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ORIGINAL ARTICLES

Maternal Blood Lead, Sociodemographic And Clinical Risk Factors Of Unfavourable Pregnancy Outcomes: A Case Control Study Among Pregnant Women In Egypt

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ABSTRACT

Introduction: Risk factors of unfavourable pregnancy outcomes include high levels of chemicals exposures, sociodemographic and clinical factors. Data are contradctory about the impact of environmental chemical pollutants exposures on pregnancy outcomes. **Objectives**: This study aimed to investigate risk factors of unfavourable pregnancy outcomes among pregnant women in Assiut city, Egypt and to define the impacts of high maternal blood lead level on the mother, fetus and infant. **Subjects and methods**: A case-control, hospital based study was carried out at the Obestetrics Emergency Room, in Aussiut University Hospital. The pregnants attended the Emergency Room for abortion or labor were recruited. The cases of unfavourable pregnancy outcomes represented the study group, 246 cases. An equal number of women with favourable pregnancy outcome was recruited as a control group. The required data were obtainned. Blood samples were collected from cases, controls, and their live borne infants and husbands to determine their blood lead and hemoglobin levels. **Results**: Mean blood lead level of women with unfavourable and favourable pregnancy outcomes were 29.46±6.72 and 28.61±6.53 μg/dL, respectively with a statistically insignificant difference. Gestational hypertension, pr-eclampsia/eclampsia, unfavourable pregnancy outcomes, and neonatal intensive care admission were more common among women with blood lead levls ≥30 μg/dL compared to women with <30 μg/dL, with statistically significant differences (P=0.006, 0.03, 0.000, 0.0001 and 0.000, and 0.000, respectively**)**. One and 5- minutes Apgar scores, maternal and infant Hb were lower among women with blood lead levls ≥30 μg/dL with statisticaly significant differences (P=0.000 for each of them). Factors, significantly, put women at risk to develop unfavourable pregnancy outcomes were maternal age group 30-35 years (OR=6.13), interpregnancy space <2 years (OR=4.15), preveious unfavourable pregnancy outcomes (OR=3.08), primiparous (OR=2.58), and low socioeconomic level (OR=2.45). Also; living nearby hazardous environment (OR=3.2), hazardous maternal occupations (OR=2.81), and unusual exertion/heavy lifting (OR=2.53) were significant risk fators for unfavourable pregnancy outcomes. No regular antenatal care, no adequate diet intake and eating foods exposed to lead pollutants were significant risk factors (OR=2.77, 2.85, and 2.13, respectively). Maternal (OR=5.17) and paternal (OR=3.66) smoking, and traditional herbal medication use (OR=2.83) were sinificant risk factors. Lastly, hypertension (OR=5.71), stress (OR=4.56) and urinary tract infections (OR=3.19) were sinificant medical risk factors. **Recommendations**: Women at risk for unfavourable pregnancy outcomes should have frequent antenatal care for monitoring and evaluation their conditions. Environmental, nutritional, and behavioral interventions are indicated for all pregnant women in order to prevent undue exposures to the women, fetus, newborn and infant. Lastly, further studies in different areas in Egypt are needed to investigate this health problem.

Key wrodss:

Introduction

Pregnancy is an important and unique period of a woman's life. During pregnancy there is high sensitivity to toxic substances. Increased blood lead (Pb), either endogenous (bone saved) or from ambient pollution, affects health in pregnancy and could be extremely harmful to the rapidly developing central nervous system of the fetus (Rastogi *et al.*, 2007). Further, research findings suggest that it can adversely affect maternal and child health across a wide range of maternal exposure levels (Ettinger and Wengrovitz, 2010). Also, lead exposure during pregnancy and breastfeeding can result in lasting adverse health effects independent of lead exposure during other life stages (Grandjean *et al.*, 2008). So, lead exposure remains a public health problem for subpopulations of women of childbearing age and for the developing fetus and nursing infant for several important reasons. First, prenatal lead exposure has known influences on maternal health, and infant birth and neurodevelopmental outcomes (Bellinger, 2005). Second, bone lead stores are mobilized during periods of

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increased bone turnover such as pregnancy and lactation for women with prior lead exposure. This may results in redistribution of cumulative lead stores, which is a concern since lead released into maternal blood and breast milk can adversely affect the fetus or newborn (Gulson *et al.*, 2003).

Lead has many, other, adversely influences on the health. Health effects of chronic low-level exposure include pregnancy induced hypertension/pre-eclampsia (PE) (Yazbeck *et al.*, 2009), cognitive decline, defects in hematopoietic and renal impairment, spontaneous abortion, alteration of fetal anthropometric characteristics and birth weight, and preterm labor (Jelliffe-Pawlowski *et al.*, 2006 and Agency for Toxic Substances & Disease Registry, 2007). Further, there is evidence that risk for unfavourable pregnancy outcomes such as spontaneous abortion is increased by maternal exposure to high levels of lead. Also, the researches suggest, but are inconclusive, that fetal lead exposure at levels found in U.S. results in low birth weight (LBW) (Ettinger and Wengrovitz, 2010). Moreover, women exposed to lead at work before pregnancy have increased rates of miscarriages, stillbirths, and LBW infants (Lamadrid-Figueroa *et al.*, 2007).

There is evidence that a significant number of pregnant women, and presumably their infants, are being exposed to lead in U.S. today. It is clear exposed subgroups do exist and some may be highly exposed; particularly recent immigrants (Graber *et al.*, 2006), workers in specific high-risk occupations (Calvert and Roscoe, 2007), and those practicing certain behaviors such as pica (Shannon, 2003), use of culturally-specific remedies and products (Saper *et al.,* 2008), and renovating older homes (Jacobs *et al.,* 2002). Women living near hazardous wastes site or active smelters (Garcia-Vargas *et al.,* 2001) and residents in countries still using leaded gasoline (Albalak *et al.,* 2003) may be highly exposed. Also, women with blood lead levels (BLLs) ≥10 µg/dL were more likely to report having friend or relative with high blood lead (Handley *et al.,* 2007). However, there is a significant decreasing trend in population average blood lead levels over time ($p<0.01$). Subjects studied in 1988-1991 had significantly higher weighted mean blood lead levels (2.0 µg/dL) than those in 1991-1994 (1.6 µg/dL) (Lee *et al.,* 2005).

Blood lead concentration is the primary biomarker used for monitoring exposure levels, and reflects an individual's current body lead burden (Barbosa *et al.,* 2005). Lead crosses the placenta from the maternal to the fetal circulation without impediment, as early as 12 weeks gestation, and blood lead levels in mother and fetus are virtually identical (Shen *et al.,* 1998 and Gomaa *et al.,* 2002).

Growth and development of the fetus are complex and influenced by genetic, epigenetic, maternal maturity, and environmental factors (Wu *et al.,* 2006). These factors affect the size and functional capacity of the placenta, uteroplacental transfer of nutrients and oxygen from mother to fetus, conceptus nutrient availability, fetal endocrine milieu, and metabolic pathways. Optimal fetal growth is essential for perinatal survival and has longterm consequences extending into adulthood (Gluckman and Hanson, 2007).

Study Objectives

I- Ultimate Objective:

Improve quality of the health of mothers, fetuses, infants and children in Egypt.

II- Immediate Objectives:

To investigate the role of blood lead, sociodemographic, behavioral and clinical conditions as risk factors of unfavourable pregnancy outcomes; spontaneous abortion, stillbirth, premature and LBW among pregnant women in Assiut city, Egypt; and to define the impacts of high maternal blood lead level on the health of mother, fetus and infant.

Material And Methods

I- Study Questions: Is high level of maternal blood lead risk factor for unfavourable pregnancy outcomes? Is there high blood lead level impacts on the pregnant mother, fetus andinfant? Is there unfavourable pregnancy outcomes sociodemographic, behavioral and/or clinical risk factors?

II- Study Design: A case-control, hospital based design was used to investigate the current research problem.

III- Study Setting: This study was conducted in the Obstetrics Emergency Room in Assiut Hospital, Al-Azhar University.

IV- Study Sample: All pregnant women attended the Obstetrics Emergency Room in Assiut Hospital, Al-Azhar University, during spesific period of the study, for abortion or labor were included in the study. The cases of unfavourable pregnancy outcomes; spontaneous abortion, stillbirth, premature and LBW were recruited as a study group. The sample was 246 cases. For each case of unfavourable pregnancy outcome; a case of

favourable pregnancy outcome, the first one after each studied case, was recruited as a member of the control group. So, the controls were also 246 women.

All cases must be fulfilling the following inclusion criteria: 1) They should be certain about the first day of last menstrual period , 2) Age of cases ranged from 20 to 35 years, 3) Married females, 4) Have a definite specific diagnosis of unfavourable pregnancy outcomes, 5) Have a singletone fetus, and 6) Have no positive serum antibodies against infectious agents potentially associated with pregnancy loss.

The controls enrolled in the study have fulfilled the following inclusion criteria: 1) Should be certain about the first day of last menstrual period, 2) Age of women ranged from 20 to 35 years, 3) Married females, 4) Have no history of threatened abortion in the current pregnancy, 5) Have a singletone fetus, and 6) Have favourable pregnancy outcome.

V- Ethical Considerations: The purpose of the study and procedures to be performed were explained to the cases and controls, an oral consent to participate in the study was taken accordingly.

VI- Study Tools and Methods:

1- Interview questionnaire: It was used to collect data relevant to topic of the study. The cases and controls were submitted to an interview to fill the questionnaire.

2- Diagnosis of unfavourable/favourable pregnancy outcomes: Spontaneous abortion were those cases who lost of a fetus weighing less than 500 grams, and before 28 weeks of gestation. While, stillbirth were those cases borne a fetus showing no signs of life at birth. Further, premature were those infants borne ≤37 weeks of gestation. Lastly, LBW were those infants weighted <2500 gm at birth irrespective to period of gestation. On the other hand, favourable pregnancy outcome were those women who borne an infant weighted ≥2500 gm at birth and >37 weeks of gestation (control group).

3- Clinical examinations: General and local physical examinations were done for the cases and controls. Further, pelvi-abdominal ultra-sonography examination was done for both groups (if there is time before abortion or labor) to get sure of gestational age, to exclude multiple fetuses (it may be a cause of LBW), and to detect fetal intrauterine growth resrection (IUGR). Also, Apgar scores at 1 and 5 minutes were defined for each live borne infant; favourable and unfavourable (premature and LBW).

4- Laboratory investigations: They were done for both groups. Venous blood samples, 5 ml, were collected from each legible female, case and control. Also, 5 ml of venous blood samples were collected from the husband of each woman of the cases. Only 52 of the cases husbands' were presented and agreed to give blood samples. We selected blood for analysis because most circulating lead is carried in the erythrocytes. So, venous blood lead test produce the most reliable results. Venous blood samples were collected into EDTA containing vacutainer tubes after scrubbing the arm with alcohl swabs followed by venipuncture. The samples were analyzed by flameless atomic absorption spectro-photometer model 460-graphete 2000 according to Bannon *et al.* (1994) to define blood lead levels (µg/dL). Also, hemoglobin (Hb) concentration levels (g/dL) were determined for all the cases and controls. Hb was determined by using Drabkin's photometric method. Further, umbilical cord whole blood samples, 5 ml, were collected from each live borne infant of women with unfavourable pregnancy outcomes to determine BLLs and Hb levels. Also, a control group of favourable pregnancy outcome infants was selected randomly to determine their BLLs and Hb levels. Further, midstream urine samples were taken from all women, cases and controls, for microscopical examination to detect those with urinary tract infections (UTIs). Lastly, maternal serum antibodies against infectious agents potentially associated with pregnancy loss were measured to exclude these cases.

VII- Statistical Analysis: Odds ratio (OR), t-student test, Yates corrected Chi-square (χ^2) and 2-tailed Fisher exact (FE) were used as tests of significance. The significance level for t, χ^2 and FE was accepted if the P-value <0.05. While, significance for OR was the 95% confidence interval (CI) or 95% exact confidence limits (ECL). The mean (M) ± standard deviation (SD) was used for descriptive statistics. The mean was used as a measure of central tendency, while the standard deviation was used as a measure of dispersion. The χ^2, FE and t-tests were used for analytic statistics; to test for the presence or absence of a statistically significant difference among the studied groups. While, OR was used to assess the risk factors.

Results:

Table (1) cleared frequncy distribution of the studied group of unfavourable pregnancy outcomes.

Table (2) demonstrated the statistical significance of the differences between mean blood lead and hemoglobin levels of the cases and controls. The mean blood lead levels of the total groups of cases and controls were 29.46±6.72 and 28.61±6.53 µg/dL, respectively with statistically insignificant difference (P=0.92). In details, the mean blood lead levels of the total subgroups of cases with spontaneous abortion and other cases with still birth, premature and LBW infants were 29.68±6.73, 29.43±6.64, 29.41±6.61, and 29.42±6.60 µg/dL, respectively compared to 28.61±6.53 µg/dL with statistically insignificant differences (P=0.95, 0.58, 0.70, and 0.69, respectively). Also, the mean hemoglobin levels of the total groups of cases and controls were 9.83±1.47 and 11.15±1.32 mg/dL, respectively with statistically significant difference (P=0.000).

Table (3) illustrated the statistical significance of the differences between mean blood lead levels of the studied cases and their infants. The mean blood lead levels of the cases with unfavourable pregnancy outcomes (premature and LBW infants) and their infants were 29.42±6.63 vs. 25.23±5.41 µg/dL, 29.41±6.61 vs. 25.22±5.42 µg/dL and 29.42±6.60 vs. 25.24±5.43 µg/dL, respectively with statistically insignificant differences (P=0.99, 0.99, and 0.99, respectively).

Table (4) showed the statistical significance of the differences between mean blood lead levels of the cases and their husbands who presented and agreed to give blood samples. The mean blood lead levels of the cases with unfavourable pregnancy outcomes; spontaneous abortion and still birth, premature, and LBW infants compared to their husbands were 29.46±6.72 vs. 29.94±4.28, 29.68±6.73 vs. 29.98±4.31, and 29.42±6.61 vs. 29.82±4.24 µg/dL, respectively with statistically insignificant differences (P=0.25, 0.34, and 0.36, respectively).

Table (5) cleared mean blood lead and hemoglobin levels of the LBW and premature infants and their control infants. The mean blood lead levels of live borne infants of women with unfavourable pregnancy outcomes and their control infants were 25.23±5.41 and 23.19±5.11 µg/dL, respectively with statistically insignificant difference (P=0.96).

Table (6) showed impacts of maternal blood lead levels ≥30 µg/dL on the studied groups of mothers. We decided to consider the maternal blood lead level 30 µg/dL a cutoff point as a biological exposure index **(Wu, 2006)**. Gestational hypertension, and PE/eclampsia were more common among mothers with blood lead levls ≥30 compared to mothers with BLLs <30 µg/dL (18.8% and 9.4% vs. 9.7% and 4.1%, respectively), with statistically significant differences (P=0.006 and 0.03, respectively**)**. Also, women with spontaneous abortion and still birth, premature, and low birth weight, and favourable pregnancy outcomes among mothers with blood lead levls ≥30 and <30 µg/dL were 61.6%, 15.2% and 23.2% vs. 23.1%, 4.5% and 72.4%, respectively with statistically significant differences (P=0.000, 0.0001 and 0.000, respectively**)**. Further, neonatal intensive care admission was common among mothers with blood lead levls ≥30 µg/dL (27.7%) than <30 µg/dL (2.4%) with statisticaly significant difference (P=0.000). As respect 1- and 5- minutes Apgar scores, maternal Hb and infant Hb, they were lower among mothers with blood lead levls ≥30 than <30 µg/dl (4.14±1.26, 6.01±1.42, 9.62±1.36 mg/dL, and 13.10±3.32 mg/dL vs. 6.06±1.02, 8.24±1.02, 11.34±1.45 mg/dL, and 17.52±4.67 mg/dL, respectively with statisticaly significant differences (P=0.000 for each of them). On the other hand, congenital anomalies and infant perinatal deaths were common among mothers with blood lead levls ≥30 than <30 µg/dL with statisticaly insignificant differences.

Table (7) clarified distribution of the cases and controls according to their socioeconomic risk factors. Low maternal and paternal education are risk factors for unfavourable pregnancy outcomes (OR=2.41, 95% CI: 1.58-3.67 and OR=2.17, 95% CI: 1.41-3.37, respectively). Also, maternal semi-skilled and skilled labor is risk factor for unfavourable pregnancy outcomes (OR=2.11, 95% CI: 1.32-3.39). Collectvely, low socioeconomic level is risk factor for unfavourable pregnancy outcomes (OR=2.45, 95% CI: 1.61-3.73).

Table (8) illustrated distribution of the cases and controls according to their personal risk factors. Higher maternal age (30-35 years) is statisticaly sinificant risk factor (OR=6.13, 95% CI: 3.92-9.63). Also, primiparous, interpregnancy space <2 years, history of menstrual disorders, and preveious unfavourable pregnancy outcomes are statisticaly sinificant risk factors (OR=2.58, 95% CI: 1.76-3.77; OR=4.15, 95% CI: 2.8-6.16; OR=1.97, 95% CI: 1.19-3.26 and OR=3.08, 95% CI: 1.45-6.69, respectively). Further, urban residence; living nearby heavy traffic, chimney and burned garbage; living in old home are statisticaly sinificant risk factors (OR=1.72, 95% CI: 1.18-2.49; OR=3.2, 95% CI: 2.14-4.79 and OR=2.83, 95% CI: 1.87-4.27, respectively). Hazardous maternal and paternal occupations are statisticaly sinificant risk factors (OR=2.81, 95% CI: 1.35-6.96 and OR=1.94, 95% CI: 1.09-3.47, respectively). Lastly, unusual exertion and/or heavy lifting is the only statisticaly sinificant physical risk factors (OR=2.53, 95% CI: 1.65-3.89).

Table (9) cleared distribution of the cases and controls according to their life-style and behavioral risk factors. No regular antenatal care, no adequate diet intake and eating foods exposed to lead pollutants (e.g. gasoline fumes or wrapped in news papers) are statisticaly sinificant risk factors (OR=2.77, 95% CI: 1.86-4.12; OR=2.85, 95% CI: 1.75-3.81; and OR=2.13, 95% CI: 1.46-3.11, respectively). Maternal and paternal smoking, and maternal bango/alchol use are statisticaly sinificant risk factors (OR=5.17, 95% ECL: 1.08-48.88; OR=3.66, 95% CI: 2.44-5.49; and OR=2.23, 95% CI: 1.31-3.8, respectively). Also, traditional herbal medication and traditional cosmetics (kohl) use are statisticaly sinificant risk factors (OR=2.83, 95% CI: 1.82-4.43 and OR=1.74, 95% CI: 1.16-2.6, respectively).

Table (10) clarified distribution of the cases and controls according to their medical risk factors. Hypertension, stress and urinary tract infections are statisticaly sinificant risk factors (OR=5.71, 95% ECL: 1.22-53.41; OR=4.56, 95% ECL: 1.9-12.56; and OR=3.19, 95% CI: 1.5-6.92, respectively).

Discussion:

Lead is toxic to living things (Sanín *et al.,* 1998). There is increasing awareness that unintended exposure to environmental/occupational contaminants, as lead, adversely affect maternal, fetal and infant health, including

the ability to become pregnant, maintains a healthy pregnancy and has a healthy baby. Evidence suggests that acute and chronic low-level lead exposure has these adverse health effects (Ettinger and Wengrovitz, 2010). So, there is great concern in avoiding the presence of pregnant women in endemic areas of lead contamination in order to protect their reproductive health and the development of their children (Gulson *et al.,* 1998).

We cleared spontaneous abortion is the most common type of the unfavourable pregnancy outcomes. Our result is consistent with McLaughlin Centre (2002), it showed its incidence was estimated to be 50.0% of all pregnancies, based on the assumption that many pregnancies abort spontaneously with no clinical recognition.

In the general public, exposure to lead occurs primarily through the oral route, with contribution from inhalation. In contrast, in the occupational setting, inhalation of lead in the form of fumes, mists, dusts and vapours is a major route of exposure. But, the toxicological effects are the same (Agency for Toxic Substances and Disease Registry, 2005). Dermal absorption of lead compounds is generally low (Department for Environment Food and Rural Affairs and Environment Agency, 2002).

Concentration of lead in blood is an important biomarker for monitoring exposure. It reflects current body lead burden (Barbosa *et al.,* 2005). But, because there is no apparent threshold below which adverse effects of lead do not occur, Centers for Disease Control and Prevention (CDC) has not identified an allowable exposure level, level of concern, or any other line intended to connote a safe or unsafe level of exposure for either mother or fetus. The CDC recommends follow-up activities beginning at BLLs ≥5 µg/dL in pregnant women. This BLL serves a different purpose; it flags the occurrence of prior or ongoing lead exposure above background levels, which may not be recognized. Vulnerability of the developing fetus to adverse effects and the possibility of preventing additional exposures postnatally justify intervention for pregnant women showing evidence of lead exposure above background levels. Further, the 95th percentile of BLLs among U.S. women aged 15-49 was 2.4 µg/dL. Estimates suggest 1.0% of women of childbearing age (15-44 years) have BLLs ≥5 µg/dL (Ettinger and Wengrovitz, 2010). The current reference range for acceptable BLLs in healthy persons without excessive exposure to environmental sources of lead is <10 µg/dL for children and <25 µg/dL for adults (Gwiazda *et al.,* 2005). The mean BLL in U.S. women of childbearing age, 20-49 years, was 1.78 µg/dL (range 0.7-31.1). Approximately 30.0%, 6.0% and <1.0% of the women had BLLs ≥2.5 µg/dL, ≥5 µg/dL, and ≥10 µg/dL, respectively (Lee *et al.,* 2005). Also, the mean BLL of women aged 20-49 years was 1.3 µg/dL (range 0.33-27.3). Approximately 10.5%, 1.4% and 0.2% of the women had BLLs ≥2.5 µg/dL, ≥5 µg/dL, and ≥10 µg/dL, respectively (McKelvey *et al.,* 2007). Further, among women aged 16-44 years, 13.0% had BLLs ≥5 µg/dL; 4.5% had BLLs ≥10 µg/dL, and less than 1.0% had BLLs ≥25 µg/dL (CDC, 2007). The current biological exposure index (a level that should not be exceeded) for lead-exposed workers in U.S. is 30 µg/dL (randomly) (Wu, 2006).

Increased risk for spontaneous abortion appears to be associated with BLLs ≥30 µg/dL. Limited evidence suggests that maternal BLLs 10-30 µg/dL could also increase the risk for spontaneous abortion, although these findings remain to be confirmed (Ettinger and Wengrovitz, 2010). Few studies have addressed the risk for spontaneous abortion at lower levels of exposure. But, most reports of those studies provide limited evidence to support an association between maternal BLLs of 0 to 30 µg/dL and increased risk for spontaneous abortion (Lindbohm *et al.,* 1992 and Tabacova & Balabaeva, 1993). Our result was supported by Borja-Aburto *et al.* (1999); they showed a statistically significant dose-response relationship between mean maternal BLL 11.0 µg/dL and risk for spontaneous abortion. Odds ratios for spontaneous abortion for the blood lead groups 5-9, 10-14, and >15 µg/dL were 2.3, 5.4, and 12.2, respectively, in comparison to the reference group (<5 µg/dL) (p for trend=0.03) with an estimated increased odds for spontaneous abortion of 1.8 (95% CI: 1.1–3.1) for every 5 µg/dL increase in blood lead. Further, in the multiple condition logistic regression model predicting spontaneous abortion, the established risk factor was BLL. So, their study provides evidence that BLLs once considered moderate may be associated with an increased risk of spontaneous abortion. Also, Lamadrid-Figueroa *et al.* (2007); cleared pregnant women (mean BLL=6.2 µg/dL), a 0.1% increment in the maternal plasma-to-blood lead ratio was associated with a 12.0% greater incidence of reported history of spontaneous abortion (p=0.02). However, with each additional abortion experienced, women had an 18.0% greater plasma-to-blood lead ratio (p=0.01). Women with a larger plasma-to-whole blood lead ratio may be at higher risk for miscarriage due to a greater availability of lead in plasma, which more readily crosses the placental barrier.

Absorption of lead depends on the physical and chemical state of the metal. Also, it is influenced by age, and physiological and nutritional status. The route of absorption has little effect on the distribution of lead. Absorbed lead is distributed by blood to mineralising systems (bone, teeth) and soft tissue (liver). The half-life of lead in blood, soft tissue and bone is approximately 36 days, 40 days and 27 years, respectively. Bone accumulates lead throughout most of the human life span but, at the same time, lead is mobilised from bone by remodelling. So, after removal the subject from environmental exposure, the decline in blood lead level occurs relatively rapidly at first as half-life of lead in blood is ~36 days (International Programme on Chemical Safety, 1995). Then it is followed by a slow continuing decline over several months to years. In addition to exogenous sources of lead, blood lead represents the contribution of past environmental exposure being mobilized from bone stores (Ettinger and Wengrovitz, 2010).

Blood lead level has been reported to be increased in pregnant than in non-pregnant women, because of bone remodeling (Tellez-Rojo *et al.,* 2004). In pregnancy, bone lead released into the blood varies from subject to subject, but there is an estimated 20.0% increase in blood lead (Gulson *et al.,* 2003), leading to speculation; in pregnancy lead is released from the skeleton and potentially available to the fetus (Rothenberg *et al.,* 1994). Lead crosses the placenta by passive diffusion (Goyer, 1990). So, it is readily transferred from mother to developing fetus. Lead concentration in cord blood may be 80.0% (Gulson *et al.,* 2003) to 85.0-90.0%, and this suggesting a near-perfect linear relationship of maternal blood (Goyer, 1990 and International Programme on Chemical Safety, 1995), hence posing a risk for the fetus. This is consistent with our result. So, umbilical cord whole blood lead collected at delivery has been widely used as a measure of fetal exposure. Studies suggest that maternal blood lead and umbilical cord lead levels, at delivery, are highly correlated (Rothenberg et al., 1996 and Harville *et al.,* 2005). We reported infant mean lead level is lower than, by ~14.0%, the mean maternal blood lead at delivery. Hamilton *et al.* (2001) found maternal BLLs of 119.4 µg/dL and 113.6 µg/dL in the cord blood. However, some studies have shown umbilical cord lead to be higher than maternal BLLs at delivery (Rothenberg *et al.,* 1996 and Harville *et al.,* 2005). A single blood lead test may not reflect cumulative lead exposure and may not be sufficient to establish the full nature of the developmental risk to the fetus/infant. Physiologic changes, such as decreasing hematocrit, saturation of red cell lead-binding capacity, and increased bone resorption or intestinal absorption of lead, may influence the interpretation of BLLs during pregnancy. In addition, it is well known that the vulnerability of developing organ systems to environmental toxicants can vary widely over the course of pregnancy (Mendola *et al.,* 2002). Also, studies have shown variation in BLLs during gestation with a substantial increase in late pregnancy (Rabinowitz, 1991). This increase may be linked to increased calcium demand and changes in calcium-related regulatory factors, which affect lead compartmentation (Silbergeld, 1991). Further, elevated maternal BLLs are linked to decreased calcium uptake by syncytiotrophoblasts, suggesting that exposure to lead can modify calcium transfer in these cells (Lafond *et al.,* 2004). Also, Rothenberg *et al.* (1996) showed cord BLLs were lower and higher than maternal BLLs at delivery in 67.0% and 33.0%, respectively of their cases. Further, Vigeh *et al.* (2006) repoted cord BLLs were significantly higher (4.30±2.49 µg/dL) among infants of postpartum women, with pre-eclampsia compared to infants of normotensive controls (3.5±2.09 µg/dL). Chuang *et al.* (2001) modeled the interrelations of lead levels in bone, venous blood, and umbilical cord blood with exogenous lead exposure through maternal plasma lead in peripartum women. An interquartile range increase in bone lead was associated with an increase in cord blood lead by about 1 µg/dL. An increase of 0.1 $\mu g/m^3$ in air lead was associated with an increase in the mean level of cord blood lead by 0.67 µg/dL. The model suggested the contributions from endogenous (bone) and exogenous (environmental) sources were relatively equal, and that maternal plasma lead varies independently from maternal whole blood lead.

We showed mean hemoglobin levels were lower among cases and their live borne infants than controls and their infants. These results are in accordance with Ettinger and Wengrovitz (2010). Further, they stated; it may increase lead absorption and also has an additional independent negative impact on fetal development. West *et al.* (1994) reported a significant negative correlation between hemoglobin and maternal BLL. Further, Harville *et al.* (2005) found higher maternal hemoglobin and presence of the sickle cell trait were associated with lower cord blood lead in comparison to mother's blood lead, suggesting that iron status may be an important factor in the maternal-fetal transfer of lead across the placenta. Lead produces range of effects, primarily on the haematopoietic system, the nervous system, and the kidneys. Lead binds to sulfhydryl and amide groups, frequent components of enzymes, altering their configuration and diminishing their activities. It may also compete with essential metallic cations for binding sites, inhibiting enzyme activity, or altering the transport of essential cations such as calcium (Flora *et al.,* 2007). Also, lead inhibits many stages in the pathway of haem synthesis aminolevulinic acid dehydratase (ALAD), which catalyses the formation of porphobilinogn from aminolevulinic acid (ALA) and ferrochelatase that incorporates iron into protoporphyrin (Jaffe, 1995). It is suggested that the inhibition of ALAD can occur at blood lead as low as 5 µg/dL. A significant correlation coefficient between lead in blood and ALA-U or ALAD has been suggested (Wetmur, 1994 and Jaffe, 1995). Ferrochelatase catalyzes the incorporation of iron into the porpohyrin ring. As a result of lead toxicity, the enzyme is inhibited and zinc is substituted for iron, and zinc protoporphyrin concentration is increased (Gurer *et al.,* 1998). The major consequences of this effect are reduction of haemoglobin and the inhibition of cytochrome P 450- dependent phase-I metabolism. Lead inhibits normal haemoprotein function in both respects, which results in basophilic stippling of erythrocytes related to clustering of ribosome and microcytosis (Lanphear *et al.,* 2000).

We reported men have insignificant higher blood lead levels than women. Blood lead level reflects the exposure in both genders and is influenced by genetic factors possibly related to uptake and storage (Bjorkman *et al.,* 2000). Our results are in accordance with Leroyer *et al.* (2001) and Nriagu *et al.* (2006); they stated many epidemiological studies of occupational and environmental exposures have shown men generally have higher concentrations of blood lead than women. Also, BLLs exceeding 10 µg/dL (the level that the CDC recommends 'not to be exceeded') were found several times more frequently among men than among women (Leroyer *et al.,*

2001). There are two reasons for higher BLLs in men; first, men are generally at higher risk of exposure to increased levels of lead than women (Kim *et al.,* 2006), and second, higher blood hematocrit in men causes accumulation of more lead in men's blood because a large proportion of lead binds to erythrocytes (Becker *et al.,* 2002). Like blood lead, the bone lead level is higher in men than in women. In addition, lead stored in bone is released more slowly into the blood in women than in men (Popovic *et al.,* 2005). So, blood lead levels remain high much longer after the cessation of occupational/environmental exposure, reflecting the endogenous source of lead in women (Tellez-Rojo *et al.,* 2004). The accumulated lead in women's bones is released more quickly during periods of increased bone turnover, particularly in pregnancy (Rabinowitz, 1991 and Manton *et al.,* 2003). Because lead stays in women's bone for years to decades, its mobilization during pregnancy may pose a significant fetal exposure risk long after maternal lead exposure has ceased (Gonzalez-Cossio *et al.,* 1997).

We observed lead exposure and increasing levels of lead in blood has been associated with increased risk for gestational hypertension but the magnitude of the effect, the exposure level at which risk begins to increase, and whether risk is associated with acute or cumulative exposure, remain uncertain. Epidemiologic and toxicologic studies demonstrate that health effects can occur at low to moderate blood lead levels without previously recognized harm. However, prevalence of gestational hypertension has been shown to be increased even at blood lead levels <5 µg/dL (Agency for Toxic Substances and Disease Registry, 2007). It is unclear whether lead-induced increases in blood pressure during pregnancy lead to severe hypertension or pre-eclampsia (PE). Further, causality is unclear since preexisting hypertension reduces renal function that in turn could result in retention of lead (Ettinger and Wengrovitz, 2010). Also, evidence showed lead damages the vascular endothelium (Vaziri and Sica, 2004) and endothelial dysfunction is an important mediator of gestational hypertension (Karumanchi *et al.,* 2005). Our result was consistent with Rabinowitz *et al.* (1987); they cleared that incidence of pregnancy hypertension and elevated blood pressure at delivery increased significantly as blood lead increased (6.9±3.3 µg/dL). During delivery, lead levels correlated with both systolic (p=0.0001) and diastolic (p=0.002) blood pressure. Using a reference level of 0.7 µg/dL, the relative risk doubled when BLL approached 15 µg/dL. Further, Dawson *et al.* (2000) showed significant differences between normotensive and hypertensive pregnancies as regard to red blood cell (RBC) lead content. Maternal blood pressure was found to be directly proportional to RBC lead content. Also, our result was accordance with Sowers *et al.* (2002); they stated that maternal blood lead was significantly associated with gestational hypertension in a cohort of women with BLL of 1.2±0.03 µg/dL. Further, Magri *et al.* (2003) reported women with gestational hypertension had significantly higher BLLs (9.6±6 µg/dL) compared to normotensive controls (5.8±3 µg/dL). Also, Vigeh *et al.* (2004) cleared mean postpartum BLL was significantly higher in cases with hypertension (5.7±2.0 µg/dL) compared to age-matched normotensive controls (4.8±1.9 µg/dL). Also, BLLs have been associated with the risk for PE, although the evidence is less clear than for gestational hypertension (Ettinger and Wengrovitz, 2010). Our result was accordance with Dawson *et al.* (2000); they observed significant differences between normotensive and pre-eclamptic pregnancies with respect to RBC lead content. Also, Vigeh *et al.* (2006) found BLLs were significantly higher (5.09±2.01 µg/dL) among postpartum women with PE compared to normotensive controls (4.82±2.22 µg/dL). A 13-fold increased risk for PE compared to normotensive controls (mean blood lead 3.52±2.09 µg/dL) was observed for every log-unit increase (~3 µg/dL) in blood lead. On the other hand, Rabinowitz *et al.* (1987) found no association between BLL and risk for PE among women at delivery. Also, Vigeh *et al.* (2004) noted that there were no significant differences in BLLs among hypertensive cases with- and without proteinuria.

In this study we revealed maternal blood lead levels ≥30 µg/dL had significantly many negative impacts compared with mothers who had blood lead levels ≤30 µg/dL. Maternal lead exposure may increase the risk for preterm delivery (Ettinger and Wengrovitz, 2010). Our finding is in accordance with Torres-Sanchez *et al.* (1999); they found cord blood lead to be higher in preterm compared to term infants (mean 9.8 vs. 8.4 µg/dL). Also, lead's adverse effects are associated with several negative pregnancy outcomes as LBW (Bellinger *et al.,* 1991). The epidemiologic studies on prenatal lead exposure in relation to gestational age and birth weight were contradictory. The well-designed of those studies suggest that maternal lead exposure during pregnancy is inversely related to fetal growth, as reflected by duration of pregnancy and infant size (Andrews *et al.,* 1994 and Lamadrid-Figueroa *et al.,* 2007). Also, epidemiologic cohort studies suggest, but inconclusive, prenatal lead exposure, at levels found in U.S. or even at maternal blood lead levels <10 µg/dL, is also inversely related to fetal growth/LBW. But, maternal BLL at which the risk begins to increase has not been determined (Ettinger and Wengrovitz, 2010). Also, Irgens *et al.* (1998) showed women occupationally exposed to lead were more likely to deliver a LBW infant than non exposed women (OR=1.1, 95% CI: 0.98-1.29). Rothenberg *et al.* (1999) found over 1-35 µg/dL range of maternal blood lead at 36 weeks of pregnancy, the estimated reduction in 6-month infant head circumference was 1.9 cm (95% CI: 0.9-3.0). Further, maternal bone lead burden was found to be inversely related to birth weight (Gonzalez-Cossio *et al.,* 1997), birth length and head circumference at birth (Hernandez-Avila *et al.,* 2002). On the other hand, West *et al.* (1994) showed the mean maternal BLL was not significantly different (6.29±0.25 vs. 7.61±1.18 µg/100 ml, p=0.066) between mothers who gave LBW infants and controls with normal weight infants. Also, IUGR and LBW have been linked to alterations of

respiratory function at all stages of postnatal life and IUGR may lead to increased susceptibility to air pollution exposure and other environmental factors (Wang and Pinkerton, 2007).

In the present study we showed congenitl anoalies was insignificantly common among cases with higher blood lead levels, ≥30 μg/dL. The periods of embryonic and fetal development are remarkably susceptible to environmental hazards (Grandjean *et al.,* 2008). Lead has long been suspected to be a teratogen (O'Halloran and Spickett, 1992). It is one of the known human teratogens, depending on the timing of exposure i.e. the state of fetal development many insults may occur in the preterm delivery (Osorio and Windham, 1997). It may influence crucial cellular functions during these critical periods of fetal development and permanently alter the structure or function of specific organ systems (Grandjean *et al.,* 2008). Further, the fetal environment is determined by the maternal environment and by maternal and placental physiology (Wu *et al.,* 2006). Data are inadequate to establish presence or absence of an association between maternal lead exposure and major congenital anomalies in the fetus (Ettinger and Wengrovitz, 2010). But, minor malformations such as birth marks and nevi among people exposed to chemicals were common (Ahlborg and Hemminki, 1995). Also, adverse effects of occupational lead exposure may be manifested in congenital malformations (Joffe, 1993). Emerging evidence shows that redox-sensitive signal transduction pathways are critical for developmental processes, including proliferation, differentiation, and apoptosis. As a consequence, teratogens that induce oxidative stress may induce teratogenesis via the misregulation of these pathways. Oxidizing and reducing equivalent imbalance in turn leads to macromolecule damage, namely protein modification, lipid peroxidation, and DNA oxidation, and if unchecked, oxidative damage can lead to cell death. However, oxidative stress as a mechanism does not satisfactorily explain how it might serve as a mechanism of teratogenesis (Jason and Hansen, 2006). In conditions of severe intrauterine deprivation, there is a capacity to lose structural units such as nephrons or pancreatic beta-cells in developing organ systems. It is not clear if such responses are either adaptive or predictive, although it is obvious that they will result in the programming of a reduced functional capacity for life (Gluckman and Hanson, 2007). Lead poisoning during period of organogenesis can induce disturbances in the development and differentiation of the fetal stomatognathic system (Brandini *et al.,* 211). Further, disturbances during the developmental period may result in transient or irreversible long term effects. Birth defects associated with the common air pollutants may potentially result in increased vulnerability of the respiratory and cardiovascular systems during infancy and childhood (Wang and Pinkerton, 2007).

We showed that low education level was significant risk factor for unfavourable pregnancy outcomes. This result is consistent with Restrepo *et al.* (1990), they observed the majority of their studied subjects with poor reproductive health outcomes had primary education or illiterates. Also, Lee *et al.* (2005) showed lower educational level and poverty were associated with higher blood lead levels. Further, McKelvey *et al.* (2007) found blood lead was inversely proportional to educational level. On the other hand, Borja-Aburto *et al.* (1999) found no differences for self reported education. Also, we cleared low occupational level was significant risk factor for unfavourable pregnancy outcomes. This result is in accordance with Restrepo *et al.* (1990), they showed that the majority of their studied subjects with poor reproductive health outcomes were workers. Ettinger and Wengrovitz (2010) stated certain populations of women at increased risk for exposure have been identified and may be highly exposed, particularly workers in certain occupations. Also, Graber *et al.* (2006) cleared foreign-born recent immigrants are more exposed. Collectively, we notised low socioeconomic level was significant risk factor for for unfavourable pregnancy outcomes. Our result is in accordance with Judith *et al.* (1994), they found an increase in miscarriage in those with low socioeconomic status among women exposed to environmental chemicals. Moreover, Lee *et al.* (2005) showed in U.S. women of childbearing age, 20-49 years, that Black or Hispanic race/ ethnicity and poverty were associated with higher blood lead levels. Also, McKelvey *et al.* (2007) found blood lead was positively associated with non-Hispanic Black, White, or Asian race/ethnicity, compared to Hispanic and foreign birth. Also, Handley *et al.* (2007) illustrated that prevalence of blood lead levels ≥10 μg/dL was 12% in Latin, much higher than concurrent blood lead levels in U.S. population in general. Those women were more likely to be born in Mexico (96.0%).

We showed older age is risk factor for unfavourable pregnancy outcomes. This result was consistent with Arbuckle and Sever (1999). Further, bone lead has greater bioavailability in younger women than in olders; this could strongly contribute to higher BLLs in women of childbearing age (Rabinowitz, 1991 and Manton *et al.,* 2003). Bone lead is readily mobilised to blood, the effect of which is most apparent in older people (International Programme on Chemical Safety, 1995). Also, Lee *et al.* (2005) cleared in U.S. women of childbearing age, 20-49 years; higher maternal age was associated with higher BLLs. Further, McKelvey *et al.* (2007) found blood lead was positively associated with age. On the other hand, Graber *et al.* (2006) showed mean BLLs decreased with age by 0.032 μg/dL/year.

We reported primiparous was significant risk factor for unfavourable pregnancy outcomes. Multiparous women tend to have lower lead levels than primiparous women and the increases in maternal blood lead occurring during late pregnancy and lactation are lower relative to those in the first pregnancy (Rothenberg *et al.,* 1994). Blood lead level significantly decrease in a stepwise manner from pregnancy to pregnancy in multiparous women, implying that the greatest risk of lead toxicity lies with the first pregnancy (Manton *et al.,* 2003). Also,

spontaneous abortion was more frequent in primigravidas (Borja-Aburto *et al.,* 1999). Further, there is evidence that with closely spaced multiple pregnancies, maternal BLLs in subsequent pregnancies are lower (Rothenberg *et al.,* 1994). We observed menstrual disorder was significant risk factor. Kersemaekers *et al.* (1995) found association between occupational chemical exposures and menstrual disorders. Further, studies demonstrate high-level exposure to certain environmental chemicals can impair fertility, but the relationship to endocrine disruption remains speculative (Damstra *et al.,* 2002). Menstrual disorders/disturbances of ovulation may occur at BLLs of 2-3 μmol/L (Osorio and Windham, 1997). Also, we showed previous unfavourable pregnancy outcome was significant risk factor for unfavourable pregnancy outcomes. Borja-Aburto *et al.* (1999) cleared that their cases of spontaneous abortion were more likely to report a previous spontaneous abortion. Further, they observed that established risk factor was a previous spontaneous abortion.

We noticed urban residence was risk factor for unfavourable pregnancy outcomes. Lead's adverse effects associated with several negative pregnancy outcomes are reported to be widespread in urban cities (Bellinger *et al.,* 1991). Heavy traffic represents a source of lead exposures (Pocock *et al.,* 1994). Residents in countries still using leaded gasoline may be highly exposed (Albalak *et al.,* 2003). The recognition of the toxic effects of lead has prompted interventions that have resulted in reductions in lead exposure in many countries (Ettinger and Wengrovitz, 2010). In U.S., the sale of leaded fuel for use in on-road vehicles was banned (U.S. Environmental Protection Agency, 1996). A worldwide initiative to phase-out lead in gasoline has already stimulated important reductions in ambient air lead levels and population BLLs in some countries (Cortez-Lugo *et al.,* 2003). A complete phase-out of leaded gasoline was completed throughout the Latin American and Caribbean region by 2005 (Walsh, 2007). However, in some parts of Africa, Asia, and the Middle East, leaded gasoline is still common (Partnership for Clean Fuels and Vehicles, 2007). The impact of leaded fuel is more important in urban settings, given their higher vehicular density (Ettinger and Wengrovitz, 2010). Atmospheric lead in Europe ranges from 0.5 $\mu g/m^3$ in urban areas to 0.1 $\mu g/m^3$ in rural areas (Factor *et al.,* 1996). Meanwhile, the atmospheric lead levels encountered in Tahreer Square, Ramses street and Abasya Square in Cairo, Egypt, were 5, 4.5, and 4.5 $\mu g/m^3$, respectively (Fahim *et al.,* 1976). We sure these levels are now much more higher in Egypt on the assumption that there is much more higher increase in numbers of useing on-road vehicles. Ambient air lead should not exceed 1 $\mu g/m^3$ (International Programme on Chemical Safety, 1995). Also, we reported that living nearby hazardous environmental pollutants was risk factor for unfavourable pregnancy outcomes. Women living near hazardous wastes site or active smelters might be highly exposed (Garcia-Vargas *et al.,* 2001). Further, we showed living in old home was significant risk factor for unfavouable pregnancy outcomes. Our result is in consistent with Lee *et al.* (2005), they illustrated year house was built was associated, but not significantly, with higher BLLs. Also, renovating older homes exposed subgroups to lead. Lead-based paint was commonly used, but it was not banned from sale for residential use in U.S. until 1978 (Jacobs *et al.,* 2002). Lead-based paint hazards were more common in homes with low incomes (35.0%) vs. in homes with high incomes (19.0%) (Ettinger and Wengrovitz, 2010). Lead in paint and house dust is among the most common sources of exposure in U.S. adults. Exposure to lead-based paint and construction-related lead hazards occurs mainly during home repair, renovation, and remodeling activities conducted by the residents themselves or due to improper work practices of tradesmen and contractors (CDC, 2009). Also, lead still can be found in some metal water taps, interior water pipes, or pipes connecting a house to the main water pipe in the street (CDC, 2004). Lead found in tap water usually comes from the corrosion of older fixtures or from the solder that connects pipes. When water sits in leaded pipes for several hours, lead can leach into the water supply. Consumption of lead-contaminated water alone would not be likely to elevate BLLs in most adults to a level that is toxicologically significant, even exposure to water with a lead content of 15 ppb (U.S. Environmental Protection Agency, 1991). Risk will vary, according to the individual, the circumstances, and the amount of water consumed (Baum and Shannon, 1997). Also, Lee *et al.* (2005) added type of drinking water was associated, but not significantly, with higher BLLs.

Our study observed cigarette smoking and bango use were significant risk factors for unfavouable pregnancy outcomes. Lead exposures include smoking (Pocock *et al.,* 1994). Also, lead exposure can take through other sources as *Cannabis sp*; it can intoxicate user women (Gulson *et al.,* 1998). Cigarettes smoking and alcohol use have been associated with higher lead levels and should be avoided during pregnancy and lactation (Ettinger and Wengrovitz, 2010). They have an impact, alone and in combination and substance abuse related to cocaine and other drugs may also be associated with feto-toxic responses (Arbuckle and Sever, 1999). Windham *et al.* (1999) proved a moderate association with maternal smoking (adjusted OR for ≥5 cigarettes/day =1.3, 95 % CI: 0.9-1.8). Also, Chatenoud *et al.* (1998) showed women who smoked >10 cigarettes/day in the first trimester were at increased risk of miscarriage (OR=1.2, 95% CI: 1.0-2.1), but there are no relationship was evident between the number of cigarettes smoked before conception and the risk of spontaneous abortion. Also, our results were consistent with Lee *et al.* (2005), they showed alcohol use and cigarettes smoking were associated with higher BLLs. Further, McKelvey *et al.* (2007) found blood lead was positively associated with former and current smoking. Also, Borja-Aburto *et al.* (1999) showed cases of spontaneous abortion reported

spending time near a greater number of smokers at their homes and workplaces. Further, the cases were more likely to report alcohol use. But, the subclinical intoxication of non-pregnant women can cause fetal alterations in later pregnancies, by releasing of lead stored in the maternal bones. Because of misdiagnosis most of the time, the problem is not considered (Gulson *et al.,* 1998). On the other hand, Han and Gan (2003) stated the risks associated with environmental tobacco smoke exposure during pregnancy on its outcomes such as LBW, preterm delivery, spontaneous abortion and stillbirth were increased among non-smokers who had moderate alcohol or heavy caffeine consumption. Also, Harville *et al.* (2005) showed alcohol consumption was associated with higher cord lead relative to blood lead of the mother.

We rvealed there are physical risk factors for unfavourable pregnancy outcomes. These risk factors include exertion (Florack *et al.,* 1993), heavy lifting (Ahlborg *et al.,* 1990), noise exposure, shift work, night shifts (Nurminen, 1995), and exposure to X-Ray, high usage of magnetic fields and radiation (Magnavita and Fileni, 1995).

Our results cleared eating inadequate, unhealthy diet was significant risk factor for unfavouable pregnancy outcomes. This may make women more susceptible to increase blood lead. Adequate dietary intake of certain key nutrients (calcium, iron, zinc, and vitamins; C, D and E) is known to decrease lead absorption (Mahaffey, 1990). Low iron level (iron deficiency anemia) is associated with elevated blood lead levels. Also, calcium deficiency may increase bone turnover since maternal bone is a major source of calcium for the developing fetus and nursing infant (Ettinger and Wengrovitz, 2010). Also, low levels of phosphorus in the diet or high levels of fat can increase lead absorption (Department for Environment Food and Rural Affairs and Environment Agency, 2002). Further, lead can enter the food chain from contaminated soil or water, deposition from the air, or contact with food containers and processing. In U.S., dietary intakes of lead have been reduced due to removal of lead from gasoline, elimination of lead-soldered cans and lead-based printing ink on candy wrappers and bread bags, and changes to agricultural practices, such as banning of lead-arsenate pesticides (Bolger *et al.,* 1996). Traditional food products that are contaminated with lead may be brought into U.S. through unregulated routes (Handley *et al.,* 2007). Also, calcium supplements derived from animal bone may contain lead (Ross *et al.,* 2000).

We showed that women using tradetional medications as herbs are at risk for unfavourable pregnancy outcomes. Using of culturally-specific remedies and products is another source of lead exposure. Lead has been found in some alternative medicines and therapeutic herbs traditionally used by East Indian, Indian, Middle Eastern, and Hispanic cultures (Saper *et al.,* 2008). These alternative medicines can contain herbs, minerals, metals, or animal products. Lead and other heavy metals are put into certain folk medicines intentionally because these metals are thought to be useful in treating some ailments. Sometimes lead unintentionally gets into the folk medicine during grinding, coloring, or other methods of preparation. Lead has been found in powders and tablets given for arthritis, infertility, upset stomach, menstrual cramps, colic, etc. Chinese herbal tea is an example of these alternative therapies (Markowitz *et al.,* 1994). BLLs in individuals consuming contaminated herbal medicines have ranged from 90-137 µg/dL in (Wu, 2006). Also, we cleared traditional cosmetic use (as kohl) is significant risk factor for unfavourable pregnancy outcomes. Lead can be found in products such as kohl (Guidotti and Ragain, 2007). Kohl is a gray or black eye cosmetic applied to the conjunctival margins of the eyes, can contain up to 83.0% lead (Parry and Eaton, 1991). So, it can increase maternal BLLs. It is used in the Middle East, India, Pakistan, and some parts of Africa for medicinal and cosmetic reasons. It may be used by women of childbearing age (Moghraby *et al.,* 1989).

We reported stress is significant risk factor for unfavourable pregnancy outcomes. Stress produces physiologic reponses e.g. increases in catecholamines, and increases in use of alcohol, tobacco, and caffeine (Coulam and Stren, 1994). Catecholamines are able to reduce fetal vascularization and oxgen supply and thus, possibly induce abortion (Adler *et al.,* 1993). Also, higher maternal blood pressure was associated with higher cord lead relative to blood lead of the mother (Harville *et al.,* 2005).

Lastly, the most important limitations of this study were small sample size, limited geographical distribution, nature of the exposure, selection biases, and poor differential recall rates among cases and controls.

Conclusions And Recommendations:

The results of this study revealed gestational hypertension, PE/eclampsia, unfavourable pregnancy outcomes and neonatal intensive care admission are significantly common among women with BLLs ≥30 µg/dL. Women at risk to develop unfavourable pregnancy outcomes are those with low socioeconomic level, age group 30-35 years, interpregnancy space <2 years, preveious unfavourable pregnancy outcomes, primiparous, living in hazardous environment, and have hazardous occupations. No regular antenatal care, no adequate diet intake and eating foods exposed to lead pollutants are sinificant risk factors. Further, parental smoking, and traditional herbal medication use are sinificant risk factors. Also, hypertension, stress and UTIs are sinificant medical risk factors. We recommend women with risk factors for unfavourable pregnancy outcomes should have a more frequent antenatal care for monitoring and evaluation their conditions. Also, environmental, nutritional and

behavioral interventions are indicated for pregnant women to prevent undue exposures to the women, fetus and newborn. Smoking cessation and a strict policy of environmental lead exposure control can bring great benefits to the generations of children. Also, there is a substantial need to improve methodology that investigate the associations between lead exposure and unfavourable pregnancy outcomes. Lastly, further researches are needed for better understanding of biomedical and demographic risk factor issues of unfavourable pregnancy outcomes. Also, further studies in different areas and among different population in Egypt are needed to investigate this health problem.

Table 1: Frequncy distribution of the studied group of mothers with unfavourable pregnancy outcomes.

Types of cases	Number=246	Percent
All cases of mothers with unfavourable pregnancy outcomes (cases):		
Spontaneous abortion	200	81.3
Still birth	4	1.6
Premature	22	8.9
Low birth weight	20	8.1

Table 2: Blood lead and hemoglobin levels of the studied groups of women with unfavourable and favourable pregnancy outcomes.

Variables	Studied groups Cases (n=246) M±SD	Controls (n=246) M±SD	t-values	P-values
Blood lead levels (µg/dL)				
All women with unfavourable pregnancy outcomes (n=246):	29.46±6.72	28.61±6.53	1.423	0.9224
Spontaneous abortion (n=200)	29.68±6.73	28.61±6.53	1.692	0.9542
Others (still birth/premature/low birth weight) (n=46):	29.42±6.61	28.61±6.53	0.764	0.7752
Still birth (n=4)	29.43±6.64	28.61±6.53	0.245	0.5876
Premature (n=22)	29.41±6.61	28.61±6.53	0.544	0.7052
Low birth weight (n=20)	29.42±6.60	28.61±6.53	0.528	0.6981
Maternal hemoglobin levels (mg/dL)				
All women with unfavourable pregnancy outcomes (live born infants) (n=246):	9.83±1.47	11.15±1.32	-10.479	0.000
Spontaneous abortion (n=200)	9.84±1.49	11.15±1.32	-9.715	0.000
Others (still birth/premature/low birth weight) (n=46)	9.82±1.46	11.15±1.32	-5.754	0.000

Table 3: Blood lead levels of cases with unfavourable live borne infants and their infants.

Blood lead levels (µg/dL)	Cases (n=42) M±SD	Infants (n=42) M±SD	t-values	P-values
Cases with unfavourable pregnancy outcomes (live born infants) (n=42):	29.42±6.63	25.23±5.41	3.173	0.999
Premature (n=22)	29.41±6.61	25.22±5.42	2.557	0.993
Low birth weight (n=20)	29.42±6.60	25.24±5.43	2.463	0.991

Table 4: Blood lead levels of cases with unfavourable pregnancy outcomes and their husbands who presented and agreed to give blood samples.

Blood lead levels (µg/dL)	Cases (n=246) M±SD	Husbands (n=52) M±SD	t-values	P-values
Cases with unfavourable pregnancy outcomes (n=246):	29.46±6.72	29.94±4.28	-0.656	0.256
Spontaneous abortion (n=200)	29.68±6.73	29.98±4.31	-0.393	0.347
Others (still birth/premature/low birth weight) (n=46)	29.42±6.61	29.82±4.24	-0.351	0.363

Table 5: Blood lead and hemoglobin levels of the live borne infants of women with unfavourable pregnancy outcomes and their control infants.

Variables	Live borne infants of cases (n=42) ±SD	Infants of controls (n=42) M±SD	t-values	P-values
Blood lead levels (µg/dL)	25.23±5.41	23.19±5.11	1.777	0.96056
Hemoglobin levels (mg/dL)	13.16±3.48	15.47±4.82	-4.698	0.000001

Table 6: Impacts of maternal blood lead levels ≥30 µg/dL of the studied groups on the mothers and pregnancy outcomes.

Variables	Mothers' blood lead ≥30 µg/dL (n=224)		Mothers' blood lead <30 µg/dL (n=268)		χ^2 t*-values	P-values
	No.	%	No.	%		
Gestational hypertension: Yes	42	18.8	26	9.7	7.64	0.006
Pre- eclampsia/eclampsia: Yes	21	9.4	11	4.1	4.74	0.03
Unfavourable pregnancy outcomes:						
Spontaneous abortion	138	61.6	62	23.1	73.27	0.000
Others (still birth/premature/low birth weight)	34	15.2	12	4.5	15.25	0.0001
Favourable pregnancy outcomes	52	23.2	194	72.4	161.63	0.000
Congenital anomalies:	(n=83)		(n=205)			
Yes	3	3.6	1	0.5	2.24	0.134

1-minute Apgar score (M±SD)	(n=83) 4.14±1.26		(n=205) 6.06±1.02		12.342*	0.000
5-minute Apgar score (M±SD)	(n=83) 6.01±1.42		(n=205) 8.24±1.02		13.012*	0.000
Maternal Hb (g/dL) (M±SD)	9.62±1.36		11.34±1.45		13.555*	0.000
Infant Hb (g/dL) (M±SD)	(n=83) 13.10±3.32		(n=205) 17.52±4.67		9.038*	0.000
Neonatal intensive care admission:	(n=83)		(n=205)			
Yes	23	27.7	5	2.4	40.16	0.000
Perinatal deaths:	(n=83)		(n=205)			
Yes	2	2.4	1	0.5	0.66	0.416

Table 7: Distribution of the studied cases of unfavourable pregnancy outcomes and control group according to their socioeconomic risk factors.

Items of parental socioeconomic levels	Studied groups				OR (95% CI)
	Cases (n=246)		Controls (n=246)		
	No.	%	No.	%	
Maternal					
Educational status:					
Illiterate, read and write	95	38.6	51	20.7	2.41 (1.58-3.67)
Elementary	37	15.0	57	23.2	0.59 (0.36-0.95)
Secondary	93	37.8	111	45.1	0.74 (0.51-1.08)
University	21	8.6	27	11.0	0.76 (0.40-1.43)
Occupation status:					
House wife	97	39.4	149	60.6	0.42 (0.29-0.62)
Unskilled labor	57	23.2	41	16.7	1.51 (0.94-2.42)
Semi-skilled/skilled labor	67	27.2	37	15.0	2.11 (1.32-3.39)
Professional	25	10.2	19	7.7	1.35 (0.69-2.64)
Paternal					
Educational status:					
Illiterate, read and write	82	33.3	46	18.7	2.17 (1.41-3.37)
Elementary	39	15.9	57	23.2	0.62 (0.39-1.01)
Secondary	97	39.4	112	45.5	0.78 (0.54-1.13)
University	28	11.4	31	12.6	0.89 (0.50-1.59)
Occupation status:					
Unskilled labor	118	48.0	81	32.9	1.88 (1.28-2.75)
Semi-skilled/skilled labor	107	43.5	136	55.3	0.62 (0.43-0.90)
Professional	21	8.5	29	11.8	0.70 (0.37-1.31)
Socioeconomic level					
Low	96	39.0	51	20.7	2.45 (1.61-3.73)
Middle	129	52.4	168	68.3	0.51 (0.35-0.75)
High	21	8.6	27	11.0	0.76 (0.40-1.43)

Table 8: Distribution of of the studied cases of unfavourable pregnancy outcomes and control group according to their personal risk factors.

Personal and clinical risk factors	Cases (n=246)		Controls (n=246)		OR (95% CI)
	No.	%	No.	%	OR (95% ECL)*
Mother's age (years):					
20-24	21	8.6	130	68.3	0.8 (0.05-0.14)
25-29	95	38.6	78	31.7	1.36 (0.92-2.00)
30-35	130	52.9	38	15.5	6.13 (3.92-9.63)
Parity:					
Primi	158	64.2	101	41.1	2.58 (1.76-3.77)
Multi	88	35.8	145	85.9	0.39 (0.27-0.57)
Interpregnancy space (years):					
<2	167	67.9	83	33.7	4.15 (2.80-6.16)
≥2	79	32.1	136	55.3	0.38 (0.26-0.56)
History of menstrual disorders:					
Yes	56	25.0	32	11.9	1.97 (1.19-3.26)
History of preveious unfavourable pregnancy outcomes:					
Yes	31	12.6	11	4.5	3.08 (1.45-6.69)
Residence:					
Rural	104	42.3	137	55.7	0.58 (0.4-0.85)
Urban	142	57.7	109	44.3	1.72 (1.18-2.49)
Living nearby heavy traffic/chimney/burned garbge:					
Yes	186	75.6	121	49.2	3.2 (2.14-4.79)
Living in old home:					
Yes	192	78.1	137	55.7	2.83 (1.87-4.27)
Hazardous parental occupation:					
Maternal	31	13.48	12	5.17	2.81 (1.35-6.96)
Paternal	41	86.52	23	94.83	1.94 (1.09-3.47)
Physical factors:					
Unusual exertion/heavy lifting	92	37.4	47	19.1	2.53 (1.65-3.89)
Noise exposure (community/occupational)	65	26.4	53	21.6	1.31 (0.85-2.02)
Shift work/night shifts	7	2.9	3	1.2	2.37 (0.53-14.36)*

Table 9: Distribution of the studied cases of unfavourable pregnancy outcomes and control group according to life-style and behavioral risk factors.

Variables	Studied groups Cases (N=246)		Controls (N=246)		OR (95% CI) OR (95% ECL)*
	No.	%	No.	%	
Regular antenatal care:					
No	183	74.4	126	51.2	2.77 (1.86-4.12)
Adequate, healthy diet intake:					
No	174	70.7	119	48.4	2.85 (1.75-3.81)
Eating foods exposed to lead pollutants:					
Yes	149	60.6	103	41.9	2.13 (1.46-3.11)
Maternal smoking:					
Yes	10	4.1	2	0.8	5.17 (1.08-48.88)*
Husband's smoking:					
Yes	189	76.8	117	47.6	3.66 (2.44-5.49)
Maternal bango/alchol use:					
Yes	53	21.6	27	11.0	2.23 (1.31-3.80)
Medication during 1st trimstr:					
Yes	56	22.8	37	15.0	1.66 (1.03-2.70)
Traditional herbal medication use:					
Yes	89	36.2	41	16.7	2.83 (1.82-4.43)
Traditional cosmetics (kohl) use:					
Yes	92	37.4	63	25.6	1.74 (1.16-2.60)

Table 10: Distribution of the studied cases of unfavourable pregnancy outcomes and and control group according to medical risk factors.

Medical risk factors	Cases (n=246)		Controls (n=246)		OR (95% CI) OR (95% ECL)*
	No.	%	No.	%	
Gestational diabetes mellitus	14	5.7	6	2.4	2.41 (0.85-7.78)*
Hypertension	11	4.5	2	0.8	5.71 (1.22-53.41)*
Stress	29	11.8	7	2.9	4.56 (1.9-12.56)*
Urinary tract infections (UTIs)	32	13.0	11	4.5	3.19 (1.5-6.92)

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