

Mercury Materno-fetal Burden and Its Nutritional Impact

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Abstract

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BACKGROUND: Mercury exists worldwide in food, water and air throwing its health hazards on all body systems.

AIM: To show the influence of the presence of mercury in pregnant mothers' blood on its level in the umbilical cord blood; and to display the relationship between the different foodstuff on the mercury levels in pregnant mothers' and umbilical cord blood.

PATIENTS AND METHODS: This cross-sectional study was conducted on randomly chosen 113 pregnant mothers at the time of labour and on their newborns. Full history, sociodemographic data and food frequency questionnaire for dietary assessment were recorded. The Maternal and neonatal anthropometric measurements together with the Apgar scoring were also measured. Serum mercury levels in both mothers' and umbilical cord blood were measured using the Inductively Coupled Plasma Mass Spectrometry (ICP-MS).

RESULTS: A high percentage of mothers (82.3%) were exposed to passive smoking. There was a statistically significant positive correlation between the maternal and fetal umbilical cord blood mercury levels ($p = 0.002$). There was an insignificant negative correlation between the maternal blood and fetal umbilical cord blood mercury levels on one side and each of the different foodstuff on the other side (fish, vegetables, fruits and proteins, for example, meat and legumes). An insignificant positive correlation was found between dairy products and of the maternal blood and umbilical cord blood mercury levels.

CONCLUSION: The fetal umbilical cord blood mercury levels correlate positively with the maternal blood mercury. The different foodstuff can influence the maternal and umbilical cord blood mercury levels whether by increase or decrease. Strict measures should be taken to decrease environmental mercury contamination with attention to pregnant mothers.

Introduction

Mercury is a xenobiotic heavy metal with undisputed toxicity, grading it as number three after lead and arsenic [1] [2].

Although it exists worldwide in soil, food, water and even in the atmosphere, still definitely our developing countries are the much more suffering ones. It can easily gain access to the human food chain and after that goes on bioaccumulating

Unfortunately, mercury adversities start very early where it can cause embryopathies, fetotoxicity, infantile hazards and up to older ages we can meet its detrimental health effects [3] [4].

Mercury has a wide range of catastrophic health insults starting from abortions, stillbirths, craniofacial malformations up to neural tube defects, brain damage and infantile cerebral palsy. As it throws its impact on almost all body systems, hence we encounter anaemia, immunological impairments, autoimmune conditions, renal injuries, endocrinal insults and so many others [5] [6] [7].

Our present study aims to elucidate the impact of the presence of mercury in pregnant mothers' blood on its level in umbilical cord blood and to display the influence of the different foodstuff, eaten by mothers, on the mercury levels measured in both pregnant mothers' blood and umbilical cord blood.

Patients and Methods

This is a cross-sectional study that was conducted on 113 pregnant mothers at the time of labour and their newborns. They were chosen randomly from those attending El-Galaa Teaching Hospital as a research project, funded by the National Research Center 10th research plan, entitled "Immunological Profile in Cord Blood and Growth Assessment of the Newborn About Maternal Exposure To Environmental Contaminant". The study was conducted in the period from September 2016 to June 2017.

The study protocol was approved by the Medical Ethical Committee of the National Research Centre. All mothers gained comprehensive and clear knowledge about the aim of our work, and written consents were signed before enrollment.

The mother's ages ranged between 18 and 40 years. Neonates were of both sexes. 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.

-Sociodemographic data about mothers included age, social status, economic responsibility, water source availability, sanitary disposal, smoke exposure and education.

-Food frequency questionnaire (FFQ) for dietary assessment of the different foodstuff.

-Gestational age, type of labour, history of delivery problems and chronic diseases.

-Maternal anthropometric measurements of weight in kilograms (kgs) height in centimetres (cm) [8].

-Neonatal Apgar scoring, at one and five minutes, was measured to assess neonatal condition at birth [9].

-Neonatal anthropometric measurements of weight (kgs), height (cm), head circumference and mid-upper arm circumference (MAC) in cm were all taken [10].

-10 ml of blood were collected from mothers whether in normal or section delivery at the time of labour and put in 3 EDTA tubes.

-Another 10 ml of blood were collected from the cord blood during delivery before placental separation and put in EDTA tubes.

-These blood samples were for measuring the mercury levels in mothers and umbilical cord of fetus using inductively coupled plasma mass spectrometry.

The standards for ICP-MS were prepared from stock solutions of mercury at 10 mg/L concentrations obtained from Sigma- Aldrich, Australia, and labelled as Fluka Trace Cert Ultra. From the stock, we prepared spiked solutions as much as needed. The hydrochloric acid and ultrapure nitric acid (HNO₃) were taken from J.T. Baker Inc. The other solvents and reagents in our study were analytical grade got from Sigma- Aldrich, Australia. The water for washing the laboratory apparatus and glassware together with the standard solutions and sample preparation was deionised (resistance < 18 m, Academic Milli-Q Ultra Pure Water System, Australia) [11].

The ICP-MS was calibrated through the use of standard aqueous solutions (having the same acid concentration used in the samples and additional internal standards) prepared from the stock solutions through dilution in the range of 0.05 to 10 mg/L concerning mercury. First, we prepared a solution containing 10 mg/L of mercury as mentioned before and from it, the final standard solution is made.

Before doing the analysis, there was an optimisation of the operating conditions of the ICP-MS instrument. The ICP-RF power, the nebuliser gas flow rate and the ion lens voltage(s) were particularly adjusted to give the highest possible signal intensities all while keeping low levels of oxides and doubly-charged ion production (where both have to be less than ~ 3%). The appropriate calibration standards were then measured after optimisation of the instrument.

To make a calibration curve with a correlation coefficient of 0.999 or better and as a part of the protocol of quality assurance, we did at least six-point calibrations of different ranges for mercury (0.10 to 10 mg/L and 0.05 to 2000 µg/L).

From the corresponding calibration curve, we determined the concentrations of the sample solution. To make sure that the instrument went on meeting the linearity criteria and the acceptable sensitivity, there was an analysis of the calibration standards at regular intervals during the ICP-MS analytical runs.

The analysis was performed using SPSS version 21 (SSPS Inc., Pennsylvania, USA). Mean ± SD was used for age distribution calculations. The correlation was done using Pearson correlation. $P < 0.05$ value was considered as significant and $p < 0.005$ value as highly significant.

Results

The sociodemographic data of the studied cases are shown in Table 1. It revealed that a high percentage of cases were exposed to passive

smoking (82.3%). Anthropometric and laboratory data of mothers and newborns are shown in Table 2.

Table 1: Sociodemographic data of studied cases

	No	%
Sex		
Male	51	45.1
Female	62	54.9
Delivery mode		
Normal	63	55.8
Caesarean section	50	44.2
Social status		
Married	112	99.1
Divorced	1	0.9
Economic status		
Responsible	11	9.7
Non-responsible	102	90.3
Water		
Available at home	112	99.1
Outside home	1	0.9
Sanitary disposal	113	100
Smoking exposure		
Yes	93	82.3
No	20	17.7
Mother education		
0 = illiterate	10	8.8
1 = primary education	31	27.4
2 = preparatory education	18	15.9
3 = secondary education	41	36.3
4 = high education	13	11.5

Table 3 revealed a statistically significant positive correlation between maternal blood mercury levels and the fetal umbilical cord blood ones ($p = 0.002$).

Table 2: Anthropometric and laboratory data of studied cases

	Mean	Std. Deviation
Mother:		
Age in years	26.72	5.6
Weight in kilograms (kg)	75.44	14.8
Height in centimeter (cm)	157.73	6.7
Newborn:		
Baby weight in kilograms	2.95	0.6
Baby length in centimeter(cm)	47.44	3.3
Head circumference in centimeter (cm)	34.17	1.9
Mid upper arm circumference in centimeter (cm)	10.22	1.5
APGAR 1	5.76	1.6
APGAR 5	8.03	1.6
Gestational age in months	36.90	2.1
Laboratory data:		
Serum maternal mercury (Hg) level ng/ml	28.82	11.8
Serum neonatal mercury(Hg) level ng/mL	15.65	5.9

Table 4 showed the correlation between maternal food intake during pregnancy and serum maternal and neonatal Hg levels. Negative insignificant correlations between the maternal blood mercury levels on one side and the proteins as meat and legumes, vegetables, fruits and fish food items each on the other side were found.

Table 3: Correlation between serum maternal and neonatal mercury (Hg) levels

		Neonatal Hg
Maternal Hg	Pearson Correlation	0.303**
	Sig. (2-tailed)	0.002

**Significant value at $p < 0.005$.

The same table similarly showed insignificant negative correlations between the fetal umbilical cord blood mercury levels on one side and the proteins as meat and legumes, vegetables, fruits, and fish food items each on the other side. The dairy products food item was the only one which showed an insignificant positive correlation

with both the maternal blood and umbilical cord blood mercury levels.

Table 4: Correlation between maternal food intake during pregnancy and serum maternal and neonatal mercury (Hg) levels

Maternal food intake		Maternal Hg	Neonatal Hg
Protein (meat and/or legumes)	Pearson Correlation	-0.094	-0.067
	Sig. (2-tailed)	0.350	0.509
Vegetables	Pearson Correlation	-0.124	0.000
	Sig. (2-tailed)	0.217	0.999
Fruits	Pearson Correlation	-0.145	-0.186
	Sig. (2-tailed)	0.147	0.066
Fish	Pearson Correlation	-0.147	-0.197
	Sig. (2-tailed)	0.371	0.237
Dairy products	Pearson Correlation	0.167	0.149
	Sig. (2-tailed)	0.094	0.140

Discussion

Organic mercury is the most toxic form that can readily cross the placental barrier. It comprises ethyl mercury which is present in medical preparations and can passively diffuse; while methylmercury is present in fish and seafood and can actively cross the barrier via amino acid carriers. On the other hand, inorganic mercury exists in the dental fillings and is also airborne where it is transferred via the different occupations. It is usually caught in the placental barrier [12] [13] [14] [15] [16].

Mercury health hazards are catastrophic because of two reasons. First, its prenatal exposure does not only impose its adversities on the fetus (fetotoxicity), but it can also go on throwing its mal-influences up to the age of fourteen as documented by neurophysiological tests suggesting irreversibility in many occasions [17].

Second, the capabilities of mercury to bioaccumulate seriously impeding the different body system functions. This was proved not only concerning the ingested methylmercury because it is hydrophobic, resistant to metabolism and accordingly, can be found in every level of the food chain, but also concerning mercury vapour. This latter can easily pass to the circulation and once oxidised becomes lipid soluble, hence very liable to bioaccumulate in the brain, liver and renal cortex [3] [17].

The present study showed a significant positive correlation between the maternal blood mercury levels and the umbilical cord blood ones. We resort this to several justifications. First, the capability of mercury to readily cross the placental barrier and moreover to hamper its function. This is due to its prooxidative influences and impeding the antioxidative processes both of which augment the fetal vulnerability. Similarly, other researchers were in agreement with our results [12] [16] [17] [18] [19]. Second, is the escalated binding of mercury to the fetal blood cells not only because of its heightened

affinity to haemoglobin but also due to the higher fetal haemoglobin and hematocrit levels compared to adults.

This explanation was consistent with other work studies which moreover evidenced it by their much higher levels of mercury in umbilical cord blood compared to the maternal blood ones. They also referred this to the higher affinity of methylmercury to fetal hemoglobin [12] [20] [21] [22] [23] [24] [25].

Third; we should also suggest a very important probable justification for that correlation where we found in our study a considerably high percentage of pregnant mothers exposed to smoke (82.3%). Mercury is present in air and smoke. Since it is present in the tobacco plant and cigarette filters and papers, therefore it is released in cigarette smoke. It also gets into air and smoke from the breakage of mercury-containing devices like thermometers, compact fluorescent lamps, thermostats and barometers. School laboratories and the mercurochrome antiseptic are other sources [26].

Inorganic mercury from dental fillings was also reported to be airborne [12]. That heavy load of maternal mercury rationally got to the fetus through the previously mentioned first two justifications.

Matching with our suggestion some studies found out that mercury from air and smoke goes from the respiratory system to the circulating blood, hence to the placental barrier and accordingly gets retained in the embryonic tissues, the most hazardous of which is the brain. They also reported that inhaled mercury gets retained in the body in 80% of the cases [27] [28]. Other researches declared that mercury in smoke could cause vascular endothelial damage [26].

Furthermore, cigarette smoke can cause an elevation of mercury blood levels through its content of cadmium too. Cadmium imposes metallothioneins expression and these in turn bind to zinc and selenium both of which are well known to be mercury detoxificants. Accordingly, we assume that mercury levels are supposed to increase.

Finally, we suggest that during gestation the fetus could act not only as a filter to the maternal mercury but also as a reservoir or container to that mercury; hence its mercury levels rose up to correlate positively with their mothers.

Again, this suggestion was going on with other research workers who confirmed it, reporting that the umbilical cord blood mercury levels even exceeded their mothers' to reach double or even triple those levels [29] [30] [31] [32].

Concerning the negative relation between each of the maternal blood mercury and cord blood mercury levels on one side and fish eating on the other side, this relation though insignificant but it

was surprisingly important because fish has always been reported to be a major source of mercury contamination; which could elevate its levels in cord blood (if eaten for example more than two times per week) [19].

However, our finding could resort to the pivotally beneficial fish nutritional contents. These comprise selenium, omega-3 fatty acids, vitamins A, D and calcium. Selenium, which was reported to be abundant in fish, plays a crucial role in protecting against mercury toxicity. Omega-3 fatty acids, vitamins A and D are antioxidants which alleviate methyl mercury hazards. Calcium too is very important because mercury causes cellular oxidative stress and mitochondrial affection ending in intracellular Ca-homeostasis disturbances and increased lipid peroxidation. Hence, we assume in our own words that the presence of these nutrients can lessen mercury toxic effects and levels [21] [33] [34].

Also, it is important to report that not all kinds of fish contain mercury in detrimental levels [23]. Similarly, other researchers found out the same result and gave more or less consistent explanations [35] [36] [37] [38] [39].

Very interesting Chinese work studies reported their results, which were in agreement with ours, to some other factors. These included the kind of fish, the fish organ ate, the water level from which the fish is caught, the accumulation factor of the metal itself and many other environmental risk factors [40] [41].

However, and contradictory to our findings, several researchers proved that frequent fish eating during gestation is associated with higher mercury levels [21].

Hence, fish could be considered a double-edged reciprocal weapon.

Regarding the negative correlation between maternal blood and umbilical cord blood mercury levels on one side and each of vegetables, fruits and proteins rich foods on the other side, we can mainly ascribe these relations to their vitamins, and minerals content which mitigates mercury improper levels and effects.

Concerning vegetables whether green, yellow or orange, they all provide very respectful percentages of iron, folate, zinc, calcium, potassium, magnesium and vitamins A, C, E and K. Their functions have proved to oscillate between lessening mercury influences, and ant oxidation. The Quercetin bioflavonoid present in the green ones gives them their antioxidant and anti-inflammatory qualities. Carotenoids in the yellow and orange vegetables are also antioxidants and antigenotoxic [42].

We are mainly concerned with the antioxidant effect of vegetables because it boosts the immunity where mercury is condemned for jeopardising the immunological system. It inhibits the normal polymorph nuclear cells stimulation and even function hindering their capability to destroy foreign material [3].

Going on with our results research declared that regular vegetable eating caused a decrease in mercury levels in both mothers and newborns [19].

Concerning the proteins rich foods item, we would like to add that they (particularly red meat) are proper sources of selenium which antagonises mercury.

Finally, we have found a positive correlation between each of the maternal blood and cord blood mercury levels on one side and the dairy products on the other side. We can assume that this might have been due to nutritional causes and pollution ones.

Nutritionally, dairy products are good sources of calcium and poor sources of iron and zinc [43] [44]. Since mercury competes with iron to bind to haemoglobin, causing aplastic and hemolytic anaemia's, therefore it is rational that iron plays a role in overcoming toxic mercury levels. Accordingly, if the dairy products were not properly fortified with iron, therefore this can be a justification for our results [16] [44].

Similarly, as zinc has proved to have a protective role through altering mercury metabolism, therefore its low levels in dairy products can be another justification [21] [44].

Concerning the calcium content of dairy products, though it is known to be very good, still we suppose that this might not be the case if the dairy product is of a poor quality concerning the source and or the manufacturing brand [45].

Another burden here is the mercury itself because not only does it cause cellular oxidative stress but also mitochondrial mal-affection ending in intracellular calcium homeostasis disturbances and increased lipid peroxidation.

Therefore, we can suggest that any calcium content problem in dairy products could have an undesirable effect on mercury levels and hazards [3].

As regards the pollution causes, we can say that these might have augmented the dairy products contamination with mercury to a burden level which might have surpassed the capabilities of dairy nutrients to alleviate it. These include the manufacturing processes steps where they comprise many physical and chemical properties [46]. The packaging processes and materials, storage reservoirs and transportation containers have their share too [43].

Moreover, since cow bodies were found to be "biological filters" of heavy metals, therefore pollution of their farms from sewage, wastewater, industrial wastes exhaustion gases and soil are all possible blamed sources [43] [45].

Finally, cheese types, brands, and drainage processes performed to get white cheese and Labenah all impose their influences on dairy products heavy metals content [45].

In conclusion, as mercury is very detrimental particularly to the brain and its hazards can go on up till older ages. Therefore measures for its environmental decrements in parallel with the nutritional detoxification measures are recommended.

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