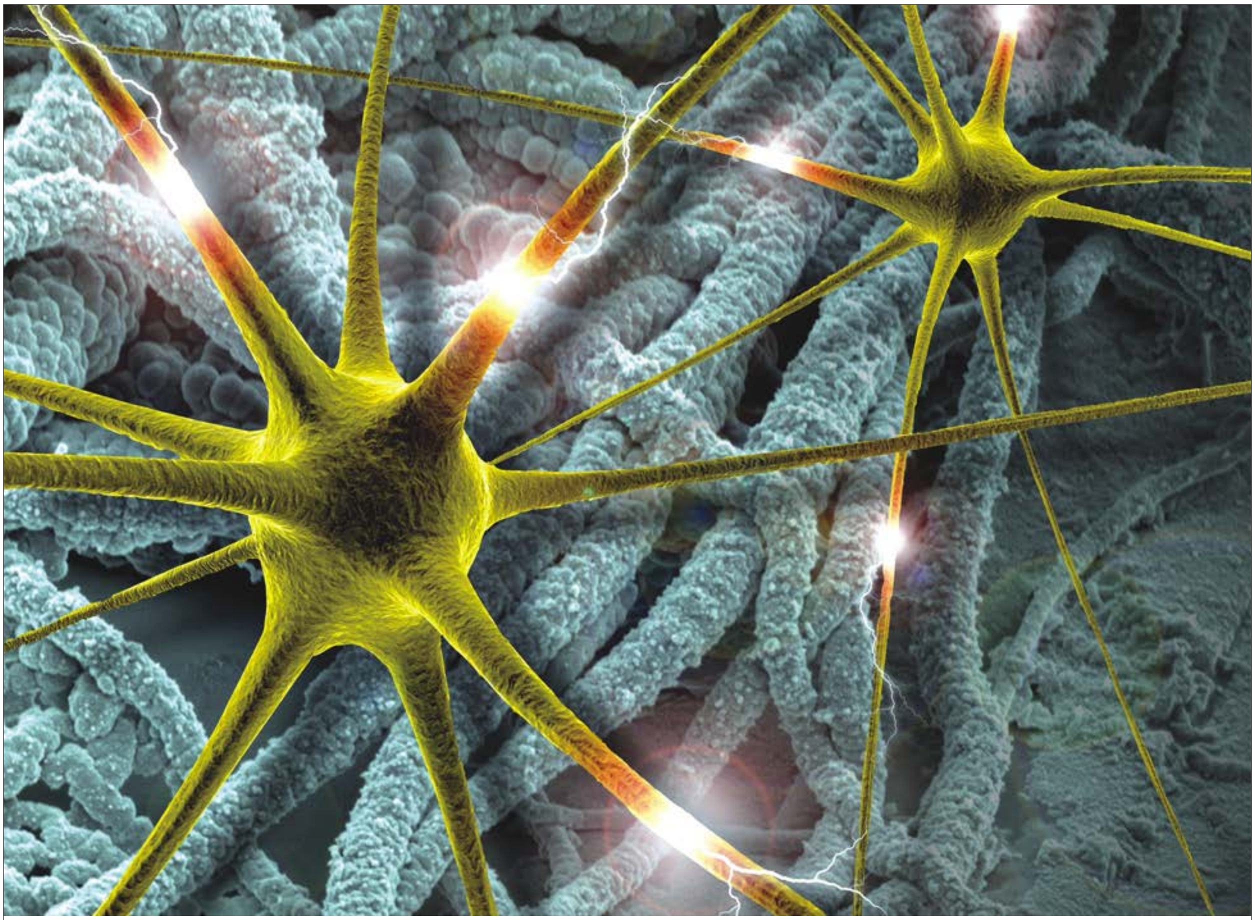

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# Correlation between Blood Lead Levels in the Pregnant Women and Infant Mental Development in Damietta Governorate

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## ABSTRACT

The impact of prenatal lead exposure on neurodevelopment may be associated with poor intellectual development in children. Aim of the study was to detect the correlation between lead levels in the pregnant women and infant mental development. One hundred pregnant women living at industrial zone of Damietta governorate were included as the study group. In addition, twenty apparently healthy pregnant volunteers, who living at non-industrial zone were included as a control group. All subjects were submitted to full medical history, clinical examination and maternal blood lead levels were measured during first, second and third trimesters. In addition, modified Bayley Scales of infant development and Electroencephalography (EEG) were conducted. Finally, lead levels were measured at umbilical cord blood at delivery and in offspring at 12 and 24 months of age. There was significant difference in maternal lead levels which were higher in the first-trimester and was correlated with infant cord blood lead levels and in infant blood lead at 24 months. In addition, there was a statistically significant difference in all infant cases in the studied group in a comparison to a control group at 12 months and at 24 months on EEG. There was a correlation between maternal plasma lead levels and poor Mental Development Index (MDI) scores in their offspring.

**Key words:** Lead, pregnancy, mental development

## INTRODUCTION

Different international studies encourage their countries to progressively reduce amount of lead exposure, due to its detrimental effect on child neurodevelopment (Lanphear *et al.*, 2005).

Since 1991, the U.S. Centers for Disease Control and Prevention (CDC) has considered values $\leq$10 μg $dL^{-1}$ (0.48 μmol $L^{-1}$) as the maximum allowable pediatric blood lead level (CDC., 1991). On the other hand, more recent research (Canfield *et al.*, 2003) and pooled analyses of seven prospective studies (Lanphear *et al.*, 2005) considered further reduction in this level.

The extent to which prenatal lead exposure may produce adverse outcomes gained attention. The substantial fetal lead exposure can occur from mobilization of maternal skeletal lead stores which in turn, can persist many years after external lead exposure has declined (Gulson *et al.*, 2003; Hu and Hernandez-Avila, 2002).

In addition, some studies have shown an inverse association between prenatal lead exposure and infant neurodevelopment (Shen *et al.*, 1998) and some has not (McMichael *et al.*, 1988).

Furthermore, some studies reported that, the detrimental effect on neurodevelopment was declined over subsequent years (Bellinger *et al*., 1992; Dietrich *et al*., 1991), while others reported a stable effect over time (Wasserman *et al*., 2010).

The experimental literature showed that, vulnerability of developing organ systems, including the brain to environmental toxicants can vary widely over the course of pregnancy. Lead exposure may be neurotoxic during a specific trimester (Mendola *et al*., 2002).

In terms of fetal exposure, ~ 1% of whole blood lead level can cross to the placenta (free lead), as 99% of blood lead levels are bound to Red Blood Cells (RBCs) (Goyer, 1990).

The objective of the present study was to detect relation between lead levels in pregnant women and infant mental development in Damietta Governorate from 1st of April 2010 to 1st of December 2012.

## MATERIALS AND METHODS

One hundred pregnant females, presented in their antenatal visit during first, second or third trimesters were included. They were recruited between 1st of April 2010 to 1st of December 2012. All mothers were informed about the study; those who agreed to participate, read and signed an informed consent. They were followed to delivery. Their offspring were evaluated at delivery, at 12 and 24 months of age. In addition, twenty healthy pregnant volunteers were included as a control group.

**Inclusion criteria:**

- Pregnant females living an industrial zone of Damietta Governorate for at least the last 6 months (study group)
- Pregnant females, matched for age and duration of pregnancy, living in non-industrial area of Damietta Governorate
- Give birth to full term neonate (≥37 weeks of gestation)

**Exclusion criteria:** Women who have any of the following were excluded:

- Women plan to leave the area in the following 5 years
- Women with a psychiatric disorder
- Women with daily consumption of alcoholic beverages
- Women with addiction to illegal drugs
- Continuous use of prescription drugs
- Diagnosis of high-risk pregnancy
- Renal or circulatory disease (for example hypertension, or gestational diabetes)
- Suffering from seizures that required medical treatment
- Being pregnant with >14 weeks of gestation

Demographic data and full medical history was obtained from all participants. Special stress was done on residency, levels of education, maternal Intelligent Quotient (IQ) and regular use of iron and calcium supplementation during current pregnancy. Clinical examination was directed for both mothers and their offspring. Sex of infant, type of feeding, Modified bayley scales of infant development (Moore *et al*., 2008) and Electroencephalography (EEG) were documented for all participants. Finally, lead levels in the maternal plasma during each trimester and umbilical cord blood lead levels were measured at delivery, then fetal plasma lead at 12 and 24 months of age.

**Maternal blood and plasma lead measurement:** Blood samples were collected during each prenatal visit of the mothers. Visits were scheduled at 12, 24 and 36 weeks of pregnancy. Subjects were instructed to fast overnight before sampling. Each subject's arm was washed with water and disinfected with alcohol. Then, 10 cc of venous blood were collected into a polyethylene tube containing sodium heparin. All samples were analyzed, using inductively coupled of an atomic absorption spectrometry (AAS)-Varian Spectra AA300/400: Graphite-furnace mode (Hernandez-Avila *et al.*, 1998; Smith *et al.*, 1998).

Potential contamination by lead from hemolyzed red cells was assessed by measuring levels of plasma iron and free hemoglobin (Smith *et al.*, 1998).

**Children's blood lead measurement:** One milliliter umbilical cord and infant venous blood samples at 12 and 24 months of venous blood were collected into trace metal-free tubes containing sodium heparin and stored at -20°C until analysis of lead.

**Measurement of child mental development:** Infant's development at 24 months was assessed by trained personnel using a modified Bayley Scales of Infant Development®-Second Edition (BSID®-II) II-Spanish version (BSID-IIS) (translated to Arabic) (Moore *et al.*, 2008). This test includes:

- **Mental scale:** Evaluates sensory/perceptual acuities, discriminations, acquisition of object constancy, memory, learning, vocalization, early verbal communication and abstract thinking, habituation, mental mapping, complex language and mathematical concept formation
- **Motor scale:** Evaluates degree of body control, co-ordination of large muscles, fine manipulation skills, dynamic movement, postural imitation and stereognosis
- **Behavior rating scale:** Measures attention, arousal, orientation and engagement, emotional regulation and motor quality

**Statistical analysis:** The collected data was organized, tabulated and statistically analyzed by using STATA (STATA Statistical Software, release 8.0; Stata Corp, College Station, TX, USA). Quantitative data was expressed as Mean±Standard Deviation (SD), while qualitative (categorical) data was expressed as relative frequency and percent distribution. Height and weight data was transformed into Z-scores by using World Health Organization (WHO)/National Center for Health Statistics/CDC reference data (WHO., 1979) and interpreted as indices of a child's nutritional status. Variables considered to be potential confounders based on biologic plausibility, regardless of statistical significance and those significantly associated with MDI scores in bivariate analyses was included in multiple linear regression models; given these criteria, confounders included were child's sex, blood lead at 24 months of age, height for age z-score and weight, as well as maternal age and intelligence quotient. Regression diagnostics were performed on all models to evaluate multicollinearity, distributional assumptions on the error term and potentially influential data points. When the latter was detected, the new models were fit excluding these observations. $p\text{-value} \leq 0.05$ was considered significant.

## RESULTS

**Demographic data:** In the present study, there was no statistically significant difference between maternal cases and control as regard demographics, except significant increase of iron and calcium supplementation in control group when compared to study group (65% vs. 20%, respectively). In addition, there was significant decrease of maternal and infant hemoglobin in study group when compared to control group (Table 1).

**Maternal clinical data:** In the present study, there was no significant difference between maternal study and control group as regard to clinical data (Table 2).

**Bayley scales of infant development:** As regard mental scale, there was significant increase of sensory/perceptual acuities, memory, learning and problem solving, vocalization and early verbal communication abstract thinking in control group when compared to study group (Table 3).

Regarding motor scale, there was significant increase of degree of body control, co-ordination of large muscles, fine manipulation skills and dynamic movement in control group when compared to study group. In addition, there was no significant difference by using behavior rating scale between study and control group (Table 3).

**Laboratory data:** As regard plasma lead levels, there was statistically significant increase of plasma lead levels in study group when compared to control group in both maternal and infant

Table 1: Comparison between maternal, infant cases and controls as regard demographic data

| | Maternal (120) | | | Infants (120) | | |
|---|---|---|---|---|---|---|
| Parameters | Cases (100) | Control (20) | p-value | Cases (100) | Control (20) | p-value |
| **Sex** | | | | | | |
| Male | - | - | | 38 (38) | 9 (45) | 0.55ns |
| Female | 100 (100.0) | 20 (100) | | 62 (62) | 11(55) | |
| Age in years (Mean±SD) | 24.12±1.96 | 23.35±1.89 | 0.11ns | | | |
| Weight (Mean±SD) in kg | 71.82±3.43 | 70.85±3.09 | 0.24ns | | | |
| **Types of infant feeding** | | | | | | |
| Breast feeding | - | - | | 80 (80.0) | 19 (95.0) | 0.11ns |
| Bottle feeding | - | - | | 20 (20.0) | 1 (5.0) | |
| Using of Ca and Fe supplementation | 20 (20.0) | 13 (65.0) | <0.001* | - | - | |
| **Levels of maternal education** | | | | | | |
| Higher | 20 (20.0) | 6 (30.0) | 0.32ns | - | - | |
| Mid or low | 80 (80.0) | 14 (70.0) | | - | - | |
| **Residence** | | | | | | |
| Rural | 15 (15.0) | 5 (25.0) | 0.27ns | - | - | |
| Urban | 85 (85.0) | 15 (75.0) | | - | - | |
| Height (cm) | 167.83±2.3 | 166.95±2.5 | 0.13ns | | | |
| BMI (kg $m^{-2}$) | 24.17±0.54 | 24.12±0.43 | 0.69ns | | | |
| Maternal IQ | 78.45±4.98 | 80.10±5.48 | 0.19ns | | | |
| Hemoglobin (g $dL^{-1}$) | 10.80±0.74 | 11.58±0.92 | <0.001* | 11.98±0.79 | 12.92±0.95 | <0.001* |
| Smoking (active or passive) | 10 (10) | 1 (5.0) | 0.47ns | 10 (10.0) | 1 (5.0.0) | 0.47ns |

Data is Mean±SD. The values in parenthesis showing percentage results, ns: Not significant, *Significant at p≤0.05

Table 2: Clinical data of the maternal cases (n = 100)

| Parameters | Study group 100 | Control group 20 | p-value |
|---|---|---|---|
| Systolic blood pressure (Mean±SD) | 120.40±5.10 | 120.75±6.12 | 0.78ns |
| Diastolic blood pressure (Mean±SD) | 78.20±4.79 | 77.0±5.93 | 0.32ns |
| Respiratory rate (cycle $min^{-1}$) | 18.32±1.06 | 18.63±1.61 | 0.33ns |
| Heart rate (beats $min^{-1}$) | 85.10±1.70 | 83.23±6.04 | 0.12ns |
| Proteinurea | 4 (4.0%) | 1 (5.0%) | 0.83ns |
| Lower limb edema | 10 (10.0%) | 1 (5.0%) | 0.47ns |

Data is Mean±SD. The values in parenthesis showing percentage results, ns: Not significant

Table 3: Clinical data evaluation of Bayley Scales of Infant Development (n = 120)

| | Cases (100) | | Control (20) | | |
|---|---|---|---|---|---|
| | Positive | | Positive | | |
| Parameters | No. | % | No. | % | p-value |
| **Mental scale** | | | | | |
| Sensory/perceptual acuities | 50 | 50 | 17 | 85 | 0.004* |
| Discriminations | 60 | 60 | 15 | 75 | 0.21ns |
| Acquisition of object constancy | 80 | 80 | 19 | 95 | 0.11ns |
| Memory | 20 | 20 | 10 | 50 | 0.005* |
| Learning and problem-solving | 20 | 20 | 10 | 50 | 0.005* |
| Vocalization | 80 | 80 | 20 | 100 | 0.028* |
| Early verbal communication abstract thinking | 70 | 70 | 18 | 90 | 0.05* |
| Habituation | 60 | 60 | 11 | 55 | 0.67ns |
| Mental mapping | 30 | 30 | 9 | 45 | 0.19ns |
| Mathematical concept formation | 65 | 65 | 16 | 80 | 0.19ns |
| Complex language | 75 | 75 | 15 | 75 | 1.0ns |
| **Motor scale** | | | | | |
| Degree of body control | 50 | 50 | 18 | 90 | 0.001* |
| Co-ordination of large muscles | 63 | 63 | 18 | 90 | 0.019* |
| Fine manipulation skills | 30 | 30 | 14 | 70 | 0.001* |
| Dynamic movement | 69 | 69 | 18 | 90 | 0.043* |
| Postural imitation | 70 | 70 | 16 | 80 | 0.36ns |
| Stereognosis | 50 | 50 | 14 | 70 | 0.10ns |
| **Behaviors rating scale** | | | | | |
| Attention | 70 | 70 | 17 | 85 | 0.17ns |
| Arousal | 60 | 60 | 15 | 75 | 0.21ns |
| Orientation and engagement | 75 | 75 | 18 | 90 | 0.14ns |
| Emotional regulation | 80 | 80 | 18 | 90 | 0.29ns |
| Motor quality | 80 | 80 | 18 | 90 | 0.29ns |

ns: Not significant, *Significant at $p \le 0.05$

pairs. In addition, there was significant decrease of plasma lead levels in maternal cases at the third trimester when compared to first trimester; while there was significant increase at 24 months when compared to values at delivery in both fetal and maternal cases (Table 4).

**Electroencephalography (EEG):** There was no statistically significant difference in all infant cases in the studied group in a comparison to a control group at 12 or 24 months (Table 5).

Table 4: Lead levels in maternal and infant cases

| Parameter | Number | Cases | Control | p-value |
|---|---|---|---|---|
| **Maternal plasma lead (μg $L^{-1}$)** | | | | |
| First trimester | 100 | 70.7±1.0 | 1.7±1.00 | <0.001* |
| Second trimester | 80 | 60.8±3.5 | 1.0±4.50 | <0.001* |
| Third trimester | 89 | 58.6±4.3$ | 1.8±3.50 | <0.001* |
| **Infant plasma lead (μg $L^{-1}$)** | | | | |
| At delivery | 100 | 51.2±44.1 | 1.02±33.1 | <0.001* |
| At 12 months | 75 | 44.9±38.1 | 1.09±77.1 | <0.001* |
| At 24 months | 96 | 81.5±10.6# | 11.5±11.60# | <0.001* |

$: Significant decrease at third trimester when compared to first trimester; #: Significant increase at 24 months when compared to lead levels at delivery

Table 5: Positive (abnormal) EEG analysis in the infant studied cases

| | EEG | | |
|---|---|---|---|
| Variables | Cases (%) | Control (%) | p-value |
| At 12 months | 70 (70) | 3 (15) | <0.001* |
| At 24 months | 75 (75) | 2 (10) | <0.001* |

## DISCUSSION

Hu *et al*. (2006) stated that lead is dissolved in a circular river (blood circulation) every day. The river is contaminated by a relatively small amount (daily lead intake) and purified by some excretion. However, it is heavily influenced by a large lake (long-term bone stores) which can be heavily contaminated. The lead contamination in the lake slowly but continuously influences the lead concentration in the river and thereby tends to contaminate all the other small lakes (body tissues and organs including brain) with which the river comes in contact.

Mobilization of maternal bone lead stores has been clearly identified as a major source of fetal lead exposure (Gulson *et al*., 2003; Hu and Hernandez-Avila, 2002) and elevated maternal bone lead stores can be expected in women with ongoing environmental exposures and in women who have retained bone lead burdens from earlier lead exposures.

This study provides a relation between lead levels in the pregnant women and infant mental development. Similar result was obtained by Hu *et al*. (2006), who reported that lead exposure has an adverse effect on neurodevelopment, with an effect, most pronounced during the first trimester and best captured by measuring lead in either maternal plasma or whole blood.

As regarded the demographic data of the studied cases, 38% of infants were males and 62% were females in the study group compared to 45% males and 55% females in the control group. There were no statistically significant difference in sex distribution between the study and control groups, similar result were obtained by Ronchetti *et al*. (2006).

As control group age was matched for study group, there was no significant difference between both groups as regard to age. In addition, maternal study and control groups were matched regarding their weight in kilogram. Comparable results were reported by Gerra *et al*. (2003).

Regarding infant feeding; breast feeding was reported in 80% and bottle feeding was reported in 20% in the study group, compared to 95% breast feeding and 5% bottle feeding in control group, with significant difference between both groups. This result was in accordance with previous studies who reported that lead level increasing four times with bottle feeding than breast feeding, due to increased amount of lead in bottle feeding. They also reported an increased level of calcium and iron supplementation; as in the present study.

In the present study, there was no statistically significant difference between cases and controls as regard to systolic and diastolic blood pressure, respiratory and heart rates, proteinurea and lower limb edema. These results are in agreement with Tokdemir *et al.* (2009) and Gerra *et al.* (2003) who reported that, there was no significant differences between studied groups as regard clinical data.

As regard plasma lead levels, there was statistically significant increase of plasma lead levels in study group when compared to control group in both maternal and infant pairs. In addition, there was significant decrease of plasma lead levels in maternal cases at the third trimester when compared to first trimester; while there was significant increase at 24 months when compared to values at delivery in both fetal and maternal cases. These results were in accordance with Hu *et al.* (2006) who found that both maternal blood lead and maternal plasma lead vary considerably over pregnancy; first-trimester levels of either measures, were better than second or third-trimester levels or levels averaged over all three trimesters at predicting infant neurobehavioral performance at age 24 months and first-trimester maternal plasma lead levels were somewhat better than first-trimester maternal whole blood lead levels at predicting infant neurobehavioral performance at 24 months of age. They added that the best-fitting model relating first-trimester plasma lead to 24-month MDI scores was one in which lead level was expressed as the natural logarithm of the measured value. This suggests that the shape of the dose-effect relationship is supra-linear, with a steeper slope at lower plasma lead levels and also this is consistent with the blood lead–IQ relationships in children reported by Canfield *et al.* (2003) in re-analyses of the boston prospective study of children (Bellinger and Needleman, 2003) and in pooled analyses that included several additional prospective studies (Lanphear *et al.*, 2005).

As regarding positive EEG finding, the results were statistically significant between cases in a comparison to a control group at 12 months and 24 months. The positive EEG in control is produced by an electrical alteration outside the brain wave; however, these disturbances do not represent brain abnormalities. Because head, jaw and eye movements cause artifacts by moving the electrodes without clinical signs or symptoms. It is described as "not evolving" and appears quite stable for its duration (Niedermeyer and Lopes da Silva, 1993). However, controversy exists in literature whether those neurophysiological methods are as sensitive as psychometric tests (Levy *et al.*, 1987; Johnston and Goldstein, 1998).

## CONCLUSION

The results of the present study revealed that there is a correlation between lead levels in the pregnant women and infant mental development, especially levels in the first trimester.

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