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Relation of Heavy Metals in Cord and Maternal Blood to Neonatal Anthropometric Indices

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ABSTRACT

Introduction: Heavy metals are environmental pollutants and can cross the placental barriers and affect fetal health and growth.

Aim: To estimate serum Cadmium (Cd), Mercury (Hg), Lead (Pb) and Arsenic (As) in pregnant mothers and their newborns and to assess the association between the levels and newborns anthropometric indices.

Materials and Methods: This cross-sectional study was conducted on 113 mothers, aged 18 to 40 years and their healthy newborns. Inductively Couples Plasma Mass Spectrometry was used to assess levels of Cd, Hg, Pb and As, in maternal and cord blood serum samples. Correlation analysis was used to elucidate the association of these heavy metals with infant anthropometric parameters.

Results: There was a significant, negative association between neonatal serum levels of As and Cd, and the neonatal birth weight (r=-0.336, -0.386; p=0.043, 0.024, respectively). Maternal serum levels of As and Cd also had a significant, negative correlation with the neonatal birth weight (r=-0.382, -0. 372; p=0.041, 0.019, respectively). Significant negative association was found between the gestational age and maternal serum As and Pb (r=-0.368, -0. 316; p=0.042, 0.035, respectively).

Conclusion: The current study provides a clinical evidence that the increased maternal exposure to Cd and As has a great burden on fetal growth, as the finding of the present research indicate an inverse correlation between Cd and As exposure and birth weight of newborns. These findings highlight the importance of monitoring populations at risk, and to enhance awareness about the hazards of heavy metals and potential sources of exposure.

Keywords: Arsenic, Cadmium, Lead, Mercury

INTRODUCTION

Several fetal health problems are attributed to the exposure of environmental toxins during pregnancy [1,2], that may extend to the early childhood life [3]. It has been vastly elucidated that the placental barriers are not absolutely impermeable to the transfer of harmful materials [4].

Heavy metals are environmental pollutants with toxic features for human [5], with a suggested contribution to adverse birth outcomes, like, premature and small for gestational age newborns [6,7]. The advanced rates of cellular division during fetal life make the embryos more vulnerable to the insult of heavy metals than their mothers [8].

Accumulating evidence supports the impact of several heavy metals including As, Cd, Pb, Hg, on the fetal health and well-being because of their capability to pass the placental barriers, producing fetal growth perturbation and fetal toxicity [9,10].

In Egypt, environmental contamination with heavy metals is a growing public health issue, and several studies investigated the potent sources of exposure. For example, Moawad EM et al., emphasised the burden of Pb poisoning in Cairo; they found higher than the recommended levels of Pb in soil, paint and dust samples [11]. In addition, another Egyptian study documented water contamination with As [12]. Moreover, high concentrations of Cd were found in food cultivated in contaminated soil [13]. Additionally, contaminated fish is considered the most important source of Hg exposure [14].

Therefore, recent studies are directed towards the progressive awareness in considering the evaluation of fetal exposure to the aforementioned heavy metals and their effects on fetal growth. For example Menai M et al., highlighted the influence of Cd on fetal growth and the close association between its blood levels and the smoking habits during pregnancy [6]. In the same context Sabra S et al., reported a negative correlation between fetal birth weight and the fetal serum level of Cd [15]. Another study in Bangladesh observed a negative effect of prenatal As exposure and neonatal birth size [7]. The influence of prenatal Hg exposure on Birth weight was found in a recent study in Japan [16]. To the best of present authors' knowledge, no obvious data have been found on the relation between prenatal exposure to heavy metals and fetal growth in Egyptian literatures, despite the rising concerns over the elevated levels of heavy metals in the urban environment of Egypt.

Therefore, this study was designed to estimate serum Cd, Hg, Pb and As in pregnant mothers and their newborns and to assess the association between their levels and newborns anthropometric indices.

MATERIALS AND METHODS

A cross-sectional study was conducted on 113 mothers and their healthy neonates, chosen randomly from those attending El Galaa Maternity Educational Hospital in the period from September 2016 to June 2017. This was a part of a research project, funded by National Research Centre 10th research plan, entitled "immunological profile in cord blood and growth assessment of the newborn in relation to maternal exposure to environmental contaminant" [17].

The mother's age ranged between 18 and 40 years. Pregnant mothers with a history of chronic diseases or major illnesses during pregnancy were excluded. Neonates with any apparent congenital abnormalities, genetic, metabolic or neurological problems were also excluded.

Informed consent was obtained from each mother for participation after receiving a detailed explanation of the study. This study was approved by the Medical Ethical Committee of National Research Centre (Registration No.16-295).

Neonatal Measures

Each neonate included in the study was subjected to:

- **Physical examination:** Neonates were subjected to thorough examination that included chest, heart, abdominal, and central nervous system examination.
- **Growth assessment:** was done for each infant by anthropometric measurements.
  - Body weight with a precision of 10 g.
  - Body length with a precision of 1 cm, crown-rump length.
  - Body circumferences: Head and mid upper arm

Cord blood sample: 10 mL was collected during delivery before placental separation and put on EDTA free tubes, then centrifuged under cooling (4°C) at 1800 × g to separate serum samples which were preserved at -70°C until analysis.

Maternal Measures

Maternal data was obtained from the medical records of the hospital, to assess the following:

Socio-demographic factors: included the order of childbirth, maternal age, residence, family income, maternal and paternal education and occupation, lifestyle factors during pregnancy (e.g., smoking and passive smoking).

Maternal medical history including history of chronic diseases before or during pregnancy, information concerning the mothers' history of congenital diseases.

Perinatal history: including gestational age, type of labour, history of delivery problems.

Maternal anthropometric measurements were made on the participants wearing a minimum amount of clothing. The weights of pregnant women were measured using a digital weighing balance with a sensitivity of 100 g. Total gestational weight gain was estimated by subtracting the early first trimester weight (self-reported in the hospital interview) from the last measured weight before delivery. Height was measured in cm. All anthropometric measurements were taken by using standard anthropometric protocols.

An amount of 5 mL of venous blood was collected from the mothers in either normal or section delivery and then centrifuged under cooling (4°C) at 1800 × g to separate serum samples which were stored at -70°C until laboratory examination.

Determination of Heavy Metals in Serum Sample

Principle: Determination of toxic elements in traditional medicine was done using Inductively Couples Plasma Mass Spectrometry (PerkinElmer ELAN ICP-MS DRC II), PIN 5989-559 IEN. This method is provided to determine As, Cd, Pb, Hg and other metals in biological samples using plasma ionisation and quadruple mass spectrometer.

Method

Sample preparation: For the determination of serum heavy metals, the serum samples were diluted with an equal volume of deionised water (1:5). The dilution ratio was adjusted to ensure that concentration falls within a suitable absorbance range.

Estimation of As, Cd, Pb and Hg in serum samples: The diluted samples were injected into Inductively Couples Plasma Mass Spectrometry (ICP mass) and the calibration curve for each metal was plotted. Then the concentration of each metal in each sample was estimated from the corresponding curve of each metal.

STATISTICAL ANALYSIS

Analysis was performed using SPSS version 23.0 (SSPS Inc., Pennsylvania, USA). Mean±SD and percent were used for parameters' distribution calculations. Correlation was done using Pearson's correlation.p<0.05 value was considered as significant and p<0.005 value as highly significant.

RESULTS

The background characteristics of the participants are presented in [Table/Fig-1]. A total of 113 mother newborn pairs were enrolled in this study. The mean maternal age was 26.72 years with SD value of 5.6. Mean gestational age was 36.9 weeks. About 56% had normal delivery, and about 46% had completed primary education. A total of 93% had passive smoking history.

Parameters		No.	Mean±SD
Maternal age (years)		113	26.72±5.62
Gestational age (weeks)		113	36.9±2.1
		No.	%
Sex of infants	Male	51	45.1%
	Female	62	54.9%
Delivery	Normal	63	55.8%
	Cesarean section	50	44.2%
Social status	Married	112	99.1%
	Divorced	1	0.9%
Occupation	Employed	11	9.7%
	Unemployed	102	90.3%
Mother's education	Illiterate	10	8.8%
	Read and write	31	27.4%
	Primary education	18	15.9%
	Secondary education	41	36.3%
	Graduate and above	13	11.5%
Availability of tap water	Available at home	112	99.1%
	Outside home	1	0.9%
Sanitary disposal		113	100%
Smoking exposure	Passive smoking	93	82.3%
	Active smoking	none	

[Table/Fig-1]: General characteristics of studied cases.

All subjects were from great Cairo region that includes Cairo, Giza, and Qalubia Governorates. Regarding the assessment of history of exposure to heavy metals, nothing specific to food habits was found. The source of drinking water in 99% of the study population was tap water which was a safer source of water in comparison to those depending on other sources such as the shallow wells. Only 9.7% of the mothers were employed in occupations not related to heavy metals exposure [Table/Fig-1].

Description of the findings regarding the maternal and fetal anthropometric measurements are shown in [Table/Fig-2]. Mean weight of the newborn at birth was 2.94 Kg. About 81 newborns (72%) had normal birth weight, while 32 newborns (28%) had low birth weight ≤2.5 kg [Table/Fig-2].

Parameters	Mean	SD
Newborn weight (kg)	2.94	0.6298
Newborn length (cm)	47.44	3.287
Head circumference (cm)	34.168	1.8811
Mid arm circumference (cm)	10.223	1.4610
Maternal weight (kg)	75.438	14.83
Maternal height (cm)	157.73	6.668

[Table/Fig-2]: Anthropometric measurements of studied subjects.

The detected concentrations of Cd, Hg, Pb, and As in the maternal, and fetal serum are listed in [Table/Fig-3].

There was a significant, negative correlation between neonatal serum levels of As and Cd, and the neonatal birth weight (r=-0.336, -0.386; p=0.043, 0.024, respectively). The other anthropometric

Parameters	Mean	SD
Maternal Pb µg/mL	23.7	13.57
Maternal As mcg/L	59.67	9.21
Maternal Cd ng/mL	0.73	0.35
Maternal Hg ng/mL	28.82	11.8
Fetal Pb µg/mL	12.36	11.05
Fetal As mcg/L	3.46	7.57
Fetal Cd ng/mL	0.71	0.32
Fetal Hg ng/mL	15.65	5.9

[Table/Fig-3]: Concentrations of serum heavy metals of studied subjects.

measures didn't show any significant correlation with neonatal serum heavy metal [Table/Fig-4].

Maternal serum levels of As and Cd also revealed a significant, negative correlation with the neonatal birth weight (r=-0.382, -0.372; p=0.041, 0.019, respectively). Significant negative association was found between the gestational age and maternal serum As and Pb (r=-0.368, -0.316; p=0.042, 0.035, respectively), [Table/Fig-5].

Variables		Newborn weight	Newborn length	HC	MAC	Gestational age
Fetal Pb	Pearson's correlation	-0.053	-0.015	-0.011	-0.013	-0.066
	p-value	0.598	0.885	0.910	0.897	0.631
Fetal As	Pearson's correlation	-0.336	0.075	0.197	0.087	0.149
	p-value	0.043*	0.459	0.051	0.392	0.284
Fetal Cd	Pearson's correlation	-0.386	0.004	-0.036	-0.129	-0.214
	p-value	0.024*	0.966	0.075	0.209	0.110
Fetal Hg	Pearson's correlation	-0.024	0.020	-0.035	0.011	0.034
	p-value	0.810	0.841	0.732	0.918	0.808

[Table/Fig-4]: Correlation between neonatal serum heavy metals and their anthropometric measures and gestational age.
*Significant test p<0.05; HC: Head circumference; MAC: Mid arm circumference

Variables		Gestational age	MAC	HC	Newborn length	Newborn weight
Hg	Pearson's correlation	0.128	0.069	-0.001	0.065	0.038
	p-value	0.344	0.491	0.993	0.513	0.704
Cd	Pearson's correlation	-0.155	0.055	-0.011	0.047	-0.372
	p-value	0.053	0.591	0.916	0.644	0.019*
As	Pearson's correlation	-0.368	0.058	-0.008	0.047	-0.382
	p-value	0.042*	0.567	0.936	0.642	0.041*
Pb	Pearson's correlation	-0.316	0.043	0.031	-0.034	-0.051
	p-value	0.035*	0.672	0.756	0.735	0.068

[Table/Fig-5]: Correlation between Maternal serum heavy metals and neonatal anthropometric measures and gestational age.
*Significant test p<0.05; HC: Head circumference; MAC: Mid arm circumference

DISCUSSION

The present study evaluated the levels of the above-mentioned heavy metals in the maternal and fetal blood, and their potential association with newborn anthropometry.

The main findings of this study indicated that the serum levels of As and Cd in the maternal and cord blood represented the most considerable burden on birth weight, as there was an inverse association between serum levels of both metals and the infantile birth-weight.

Low birth weight is believed to be a considerable public health problem, owing to its high association with infant mortality and morbidity risk in adulthood [18].

Previous research reported conflicting results regarding the influence of heavy metal exposure on anthropometric parameters of infants [1,19-21]. However, Cd has been reported to have the most evident influence on fetal growth in several studies. For example, Al-Saleh I et al., in their study on Saudi Arabian population, outlined the inverse correlation between Cd level in umbilical cord blood with baby length and birth weight, while neither Pb nor Hg levels were correlated with these variables in the same sample [20]. Moreover, a study of Kippler M et al., stated that Cd concentration in the placenta has an inverse association with birth weight [22]. In addition, research on animals had attributed various serious developmental effects to Cd exposure [23]. Nowadays, Cd is one of the essential intoxicants in the environment, as a consequence to the wide spread of several industries worldwide [24]. It has been suggested that maternal smoking might increase Cd concentration in the placenta, and there was a negative correlation between placental Cd levels and birth weight in both smokers and non-smokers [25]. In contrary to these findings, Hu and his colleagues mentioned that Cd has no statistically significant correlation with birth weight [26].

Previous research has investigated the mechanism by which Cd may induce low birth weight. Kippler M et al., suggested that, Cd may interrupt zinc transfer to the fetus, causing fetal growth retardation [22]. Cd has been also suggested to play a role in feto-placental hormonal changes, for example, it may interfere with the production of thyroid stimulating hormone and placental leptin release, which have been associated to diminished intrauterine growth [27,28]. In addition, it was reported that Cd may contribute to placental insufficiency, which inhibits the transfer of the nutrients to the fetus [29]. Moreover, it was stated that Cd exposure has an influence on the production of pituitary hormones, which have a critical role in fetal growth [30].

On the other hand, as exposure of pregnant mothers has been also suggested to play a role in impaired placental circulation, which influences fetal growth through the induction of oxidative stress [31]. Evidences from animal researches showed the role of As as an endocrine disruptor, interfering with hormonal activation of gene transcription arranged by the closely related steroid receptors, at minimal dose of exposure, influencing insulin growth factor system, and cellular growth [32,33].

Several studies have found an association between urinary concentrations of As and birth weight [7,34,35]. On the other side, urinary concentrations of As in pregnant women revealed a significant correlation with other growth parameters including, birth weight, head and chest circumference [7]. However, no significant association between As concentrations and Small for Gestational Age (SGA), was found in other studies [36,37].

In the present study, maternal and neonatal serum concentrations of Pb and Hg showed no statistically significant association with any of the infantile anthropometric parameters. Likewise, some previous studies reported, no relation of cord blood Hg and/or maternal blood Hg with, birth weight, length [38], or head circumference [38,39].

In contrast to the previous findings, Hg concentrations in cord blood have been correlated with low birth weight [40,41], and with reduced birth length [40,42], and a relation between maternal hair Hg with decreased head circumference at 20-24 weeks gestation has been reported [43].

On the opposite side, a study of 53 mother-infant pairs in Vienna documented that the maternal blood level of Pb is a predictor to birth weight, birth length, head circumference, and intrauterine growth of the fetus [39]. Nevertheless, other studies reported no relation between maternal blood Pb concentration and infantile birth weight [26,44]. Another study suggested that the birth outcome may be influenced by the timing of prenatal exposure of Pb, besides the extent of exposure [45]. That study provided an explanation to the contradictory results between studies which may be in part due to the differences between-study samples in timing or measurements of Pb exposure during pregnancy, as the exposure dosage and timing have a common role in intrauterine fetal growth [46].

LIMITATION

The small sample size hinders the generalisation of the study findings.

CONCLUSION

The outcomes of the present study provide a clinical evidence that the increased maternal exposure to Cd and As has a great burden on fetal growth, as the findings of the present research indicate an inverse correlation between Cd and As exposure and birth weight of newborns. These findings highlight the importance of monitoring populations at risk, and to enhance awareness about the hazards of heavy metals and potential sources of exposure. Further research is suggested to explore the long-term impact of early exposure to heavy metals on child growth and development.

AUTHORS' CONTRIBUTION

All authors contributed equally in all parts of this study.

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