Taiwanese Journal of Obstetrics & Gynecology 58 (2019) 60–63

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Original Article

Association of raised blood lead levels in pregnant women with preeclampsia: A study at tertiary centre

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ARTICLE INFO

Article history:
Accepted 13 August 2018

Keywords:
Lead
Preeclampsia
Heavy metal
Pregnancy

ABSTRACT

Objective: This study aims to find the blood lead levels in pregnant women and its association with pre-eclampsia.

Material and methods: The study included 44 healthy pregnant females and 23 pre-eclamptic women. Demographic data and common risk factors for lead toxicity were recorded including age, residence, occupation, husband occupation, passive smoking, use of cosmetics, kajal, surma, receiving supplements/vitamins, history of house remodelling, plumbing, source of potable water, paint in house, use of lead-glazed ceramic and pica. Venous blood was collected and lead level was determined by atomic absorption spectrometry.

Results: The mean blood lead level was 2.38 ± 2.43 ug/dL in controls and 3.42 ± 2.18 ug/dL in pre-eclamptic women which was significantly higher ($p = 0.0132$). Strong correlation of BLL was observed with blood pressure in pre-eclamptic women. Pre-eclamptic patients were observed to be at increased risk of being lead exposed in terms of occupation and living conditions.

Conclusion: Higher blood lead level is associated with increased risk of preeclampsia. Patients should be counselled for lifestyle modification to prevent complications.

Introduction

Preeclampsia is a pregnancy-specific disorder defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg beginning after the 20th week of gestation with proteinuria ≥300 mg per 24 h [1,2]. The clinical continuum of pre-eclampsia ranges from mild to severe. Preeclampsia has remained a significant public health threat in both developed and developing countries contributing to maternal and perinatal morbidity and mortality globally [3–5]. The prevalence of preeclampsia varies in different populations and in different ethnic groups [6–8]. The incidence of preeclampsia is reported to be 8–10% in India. According to a study, the prevalence of hypertensive disorders of pregnancy was 7.8% with preeclampsia in 5.6% of the study population in India [9,10].

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 developments and maternal morbidities [11]. Lead is a heavy metal widely prevalent in atmosphere and is known to cause various health related side effects. Lead is not biodegradable and exposure to even low lead levels can affect developing fetus as well as maternal health [12]. Lead is a ubiquitous toxin which accumulates in the body tissues and bones. Lead in bone is mobilized to blood stream during pregnancy [13]. Blood lead levels increase from 24 weeks of pregnancy until delivery, because of an increase in bone turnover in this period [14].

A number of studies report association of lead with a wide range of negative pregnancy outcomes including developmental delays, early membrane rupture, low birth weight, spontaneous abortion, complications during pregnancy, increased prenatal mortality and repressed postnatal growth [2]. In addition, prenatal exposure is an important cause of childhood lead poisoning [15]. The underlying pathophysiology of pre-eclampsia is not known but oxidative stress

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https://doi.org/10.1016/j.tjog.2018.11.011

is associated with it [16]. Lead can be one of the sources of oxidative stress leading to development of pre-eclampsia. We conducted a study to estimate blood lead levels (BLL) in pregnant women and its correlation with preeclampsia.

Materials and methods

This was a cross sectional study carried out in the Department of Obstetrics & Gynecology and Biochemistry at All India Institute of Medical Sciences, Jodhpur from February 2017 to October 2017. The ethical clearance from the institutional ethical committee was obtained to carry out the study. A total of 84 pregnant women attending Obstetrics & Gynecology outpatient department were screened for the study. Out of these, 11 patients did not give consent, four patients were found to have gestational diabetes mellitus, and two patients had chronic hypertension so they were excluded from the study. Forty-four healthy pregnant as controls and 23 pre-eclamptic pregnant women were included in the study. Pregnant women with normal blood pressure, absence of proteinuria and without any other systemic or endocrine disorder were taken as controls. Pre-eclampsia was considered with blood pressure of 140/90 mm Hg or more, with protein in urine with or without edema in pregnant woman after 20 weeks of gestation. All subjects included were in their third trimester. Informed consent was obtained. Patients with history of chronic hypertension, renal disease, and diabetes were excluded from the study. Thorough history with particular emphasis on environmental exposure to lead was taken. Demographic data and common risk factors for developing lead toxicity were recorded from each participant which included age, residence place, living near a busy street, occupation, husband occupation, passive smoking, use of traditional cosmetics and kajal, surma, receiving supplements/vitamins, materials used for building their house, history of house remodelling, plumbing, source of potable water, paint in house, use of lead-glazed ceramic, use of herbal medical products and pica.

Venous blood (3 ml) with aseptic precautions was collected in EDTA (ethylene di-amine tetra acetic acid) vials mixed properly and stored at −20° till further analysis. Lead was determined directly in whole blood using Graphite Furnace Atomic Absorption Spectrometry (Thermofisher Scientific, USA) using defined protocol. QuadLine background correction was used throughout during the estimation [17]. AnalaR grade Ammonium phosphate, Triton X-100 and nitric acid were used as mixed matrix modifiers. Calibration was performed by using working standards of Pb of different strengths (0,50,100 and 200 μg/dL) prepared daily in 0.2% HNO3 by serial dilution of a master standard (Pb 1000 mg/L) from Thermofisher Scientific, USA. Blood samples were prepared in acid washed autosampler cups immediately before analysis.100 μl of whole blood was added to 1900 μl of matrix modifier solution (1 g/L of $NH_4H_2PO_4$ prepared in 0.2% v/v nitric acid and 0.1%Triton X-100) to make a total volume of 2 ml for autosampler cup as described elsewhere [18]. Blood lead level was measured at wavelength of 283.3 nm. The furnace temperature was standardized (110C for 25s, 800C for 10s, 2100C for 3s and 26oo for 3s) with argon flow rate of 0.2 L/min. Three level quality control (BioRad, USA) was used before BLL estimation.

Anthropometric data and serum levels of lead in study groups were analysed using Graphpad Instat, USA. The values were expressed as mean ± SD. Pearsons correlation was performed to determine the relation of lead with maternal age, gestational age, BMI, systolic and diastolic blood pressure in control group and pre-eclamptic group. P value < 0.05 was considered significant.

Results

The mean BLL in controls was 2.38 ± 2.43 ug/dL (median 1.7 ug/dL, range 0.16–10.12 ug/dL) whereas in the pre-eclamptic pregnant women, BLL was 3.42 ± 2.18 ug/dL (median 2.96 ug/dL, range; 1.28–8.6 ug/dL) which was found to be significantly higher ($p = 0.0132$) in comparison to the controls (Table 1).

The mean age in control group and pre-eclamptic group was comparable as 24.54 ± 3.6 years and 27.34 ± 6.4 years, respectively.

Mean gestational age in control group was 30.72 ± 4.47 weeks whereas in pre-eclamptic group it was 32.17 ± 3.9 weeks which was not significantly different ($p = 0.09$). No correlation of BLL with gestational age ($r = 0.156$, $p = 0.47$) was observed.

Mean BMI in control group was 22.68 ± 4.06 kg/m^2 whereas in pre-eclamptic group it was 26.74 ± 4.04 kg/m^2 which was significantly higher in comparison to control group ($p < 0.0001$) but no correlation of BLL with BMI ($r = -0.108$, $p = 0.62$) was observed.

It was found that mean value of systolic arterial blood pressure (SBP) of control group was 105.45 ± 9.3 mmHg, while in pre-eclamptic group the SBP was 152.6 ± 12.9 mmHg. There was significant difference in the value of SBP between control and pre-eclamptic group ($p < 0.0001$).

The diastolic arterial blood pressure (DBP) was found to be significantly high in pre-eclamptic group (102.95 ± 13.34 mmHg) compared to control group (65.54 ± 7.9 mmHg) ($p < 0.001$). Pearson correlation was carried out for BLL and blood pressure, Body Mass Index (BMI) and gestational age (Table 2). Significant correlation between BLL and systolic blood pressure ($r = 0.71$, $p < 0.0001$) and diastolic blood pressure ($r = 0.57$, $p = 0.004$) was found. The demographic and other risk factors were estimated for control and pre-eclamptic group (Table 3). More percentage of pre-eclamptic group patients were illiterate (45.4%), exposed to passive smoking (72.6%), consumed no vitamin supplements (67.6%), had partners with high risk occupation (54%), and did not have water purification systems at home (96.7%). In this subset 45.45% had their houses recently painted.

Discussion

Lead is a toxic heavy metal known to cause extensive environmental pollution due to its environmental persistence and transportability with a wide range of acute and chronic toxic effects [19].

Table 1
Anthropometric data and BLL in study groups.

	Control (N = 44) Mean ± SD	Pre-eclamptic (N = 23) Mean ± SD	P value
Age (years)	24.54 ± 3.6	27.34 ± 6.4	0.08
BMI (kg/m^2)	22.68 ± 4.06	26.74 ± 4.04	<0.0001*
Gestational age (weeks)	30.72 ± 4.47	32.17 ± 3.9	0.09
Systolic blood pressure (mmHg)	105.45 ± 9.3	152.6 ± 12.9	<0.0001*
Diastolic Blood pressure (mmHg)	65.54 ± 7.9	102.95 ± 13.34	<0.001*
BLL (μg/dL)	2.38 ± 2.43	3.42 ± 2.18	0.013*

$p < 0.05$ is considered significant, BLL: blood lead level.

Table 2
Correlation of BLL with different variables in Pre-eclamptic subset.

BLL vs BMI (kg/m^2)	$r = -0.108$, $p = 0.62$
BLL vs Gestational age (weeks)	$r = 0.156$, $p = 0.47$
BLL vs Systolic blood pressure (mmHg)	$r = 0.71$, $p < 0.0001$
BLL vs Diastolic Blood pressure (mmHg)	$r = 0.57$, $p = 0.004$

Table 3
Demographic variables in pre-eclamptic and control groups.

S no.	Variables	Controls (N = 44)	Pre-eclamptic group (N = 23)
1	Age		
	<25 years	52.1%	54.5%
	>25 years	47.9%	45.5%
2	Residence		
	Urban	52.2%	45.5%
	Rural	47.8%	54.5%
3	Living near busy street		
	Yes	8.7%	9%
	No	91.3%	91%
4	Occupation		
	Housewife	78.3%	72.7%
	Employed	13%	27.3%
	Student	8.7%	–
5	Education		
	Illiterate	13.04%	45.4%
	School	47.82%	27.27%
	Graduate & above	39.14%	27.27%
6	Husband occupation		
	low risk	74%	19%
	Moderate Risk	21.7%	27%
	High Risk	4.3%	54%
7	Passive smoking		
	Yes	17.4%	72.6%
	No	82.6%	27.4%
8	Cosmetics/kajal/sindoor		
	Yes	80.6%	54%
	No	19.4%	46%
9	Vitamin consumption		
	Yes	69.5%	32.4%
	No	30.5%	67.6%
10	Herbal/ayurvedic medicines		
	Yes	17.4%	9.1%
	No	82.6%	89.9%
11	Water Purifier		
	Yes	17.4%	3.3%
	No	82.6%	96.7%
12	Building material		
	Clay	4.5%	27.3%
	Concrete	95.6%	72.7%
	Recent paint	17.4%	45.45%
	Old Paint	52.17%	54.54%
	No Paint	30.4%	–

Lead exposure for prolonged duration as well as in increased dosage can have detrimental effects on various organ systems including reproductive system in humans. Lead poisoning is a public health problem faced by developed as well as developing countries [20].

In spite of the fact that the exact pathophysiology of this multisystem disorder is still unclear, oxidative stress is one of the mechanism implicated in pre-eclampsia [21,22]. Lead is an environmental toxicant that can result in reactive oxygen species (ROS) generation leading to oxidative stress [23]. Therefore, lead may be one of the sources of oxidative stress resulting in pre-eclampsia. Some studies report blood lead level association with pre-eclampsia [24,25] and others did not find any association [26]. Different ethnicities have been linked with higher blood lead level [27].

In the present study, controls and pre-eclamptic subset were comparable in age. The mean BLL in controls was 2.38 ± 2.43 ug/dL (median 1.7 ug/dL, range 0.16–10.12 ug/dL) whereas in the pre-eclamptic pregnant women, BLL was 3.42 ± 2.18 ug/dL (median 2.96 ug/dL, range; 1.28–8.6) which was found to be significantly higher in comparison to the controls. Others have reported much higher BLL in pre-eclamptic [24,25] as well as normal pregnant women who were not occupationally exposed to lead [28]. In addition to this BLL was significantly associated with blood pressure in pre-eclamptic subjects which is in accordance with other reports [29,30]. Recent meta-analysis reported blood lead concentrations in pregnant women to be the strongest risk factor for preeclampsia with an increase of 1 μg/dL associated with a 1.6% increase in likelihood of preeclampsia [31]. Low BLLs are associated with blood pressure [32]. There is evidence of a causal relationship between lead exposure and hypertension [20,33]. The underlying pathophysiology has been explored in several reports. It has been suggested that dysregulation of the renin-angiotensin-aldosterone system, along with effects on the endothelium and vascular smooth muscle, and stimulation of the sympathetic nervous system due to elevated production of catecholamines may be responsible [34]. Lead directly by generating reactive oxygen species or indirectly by binding to the antioxidant glutathione can result in the oxidative stress which is linked with decreased nitric oxide production affecting vasodilatation. It has been seen that lead encourages endothelial release of endothelin; increases serum levels of norepinephrine, angiotensin-converting enzyme, and thromboxane; and leads to diminution of prostacyclin production which endorse vasoconstriction [35].

The BMI of patient subset was significantly higher in comparison to controls but no correlation of these variables was observed with BLL. This could be partly due to increased gestational age observed in patient subset.

Increased gestational age has been associated with increased BLL possibly due to mobilization of stored lead in bone to circulation after 24 weeks of pregnancy [14]. Although the gestational age was slightly higher in pre-eclamptic subset in comparison to controls, no correlation was observed with BLL in our study. This may be explained by the fact that the BLL observed in the patient subset is much lower in comparison to other reports [24,25] as well as lesser number of the participants in our study.

To conclude**,** BLL is significantly higher in pre-eclamptic pregnant women in comparison to healthy pregnant women**.** This subset of patients were found to be more illiterate, exposed to passive smoking, consumed lesser vitamins, had spouses who occupationally belonged to high risk, had their houses painted and did not use water purification system.

The present study adds value and information to the risk assessment of lead exposed pregnant women, although larger studies are required further to assess the actual risk. It will aid in counseling of the affected individuals for lifestyle modification and prevention of complications.

Conflict of interest

The authors declare no conflict of interest.

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