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Lead Level in Pregnant Women Suffering from Pre-eclampsia in Dakahlia, Egypt

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Abstract

Background: Lead toxicity is a prevalent health problem in both developed and developing countries. One of the proposed mechanisms for lead-induced organ damage is oxidative stress. Oxidative stress is well-associated with the pregnancy disorder, pre-eclampsia. Exposure to lead may be one of the sources of the oxidative stress that leads to development of pre-eclampsia in pregnant women.

Objective: To test if blood lead level of pregnant women suffering from pre-eclampsia is higher than the normal limit.

Methods: Using atomic absorption spectrophotometry, blood lead level was measured in 115 pregnant women suffering from pre-eclampsia and compared to its level in a comparison group of 25 healthy pregnant women in Dakahlia governorate, Egypt.

Results: The mean±SD blood lead level was 37.68±9.17 µg/dL in women with pre-eclampsia; the value in the comparison group was 14.5±3.18 µg/dL (p<0.001).

Conclusion: Pre-eclampsia is significantly associated with a high blood lead level.

Keywords: Lead poisoning; Pre-eclampsia; Pregnancy complications

Introduction

Lead is toxic and induces a broad range of harmful effects on various organs including the reproductive system.¹ Lead poisoning remains an urgent public health problem in both developed and developing countries.²

Pre-eclampsia, the most common medical complication of pregnancy, is as-

sociated with oxidative stress.³ One of the most contributors to the state of oxidative stress is exposure to excess toxic metals in the environment and the deficiency of bio-elements necessary for antioxidant defense mechanisms.⁴

Long-term exposure during pregnancy to even low concentrations of toxic metals, which have the ability to accumulate, often leads to irreversible damage to fetal

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developments and maternal morbidities including pre-eclampsia.⁵

Lead is one of the heavy metals people most commonly exposed to in the environment. Lead is not biodegradable and the concerns for ecotoxicity of lead are increasing.⁶ Placental blood lead levels at or even below 10 µg/dL were associated with adverse pregnancy outcomes.⁷

As a result of mining and industrialization, lead is ubiquitous in the environment. Lead is found in air, water, soil and as a contaminant in humans as it has no known physiological function.⁸ Common sources of lead exposure include industrial and mining activities, paint, dust, soil, water, air, workplaces, food, trinkets, ethnic folk remedies and cosmetics.⁹

The black eye cosmetic, *kohl*, the main component of which is lead sulfide, has very high lead concentration, and is considered an important source of lead exposure, particularly for women and children.¹⁰

Pregnant women are exposed to lead through occupational and non-occupational sources. Some sources are more common in pregnant women; for example, they may use more herbal products to treat the symptoms of pregnancy. Also, pica is reported to be one of the common causes of high lead levels in women.¹¹ We conducted this study to compare the blood lead level (BLL) of pregnant women suffering from pre-eclampsia with a comparison group.

Patients and Methods

In this cross-sectional study we compared 115 pregnant women suffering from pre-eclampsia with a comparison group consisted of 25 full-term healthy pregnant women. The participants were recruited from Obstetrics and Gynecology Department and out-patient clinic of Mansoura University Hospital (MUH), Mansoura,

Egypt.

The study was approved by the local ethical committee before beginning and informed written consents were obtained from all patients included in this study after explaining the study objectives.

A thorough history with particular attention to environmental exposure to pollutants was taken from each participant. Demographic data and common risk factors for developing lead toxicity were gathered from each participant; they included age, residence place, living near a busy street, occupation, their husband occupation, passive smoking, use of traditional cosmetics and *kohl*, receiving vitamins, materials used for building their house, history of house remodeling, use of canned food, use of lead-glazed ceramic, use of herbal medical products and pica. Pre-eclampsia was considered if the blood pressure increased to 140/90 mm Hg or more, and if protein is detected in urine with or without edema in a pregnant woman after 20 weeks of gestation.¹²

Occupations were classified according to Callan and Hinwood.¹³ They reviewed different sources of lead exposure and various scenarios that could explain why lead still remains a pollutant of concern. They stated that several occupations are considered “high-risk” for lead exposure. Some of high-risk occupations are painting, construction work (*e.g.*, sanding, scrapping, blasting), mining, and lead-acid battery manufacturing which are still important sources of lead exposure in developing countries. Some jobs are considered “moderate-risk” for lead exposure; they are glass blowing, wire and cable manufacturing and mechanics repairing.¹³ Occupations “low-risk” for lead exposure include jobs where there is exposure to lead fumes as car drivers, gas-station attendants and traffic police officers particularly in developing countries where leaded-gasoline is still used.¹³

For more information on blood lead level and pregnancy outcome see www.theijoem.com/ijoem/index.php/ijoem/article/view/94/187

For more information on lead and infertility see www.theijoem.com/ijoem/index.php/ijoem/article/view/64/145 and www.theijoem.com/ijoem/index.php/ijoem/article/view/85/185

For more information on lead poisoning in the world and Iran see www.theijoem.com/ijoem/index.php/ijoem/article/view/28/61

TAKE-HOME MESSAGE

- Maternal blood lead level is closely related to pre-eclampsia/hypertension of pregnancy.
- Lead is a ubiquitous environmental toxin that is accumulated in the body tissues and bone.
- Lead in bone is mobilized during pregnancy to the blood stream.
- Good nutrition and calcium supplementation is mandatory during and, even before pregnancy to minimize lead release from bone stores.
- Screening for blood lead level may be useful for women with history of pre-eclampsia to begin chelation therapy before deciding to be pregnant again.
- There should be searching for new sources of lead exposure and development of strict preventive measures for this public health problem.

Blood sampling and analysis

Three mL of peripheral venous blood were taken and collected in tubes with heparin for blood lead level measurement. Sample preparation was carried out under clean conditions using deionized water.¹⁴ All chemicals were ultra pure reagent grade, nitric acid (HNO₃) BDH 69% and perchloric acid (HClO₃) 70%. All glassware and plasticware were acid-treated—washed three times with deionized water then soaked in 20% HNO₃ overnight and then rewashed three times with deionized water and dried until used.

The first step in the analysis was nitric acid-perchloric acid digestion. One mL whole blood was pipetted into 50 mL pyrex beaker; then, 4 mL nitric acid was added. A watch glass was placed on the

top of a beaker. This mixture was placed on low heat; the temperature was then slowly increased to 120 °C—the point at which nitric acid began to distill. Then, the heating rate increased gradually. Near dryness, the watch glass was removed and 1 mL perchloric acid was added and the digestion was continued. The process was complete with the appearance of a white fume of perchloric acid. Near dryness, the watch glass was removed; few mL of deionized water were added and heating was stopped. After cooling, the digestion was completed to 10 mL by deionized water and stored in 10 mL acid-treated polyethylene tube.¹⁴

Measurement of lead was made by a Perkin-Elmer double beam 2380 atomic absorption spectrophotometry that adapted Perkin Elmer hollow-cathode lamps and conventional 10 cm slot burner heat for an air-acetylene flame.

We used the optimum instrumental conditions for determination of lead provided by AAS.¹⁵

Statistical analysis

We used SPSS® ver 10 for Windows® (SPSS, Inc., Chicago, IL, USA) for data analysis. Qualitative data were presented as number and percentage; quantitative data were presented as mean±SD. The χ^2 test was used to test the association between two categorical variables. Correlation between BLL and manifestations of pre-eclampsia was measured by Pearson correlation coefficient. A p value <0.05 was considered statistically significant.

Results

The mean±SD blood lead level was 37.68±9.17 µg/dL in women with pre-eclampsia; the value in the comparison group was 14.5±3.18 µg/dL (p<0.001). Characteristics of the two groups are presented in Table 1. While more than 90%

Table 1: Frequency distribution of demographic variables and risk factors for lead toxicity in the studied women with pre-eclampsia and the comparison group

	Women with pre-eclampsia (n=115)	Comparison group (n=25)	p value
Age (yrs)			
<25	56 (48.7%)	15 (60%)	0.30
≥25	59 (51.3%)	10 (40%)	
Residence			
Rural	57 (49.6%)	15 (60%)	0.34
Urban	58 (50.4%)	10 (40%)	
Living near busy street			
No	65 (56.5%)	17 (68%)	0.29
Yes	50 (43.5%)	8 (32%)	
Occupation			
House wife	93 (80.9%)	18 (72%)	0.5
Farmer	7 (6.1%)	3 (12%)	
Employer	15 (13.0%)	4 (16%)	
Husband Occupation			
Low risk	66 (57.4%)	23 (92%)	0.004
Moderate risk	27 (23.5%)	2 (8%)	
High risk	22 (19.1%)	0 (0%)	
Passive smoking			
No	64 (55.7%)	16 (64%)	0.44
Yes	51 (44.3%)	9 (36%)	
Use of traditional cosmetics and <i>kohl</i>			
No	64 (55.7%)	15 (60%)	0.69
Yes	51 (44.3%)	10 (40%)	
Vitamin therapy			
No	16 (13.9%)	3 (12%)	0.94
Yes	99 (86.1%)	22 (88%)	

Continued

Table 1: Frequency distribution of demographic variables and risk factors for lead toxicity in the studied women with pre-eclampsia and the comparison group

	Women with pre-eclampsia (n=115)	Comparison group (n=25)	p value
Building material			
Clay	11 (11.0%)	2 (8%)	0.67
Concrete	30 (30.0%)	5 (20%)	
Recent paint	22 (22.0%)	6 (24%)	
Old paint	37 (37.0%)	12 (48%)	
House remodeling			
No	102 (88.7%)	23 (92%)	0.62
Yes	13 (11.3%)	2 (8%)	
Use of Canned Food			
No	97 (84.3%)	21 (84%)	0.96
Yes	18 (15.7%)	4 (16%)	
Use of lead-glazed ceramic and pottery			
No	84 (73.0%)	20 (80%)	0.47
Yes	31 (27.0%)	5 (20%)	
Use of herbal medicine and pica			
No	104 (90.4%)	23 (92%)	0.8
Yes	11 (9.6%)	2 (8%)	
Total	115 (100.0%)	25 (100%)	

of women in the comparison group had a husband with low-risk occupation for lead toxicity, more than 40% of women with pre-eclampsia were wives of men with a moderate- or high-risk occupations ($p=0.004$) (Table 1). The two groups had no significant difference regarding other studied demographic variables and risk factors (Table 1).

In women with pre-eclampsia, BLL was significantly correlated with proteinuria ($r=0.44$, $p<0.001$), diastolic blood pressure ($r=0.44$, $p<0.001$), and systolic

blood pressure ($r=0.26$, $p=0.01$).

Discussion

Pre-eclampsia is a complex pregnancy-specific systemic disorder that, despite its great polymorphism, the criteria for its diagnosis, *i.e.*, a systolic blood pressure > 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg and proteinuria ≥ 0.3 g/day, have not been changed over the past decade. Clinical features and laboratory abnormalities determine the severity of the

disorder.¹⁶

Abnormal vascular response to placentation is thought to be the main underlying mechanism for the development of pre-eclampsia. In spite of the fact that the exact pathophysiology of this multisystem disorder is still unclear, pre-eclampsia is associated with a state of oxidative stress.¹⁷

In this study, BLL was measured in a group of pregnant women suffering from pre-eclampsia and compared it to a comparison group of healthy pregnant ones. There was also inquiry to find the possible sources of lead exposure to the pregnant women.

We observed a statistically significant difference in the mean BLL measured in pregnant women suffering from pre-eclampsia compared to a comparison group of healthy pregnant women ($p < 0.001$). There was also a significant correlation between the BLL and manifestations of pre-eclampsia—proteinuria, and both systolic and diastolic blood pressure in women suffering from pre-eclampsia. These findings were in keeping with the results of Rothenberg, *et al*,¹⁸ who found a significant positive association between BLL and elevated blood pressure in pregnant females. The investigators also reported lead-associated elevated blood pressure during pregnancy, even when the measured BLL was within the acceptable range. Rothenberg, *et al*,¹⁹ believe that the lead accumulated in bone would cause hypertension even if the BLL is within the acceptable range.

Our findings, however, are in contrast with the findings of Yao and Huang²⁰ who measured BLL in a group of pregnant women to determine the association between maternal BLL and pregnancy complications. They recorded a mean maternal BLL of 4.34 $\mu\text{g}/\text{dL}$ and concluded that BLL is not correlated with pregnancy complications or neonatal physical and

neurobehavioral development, but it is positively correlated with maternal hemoglobin concentration. This difference can be explained by the relatively low BLL recorded in this study. At this level, lead affects hemoglobin synthesis and causes anemia; its effects on blood pressure and neonatal physical and neurobehavioral development would appear at higher blood levels.

There is evidence of a causal relationship between lead exposure and hypertension.^{21,22} A study revealed association between bone lead content and blood pressure in a cohort of 590 men.²³ A meta-analysis of 58 518 subjects from both the general population and occupationally-exposed groups from 1980 to 2001 in Belgium suggested a weak, but significant association between BLL and blood pressure.²⁴ Elevated blood pressure is more pronounced in middle age than in young age.²²

The mechanism proposed for lead-induced hypertension looks the same as the mechanism anticipated for essential hypertension. It is believed that lead-induced hypertension is mediated by vascular and nephrotoxic mechanisms.²⁵

BLL is sometimes a false indicator of the association of lead to hypertension. De Castro and Medley²⁶ noticed that relying only on BLL for assessment of the risk of lead-induced hypertension may give false results as lead has a multi-compartmental pharmacokinetic model; at the first phase, it is only in blood; later on, it will move to other organs (*e.g.*, the central nervous system and cardiovascular system). Finally, it is stored in bones. The investigators found high blood pressure in patients despite low BLLs—these patients showed elevated bone lead content.²⁷

The BLL found in the comparison group of healthy pregnant women in this study was higher than the accepted range in many countries. In the USA, strict pre-

ventive strategies have been established to prevent lead exposure to lower BLL in population to $<10 \mu\text{g}/\text{dL}$.^{28,29}

The remarkably high BLLs found in participants of this study may be attributed to the high prevalence of environmental pollution in many developing countries including Egypt.² Also, mobilization of lead from bone during pregnancy results in a significant gestational increase in maternal BLLs.³⁰

We found that exposure of husband of women with pre-eclampsia to lead was significantly higher than those of the comparison group. The at-risk husbands may expose their wives through lead particles in their clothes that they carry to home. It was shown that workers with high-risk occupations of lead exposure carry the risk of elevated BLLs for their family members.^{31,32}

Lack of association between the elevated BLL in pregnant women with pre-eclampsia and other environmental and demographic factors was also reported earlier.³³ However, this finding does not fit with that of Mitra, *et al*,³⁴ who found that children living in urban and industrialized areas have higher BLLs than those living in rural non-industrialized areas.

Lin, *et al*,³⁵ explained the elevated BLLs observed in some rural areas by the fact that some villages are polluted with high concentrations of lead in soil and household dust that subsequently carry the risk of lead exposure to the population there, causing elevated BLLs. One report stated that pregnant women may be exposed to lead from tobacco smoke.³⁶

Our findings are in keeping with the results of Bakhireva, *et al*,³⁷ who found that use of traditional/folk remedies and cosmetics, seasonings and food products are not predictive of elevated BLLs. However, some researchers found a positive association between elevated BLLs in pregnant women and pica, use of non-commercial

pottery and living in old houses. We found no association between the distribution of these risk factors and development of high BLL and pre-eclampsia.

Zolaly, *et al*,³⁸ studied risk factors of lead exposure in certain districts in Saudi Arabia and found that BLLs in women were higher than men. They found a positive association between the elevated BLLs and use of toothpaste, use of *kohl*, putting colored toys in the mouth, use of both canned food and canned juice, use of lip gloss in women, and different methods of handling newspaper while preparing food.

The insignificant difference between the women with pre-eclampsia as compared to the comparison group of healthy pregnant women regarding vitamin therapy may reflect that vitamins, despite of their antioxidant properties, could not prevent or decrease hypertension in pregnancy—it seems that the hypertension with pregnancy is, in part, caused by lead and vitamin supplementation could not counteract that. This finding is in keeping with some reports that indicated vitamins C and vitamin E supplementation, despite of their potent antioxidant properties, can neither prevent nor treat pre-eclampsia.³⁹

This cross-sectional study had some limitations; the low sample size of the studied groups, especially that of the comparison group made it difficult to evaluate the effect of studied risk factors with a high level of certainty. Future efforts are needed to examine this issue in longitudinal studies. Sources of lead exposure should be identified and strategies should be established to control lead exposure, particularly in pregnant women.

Conflicts of Interest: None declared.

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