Contamination index. A novel parameter for metal and pesticide analyses in maternal blood and umbilical cord[1]

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DOI: http://dx.doi.org/10.1590/S0102-865020160070000010

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ABSTRACT

PURPOSE: To evaluate the contamination index of metals and pesticides in pregnant women, and to relate this to perinatal outcomes.

METHODS: Descriptive, retrospective, exploratory study, developed from existing secondary data analyses at Level III maternity center. A total of 40 mothers with their newborns (NB), living in a rural area in Botucatu- Brazil and surrounding region. Blood samples from mothers and newborn were collected to determine the total contamination index for metals and pesticides. The concentrations of each metal and each pesticide were determined in blood samples of mothers and their newborns by Rudge's results. After obtaining these concentrations, the total contamination index in mother and NB was calculated, along with its correlation with clinical parameters of NB.

RESULTS: There was no correlation ($p > 0.05$) between maternal contamination index with NB clinical parameters, and NB contamination index versus NB clinical parameters.

CONCLUSION: The maternal contamination index of metals and pesticides was not related to perinatal outcomes, but it could be used as baseline parameter in future toxicological studies, regarding to long-term toxic characteristics as persistent organic pollutants, its long half-lives, bioacumulative, and expected to impose serious health effects on humans.

Key words: Pesticides. Metals. Contamination. Pregnancy.

Introduction

Human exposure to persistent toxic substances (PTS) in the living environment include toxic metals and persistent organic pollutants (POPs) with negative health effects[1]. The influence of these pollutants on public health has been increasingly acknowledged, especially during the period of growth and development. The maternal exposure to PTS may be detrimental to the developing fetus being the prenatal life considered the most sensitive stage of human development. The fetus is highly susceptible to teratogens, typically at low exposure levels that do not harm the mother[2].

The placenta serves as the point of contact between maternal and fetal circulation acting as a selective fetal-maternal barrier allowing nutrients and oxygen pass to the fetus, and protecting against the transfer of toxic substances to prevent perinatal contamination[3-5].

The exposure of pregnant women to toxic metals and transfer from the mother's blood to the developing fetus have mostly been studied in heavily exposed individuals[6-9]. There are few studies on placental concentrations of toxic metals in women living in less polluted areas[10,11], and for some metals the reported data are conflicting.

POPs present in the environmental have detrimental health effects on pregnant women and on embryonic and fetal development stages, which are the most vulnerable periods. The current review provide epidemiological evidence for the effects of a wide range of environmental contaminants on child health outcomes: fetal growth, prematurity, neurodevelopment, respiratory, immune health, childhood growth and obesity, even at lower exposure levels[12].

The Arctic Monitoring and Assessment Programme (AMAP) initiated in 1991 includes eight Arctic countries of North Hemisphere[13-15] to measure the levels of PTS investigating multiple contaminants and the relationship between the levels of these compounds with maternal health effects and birth outcomes[16,17]. After, this Programme was enlarged to involve the Southern Hemisphere in order to evaluate the levels of maternal and fetal contaminants in South Africa and Brazil. Our research group as a part of this new phase of AMAP reported the levels of cadmium, mercury, lead, manganese, cobalt, copper, zinc, arsenic and selenium in maternal and umbilical cord from delivering women from seven selected regions of South Africa that differ in their degree of environmental pollution[18,19].

A similar study in seven different regions within São Paulo State, Brazil with blood samples from 155 pregnant women to evaluate the degree of environmental contamination and possible exposure of Brazilian pregnant women to PTS was performed. Low environmental contamination of toxic and essential metals was found. These findings could indicate that pregnant women have little or no contact with pollutants, possibly due to awareness campaigns carried out by public health practitioners in Brazil. Although, it was found different metals concentrations in pregnant women from sites of São Paulo State, the highest levels in delivering was detected in pregnant women from rural areas[20].

Higher levels of pesticides in blood of delivering women mostly in rural areas. It is thought that sources of exposure to these pollutants may be both from recent and past activities[21]. The study detected 12 PCB congeners in the maternal blood but only three namely PCB118, PCB138 and PCB153 congeners were dominant (e.g. present in more than 70% samples). This indicates that dominant congeners found are the most recalcitrant to degradation and have the greatest ability to bioaccumulate and biomagnify.

Putting together both studies[20,21] it is possible to conclude that maternal contamination as well as the placental transfer to fetus is upon dependent of different concentration of these compounds on the two sides of the placental villus and from the placental and fetus mechanisms that actively or passively permits, facilitates and adjusts the amount and rate of transfer of a wide range of substances to the fetus[21,22].

The developmental stage during which the exposure occurs has a major influence on the consequences of this exposure. If exposure occurs during the time when organogenesis takes place, permanent structural changes might occur. Alternatively, exposures after complete organogenesis might result in functional consequences.

However, only the PTS and its concentration have been analyzed in quite all studies but the number of metals and pesticides to which women were exposed was not considered in these studies. Accordingly, one might expect that pregnant women and their newborns might be at a high risk when there is a sum of different PTS contaminants and concentrations. Therefore, the development of a novel parameter for environmental contaminant analysis drawn from random blood samples of delivering women was carried out to create another tool in the toxicology field in order to evaluate the degree of maternal and perinatal environmental pollution. To calculate the contamination index, not only the metal and pesticide concentrations were used, but also the number of metals or pesticides to which women and fetal were exposed. This contamination index reflects the fetal-maternal communication system as a whole being the placenta the organ of transfer from mother and fetus and from fetus to mother through the syncyciotrophoblastic of the intact villi. Little is known about possible interactions between number and concentration of metal and POPs in the maternal and perinatal outcomes.

In this context, we hypothesized that the higher contamination index leads to greater damages to mothers and newborns. Therefore, the goal of the present study was to characterize the maternal and perinatal contamination index of PTS intrauterine exposure in order to evaluate interactions between metal and POPs. This new contamination index of PTS exposure to metal and POPs reflecting the maternal transfer of a wide range of substances and its concentration to the fetus is an indicator of perinatal outcomes. In view of these observations, we therefore designed a cross-sectional study in delivering Brazilian patients to investigate the status of various environmental pollutants at different concentrations of mothers and newborns to assess the effect of these pollutants on perinatal outcomes.

Methods

The present study was approved by the Brazilian National Research Ethical Council (CONEP-Brazil; Protocol number 12388 – December 13th 2005).

The findings reported here form part of the pilot study titled "Levels of Persistent Toxic Substances (PTS) in maternal and cord blood from selected areas of São Paulo State-Brazil". The study subjects were part of a monitoring program, aiming at assessing the exposure levels of environmental pollutants, such as toxic metals and POPs. The delivering women were admitted at the institutional hospital from Botucatu city, São Paulo State, Brazil. Potential participants received plain-language information about the study and those who agreed to participate signed a written consent form, which stated that participation was voluntary, confidentiality was ensured and participants could withdraw from the study at any time. Subjects were also informed that if results were a cause for concern, they would be referred to an appropriate medical facility for further investigation. After delivery, the researcher (CVCR) extracted records from patient hospital files that included date of delivery, newborn weight and length, head circumference, gestational age at delivery.

A total of 40 delivering women and their newborns, which were living in a rural area in Botucatu-Brazil and surrounding region, participated in this study. The sociodemographic and obstetric data were acquired from a questionnaire translated and adapted for the Brazilian population[23].

The inclusion of participants included the following criteria: signing the informed consent form and agreeing to donate blood, answering a socioeconomic questionnaire, allowing access to their health and post-delivery records, gestational age higher than 37 weeks, and living in a rural area in Botucatu and surrounding region for at least one year.

The delivering women were submitted to a surgical procedure in which one or more incisions are made through a mother's abdomen, and the umbilical cord was clamped and cut to obtain blood samples immediately after delivery. The umbilical cord blood samples were used for analysis of PTS: metal (Mo, Cd, Hg, Pb, Co, As, Zn, Mn, Se and Cu) and Persistent organic pollutants (12 biphenyl polychlorine, dichlorodiphenyltrichloroethane, diphenyl dichloroethylene, hexachlorocyclohexane (α-HCH, β-HCH, γ-HCH), hexachlorobenzene (HCB), chlordane (cis- chlordane, trans-chlordane, oxy-chlordane, cis-and trans-nonachlor) levels.

For the analysis of lipid and hormonal profiles, maternal blood (10 ml) was collected by venous puncture into Vacutainer tubes (trace metal free tubes) within one day postpartum, which were stored at -4ºC and analyzed in the clinical laboratory of our institution. The triglycerides, total and fractions cholesterol levels were determined by spectrophotometer, and follicle-stimulating hormone (FSH), luteinizing hormone (LH), progesterone, prolactin and estradiol levels were measured by chemiluminescence Umbilical cord blood was collected after delivery by the surgeon , using a Vacutainer disposable system. Metal-free vessels were used to prevent contamination during collection and fractionation. All samples were stored at -20ºC and shipped in a frozen state to University of Tromso, Norway, for analytical laboratories. The metal and POPs data from delivering women were analyzed by Rudge *et al.*[20] and these results associated with unanalyzed data from newborns were assigned to be used in this study to determine the contamination index. To calculate the total contamination indexes of mothers and newborns, the metal and POPs concentrations were used according to the following formulas:

1) Maternal contamination index = (**Σ** maternal metal concentration x number of metals exposed) + (**Σ** maternal POPs concentration x number of POPs exposed).
2) Newborn contamination index = (**Σ** newborn metal concentration x number of metals exposed) + (**Σ** newborn POPs concentration x number of POPs exposed).

Design and statistical analysis

This is a descriptive, retrospective and exploratory study, developed from existing secondary data analyses. The protocol for this study has been described in detail previously[20,21].

The results were presented as the sum of the concentrations of metals and POPs to calculate the maternal, fetal and total contamination index. For the analysis of correlations between maternal contamination index *versus* newborns contamination index, maternal contamination index *versus* perinatal clinical parameters and newborn contamination index *versus* perinatal clinical parameters, Pearson's correlation was used. The level of statistical significance was taken as $p<0.05$.

Results

Socioeconomics and housing characteristics for delivering women from rural area are summarized in Table 1. It was observed that the pregnant women were predominantly older than 30. All the women of Botucatu consumed water at home, and used gas for cooking. Most of the women claimed that they were not in the habit of drinking alcohol or smoking. And those that confirmed that they smoked consumed less than a packet of cigarettes daily and had done so for more than a year.

TABLE 1 - Social and personal data (% - percentage) of pregnant women from Botucatu and region.

	%
Age	
< 21 years old	20
21 – 30 years old	35
> 30 years old	45
Residence	
House	100
Ranch/farm	0
Wood house	0
Other	0
Energy for cooking	
Gas	100
Electricity	0
Wood	0
Other	0
Water source	
House	50
Out	20
Well	30
River	0
Other	0
Smoking habit	
Paper cigarette	35
Hand-rolled cigarette	5
Majiruana	0
Non smoking	60
< 1 pack/day	100
1 pack/day	0
> 1 pack/day	0
Less than 1 year	14
More than 1 year	86
Alcohol drink	
Yes	30
Weekly	100
Daily	0
No	70

As for the environmental aspects, all the delivering women were using chemical materials to clean their own houses s. 55% of these women used poison monthly against insects and only 30% to cultivate plants for food; there was a predominance of fish consumption of locally caught fish and good air quality was reported without pollution factors (Table 2).

TABLE 2 - Maternal exposure (% - percentage) of delivering women from rural area of Botucatu and surrounding.

	%
Use of chemical material to clean house	
Yes	100
No	0
Not know	0
Frequency of use of poison to kill insects	
Weekly	0
Monthly	55
Not use	45
To plant their own food, using poison in the garden	
Yes	30
No	70
Fish consumption of locally caught fish	
Yes	65
No	35
Environmental pollution factors of residence	
Sink	5
Atmosphere pollution	20
Other	10
No	65

Table 3 shows that the women 40%admited exposure to cleaning house material.

TABLE 3 - Occupational exposure (% - percentage) of pregnant women from Botucatu and region.

	%
Women working outside home	40
Chemical used in workplace	
Solvents	0
Paints	0
Metals	0
Cleaning house materials	40
Wax	20
Paint remover	0
Greases, oils and lubricants	0
Others	20
No	20

Regarding the eating habits of delivering women, a prevalence of weekly or daily consumption of red or white meat and fruit/vegetables was observed. The fish consumption was lower than red/white meat.

The dietary intake as evaluated from dietary questionnaire appeared to be sufficient and adequate (Table 4).

TABLE 4 - Food habits (% - percentage) of pregnant women from Botucatu and region.

	%
Red and White meat	
Locally produced	
Yes	50
No	50
Frequency	0
Rarely	40
Weekly	60
Daily	
Fish	
Locally produced	
Yes	65
No	35
Frequency	35
Rarely	45
Weekly	20
Daily	
Fruits and vegetables	
Locally produced	
Yes	60
No	40
Frequency	0
Rarely	5
Weekly	95
Daily	
Milk and dairy products	
Locally produced	
Yes	25
No	75
Frequency	10
Rarely	45
Weekly	45
Daily	

The biochemical analysis of maternal blood samples are presented in Table 5. The lipid parameters in the blood of pregnant women were classified within the normal range. For postpartum women, blood hormonal parameters were consistent values of LH, FSH, prolactin and progesterone, expected for this stage.

TABLE 5 - Biochemical parameters of pregnant women from Botucatu and region.

	Concentration
Triglycerides (mg/dL)	181.20 ± 40.17
Total cholesterol (mg/dL)	180.55 ± 38.48
HDL-Cholesterol (mg/dL)	53.85 ± 13.41
LDL-Cholesterol (mg/dL)	90.96 ± 31.73
VLDL-Cholesterol (mg/dL)	36.24 ± 8.03
FSH (mIU/mL)	0.08 ± 0.01
LH (mIU/mL)	3.09 ± 1.92
Progesterone (ng/mL)	12.69 ± 7.16
Prolactin (ng/mL)	144.83 ± 33.17
Estradiol (pg/mL)	5.38 ± 5.12

Data presented as mean ± standard deviation.

Figure 1 shows the distribution of the metal contamination levels (Figure 1A), POPs (Figure 1B) and maternal, fetal and total PTS contamination index (Figure 1C). The statistical analysis showed no correlation between the studied contamination indexes.

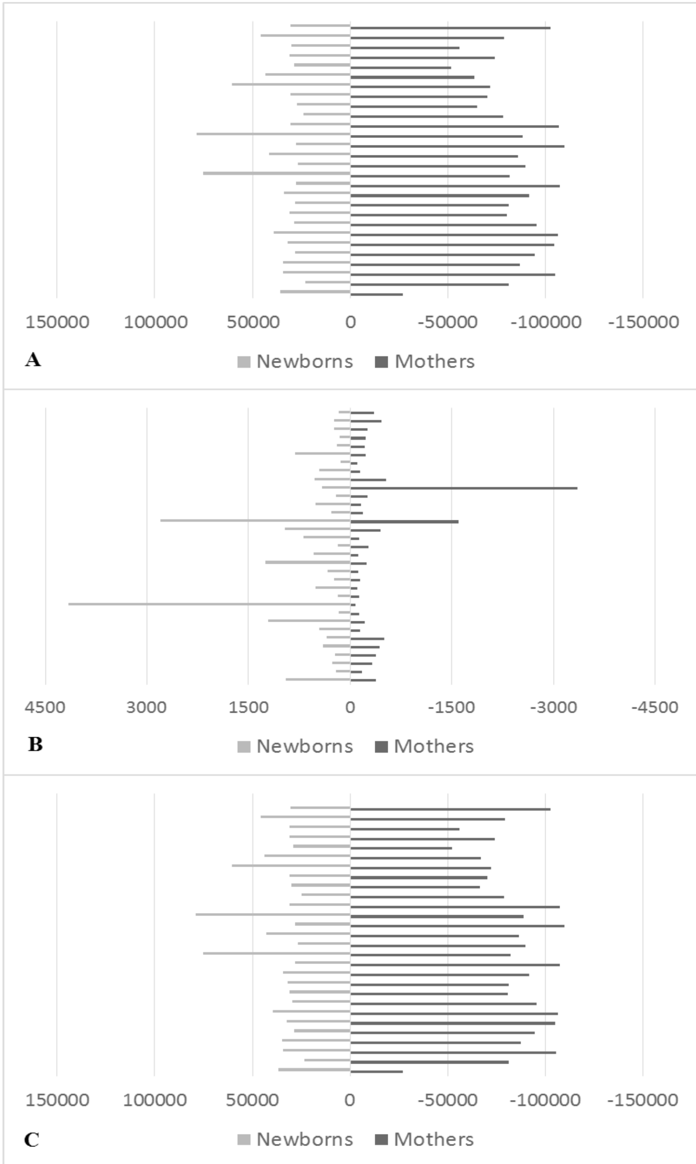

FIGURE 1 - Metal (**A**), POPs (**B**) and total PTS maternal and newborn contamination index (**C**).

Table 6 shows an analysis of correlations between maternal contamination index and their newborns, maternal contamination index *versus* perinatal clinical parameters and newborns contamination index *versus* perinatal clinical parameters. There was no correlation between any of the parameters.

TABLE 6 - Correlation analyses of maternal and newborn data.

	p	r
Newborn contamination index x newborn weight	0.38	0.15
Newborn contamination index x newborn head circumference	0.81	- 0.03
Newborn contamination index x newborn length	0.14	0.26
Newborn contamination index x maternal contamination index	0.40	0.15
Maternal contamination index x newborn weight	0.49	0.11
Maternal contamination index x newborn head circumference	0.83	0.03
Maternal contamination index x newborn length	0.29	-0.17

Pearson´s correlation test.

Discussion

This report quantifies the levels and the number of PTS in 40 paired samples of maternal and cord blood, but we are not able to demonstrate that as the maternal contamination index of PTS exposure worses, the potential of perinatal contamination index as well as some perinatal outcomes increases. As the overall PTS concentrations in the whole blood was surprising low in the patients from rural areas, the individual analysis of these patients allow us to follow another parameter that could reflect the total maternal contamination taking in account the sum of all pollutants as well as its concentration.

The coefficient values is an indicative of the degree of heavy metal and POPs trans-placental transfer between mother and fetus and suggest that the placenta might still partially hinder the passage of PTS to the fetus and reduce its toxic effect. Placenta is not only a barrier but also is a filter for maternal environmental.

In our research group, it was demonstrated a correlation for each element studied between paired maternal and cord blood; a significant correlation was shown for mercury, lead, manganese and copper in South Africa[19-24]. However, after other analyses, these authors concluded that there was low environmental contamination in São Paulo State, Brazil, suggesting that pregnant women have little or no contact with pollutants[20]. Another study performed by Rudge[21] verified that β-HCH, γ-HCH (hexachlorocyclohexanes) and HCB (hexachlorobenzene) were found to be highest in the Botucatu area.

In this study, it was found that the total contamination index was influenced by the metal contamination index, especially due to the high copper and zinc concentrations. After analysis of these indexes, it was verified that there was no correlation between maternal and newborn indexes or between these indexes and the studied perinatal clinical variables (body weight and length, and head circumference). Despite the maternal contamination index showing no correlation with perinatal outcomes, it is important to note that this index takes into account the number and concentrations of metals and pesticides that these women and newborns were exposed to. Therefore, this parameter does not establish an importance only in the short-term, but should also be used to assess long-term toxic effects, especially in relation to cognitive deficits observed in other studies[25,26]. There is evidence that exposure to persistent organic pollutants (POPs) is responsible for serious deleterious effects on the developing central nervous system during the fetal stage, resulting in decreased intelligence quotient (IQ) and behavioral problems[27-29].

In addition to the numerical parameters (concentration and index) mentioned, the toxic substances to which the women/newborns were exposed should be considered because there are metals (mercury, lead, cadmium, and arsenic) and pesticides that regardless of existing quantities in the tissue are harmful to health. However, the contamination index proposed for the contamination analysis of metals and pesticides showed no relationship between maternal exposure and such clearly apparent perinatal outcomes, but it could be a parameter to be considered in toxicology studies. A limitation of this study was the sample size of the study population. Thus, the development of epidemiological studies to investigate the effects of POPs at different stages of life is extremely important, in order to stimulate campaigns to reduce the indiscriminate use of POPs and increase awareness of the risks of these products to the population.

Conclusion

The maternal contamination index of metals and pesticides was not related to perinatal outcomes, but it could be used as baseline parameter in future toxicological studies, regarding to long-term toxic characteristics as persistent organic pollutants, its long half-lives, bioacumulative, and expected to impose serious health effects on humans.

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Acknowledgements

To staff of Laboratory of Experimental Research on Ginecology and Obstetrics; to University of Tromsø, and University of Aarhus; the Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway; and Jose Eduardo Corrente

for statistical analysis.

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Received: Mar 11, 2016
Review: May 09, 2016
Accepted: Jun 13, 2016
Conflict of interest: none
Financial source: Nordic Council of Ministers

[1]Research performed at Laboratory of Experimental Research on Gynecology and Obstetrics, Botucatu Medical School, Universidade Estadual Paulista (UNESP), Botucatu-SP, Brazil. Part of PhD degree thesis, Postgraduate Program in Gynecology, Obstetrics and Mastology. Tutors: Marilza Vieira Cunha Rudge and Débora Cristina Damasceno.