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FISH INTAKE DURING PREGNANCY AND MERCURY LEVEL IN CORD AND MATERNAL BLOOD AT DELIVERY: AN ENVIRONMENTAL STUDY IN POLAND

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Abstract

Objectives: The purpose of this study was to estimate the amount of absorbed mercury (Hg) by mothers and their infants as a result of fish consumption during pregnancy. **Materials and Methods:** The cohort consisted of 313 mother-infant pairs recruited initially from ambulatory prenatal clinics in the first and second trimesters of pregnancy. The customary pattern of fish consumption during pregnancy reported by mothers was correlated with Hg levels in cord and maternal blood at delivery. Blood Hg level was measured using atomic absorption spectrometry. **Results:** The mean Hg concentration in cord blood was markedly higher than in maternal blood at delivery (1.09 µg/L; 95%CI: 1.00–1.13 µg/L vs. 0.83 µg/L; 95%CI: 0.76–0.91 µg/L). There was significant correlation ($r_s = 0.62, 95\%$ CI: 0.55–0.69) between Hg levels in cord and maternal blood. The overall ratio of Hg in cord blood vs. maternal blood was 1.7 (95%C: 1.50–1.89). Fish consumed during the last pregnancy trimester correlated stronger with umbilical cord Hg concentrations ($r_s = 0.32; 95\%$ CI: 0.22–0.40) than with Hg in maternal blood ($r_s = 0.23; 95\%$ CI: 0.14–0.33). **Conclusions:** The study shows that in Poland, babies are exposed to moderate levels of mercury prior to birth and that fish eating in pregnancy significantly contributes to prenatal Hg exposure. The findings also suggest that the level of cord blood Hg should not be used for describing inter-individual differences in maternal exposure to Hg compounds unless a proper correction factor is introduced.

Key words:

Fish intake during pregnancy, Prenatal mercury exposure, Cohort study

INTRODUCTION

It is generally believed that fish intake during pregnancy has the favorable effect on fetal development because it is a rich source of iron and long chain unsaturated fatty acids, which are essential for healthy development and function of the nervous system. Some studies have provided evidence that fish oil supplementation of the infant formula may improve infant growth and cognitive development [1,2]. However, the issue is debatable because fish consumption during pregnancy may be implicated in adverse effects on children's cognitive development. This danger results from the fact that fish is a common source of

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methylmercury (MeHg), which absorbed by mother easily crosses the placenta and accumulates in the fetus at higher concentrations than in mothers [3–6]. The importance of prenatal mercury (Hg) exposure for children's neurode-velopment has been studied extensively after poisoning disasters in Japan and Iraq [7–9] and analyzed in the course of epidemiological studies in populations consuming large quantities of fish [10–13].

Until now environmental studies on fish-related prenatal exposure to mercury have not been performed in the countries of central and eastern Europe, and the study was undertaken to describe the usual fish consumption pattern during pregnancy and to estimate a possible amount of absorbed mercury by mothers and their infants in Poland.

MATERIALS AND METHODS

Study subjects

The cohort consisted of 313 mother-infant pairs recruited from ambulatory prenatal clinics in the first and second trimesters of pregnancy. The enrolment included only non-smoking women with singleton pregnancies, aged 18-35 years, free from chronic diseases, such as diabetes and hypertension. Upon enrolment, a detailed questionnaire was administered to each woman to elicit information on demographic data, medical and reproductive history, occupational exposures, alcohol consumption, and smoking practices of others present in the home. Maternal fish intake during various trimesters of pregnancy and in the last two weeks before the delivery was assessed by the food frequency questionnaire completed by trained interviewers twice in the gestation period. The detailed information on eating frequency of smoked, fried, roasted and grilled fish servings have been collected. To estimate the amount of fish eaten per week we assumed that each fish meal averaged 150 g.

Table 1 presents characteristics of the study population sub-grouped subsequently by the reported fish consumption in the last pregnancy trimester. Based on the amount of various fish servings (smoked, fried, roasted, and grilled) consumed in the third trimester of pregnancy, the women were divided into two subgroups. We assigned women who reported lower fish consumption (equal or less than **Table 1.** Characteristics of the total study sample and the subgroups by fish consumption during the third trimester

Variables	Total (n = 313)	Fish consumption during the third trimester		
		$\leq 150 \text{ g/week}$ $(n = 180)$	>150 g/week (n = 133)	Р
Mother's age Mean SD	27.79 3.389	27.48 3.462	28.22 3.253	0.0560
Education (years) Mean SD	15.69 2.792	15.71 2.683	15.66 2.944	0.8772
Parity 1 n (%) $\ge 2 n (\%)$	190 (60.7) 123 (39.3)	109 (60.6) 71 (39.4)	81 (60.9) 52 (39.1)	1.0000
Gender Boys n (%) Girls n (%)	159 (50.8) 154 (49.2)	87 (48.3) 93 (51.7)	72 (54.1) 61 (45.9)	0.3678
Gestational age (weeks) Mean SD	39.43 1.341	39.42 1.430	39.44 1.215	0.8893
Birth weight (g) Mean SD	3444.2 463.7	3449.3 439.9	3437.4 495.6	0.8219
Length at birth (cm) Mean SD	54.81 2.702	54.75 2.629	54.89 2.805	0.6530
Head circumference (cm) Mean SD	33.91 1.418	33.89 1.502	33.94 1.301	0.7539
Maternal blood mercury (μ g/L) Mean SD Median (Q_3 - Q_1)/2	0.833 0.681 0.600 0.300	0.718 0.534 0.600 0.249	0.988 0.817 0.720 0.350	0.0005
Cord blood mercury ($\mu g/L$) Mean SD Median ($Q_{x}-Q_{1}$)/2	1.093 0.675 0.900 0.407	0.941 0.605 0.800 0.309	1.299 0.713 1.200 0.457	0.0000
Season of birth Spring n (%) Summer n (%) Autumn n (%) Winter n (%)	81 (25.9) 61 (19.5) 93 (29.7) 78 (24.9)	42 (23.3) 38 (21.1) 53 (29.4) 47 (26.1)	39 (29.3) 23 (17.3) 40 (30.1) 31 (23.3)	0.5969
Cesarean section No n (%) Yes n (%)	255 (81.5) 58 (18.5)	151 (83.9) 29 (16.1)	104 (78.2) 29 (21.8)	0.2566

P-level of significance; SD - standard deviation.

150 g/week) to the lower exposed (LE) subgroup and those who consumed more (>150 g/week) to the higher exposed (HE) subgroup.

Blood sample collection and analysis

Cord blood and maternal blood samples were drawn at delivery into evacuated blood collection tubes that had been treated with ethylene diamine tetra-acetate (EDTA). Then the tubes were inverted several times to mix EDTA and blood to prevent coagulation. The blood for Hg analysis was refrigerated without any processing. Mercury level was measured at the Centers for Disease Control (CDC), Atlanta, GA, USA, by Zeeman graphite furnace atomic absorption spectrometry, using a phosphate/Triton X-100/ nitric acid matrix modifier. The CDC, using cold vapor atomic spectrometry following chemical reduction of Hg compounds, measures total mercury in whole blood.

Statistical analysis

In the descriptive analysis, the distribution of various characteristics of women under study in terms of the Hg exposure level has been considered. The Chi-square statistics (nominal variables) and analysis of variance (numerical variables) tested differences between subgroups with lower and higher fish intake. The relationship between the fish consumption pattern and Hg level in cord and maternal blood was measured using the Spearman correlation coefficient and linear multivariate regression. All statistical analyses were performed with STATA release 9 [14,15].

RESULTS

The women with higher fish consumption were slightly older than those consuming less fish (28.2 vs. 27.5). There was a significantly higher Hg content in the maternal and cord blood in the more exposed subgroup. In the total study group, there was 87% of women who confirmed consumption of various amounts of fish during pregnancy. Mean amount of fish intake (g/week) was much lower in the last two weeks of pregnancy (mean = 75.4 g, 95%CI: 65.4–85.4) in comparison to the average fish consumption in the first two trimesters (mean = 139.0 g;

95%CI: 125.3–152.6) and over the whole third trimester (mean = 175.8 g; 95%CI: 159.3–192.3). The Spearman correlation coefficient between the amount of fish intake (g/week) in the first two trimesters and third trimester was 0.41 (95%CI: 0.34-0.48).

The distribution of blood Hg levels in newborns and their mothers was skew to the right (Fig. 1). Among the newborns, the mean Hg concentration was markedly higher than in mothers at delivery (1.09 μ g/L; 95%CI: 1.00–1.13 vs. 0.83 μ g/L; 95%CI: 0.76–0.91). There was significant correlation ($r_s = 0.62$, 95%CI: 0.55–0.69) between Hg levels in maternal blood and cord blood. Figure 2 shows the plotting of Hg concentrations in maternal blood against those in the umbilical cord. The overall ratio of Hg concentration in cord blood vs. maternal blood was 1.7 (95%CI: 1.50–1.89).

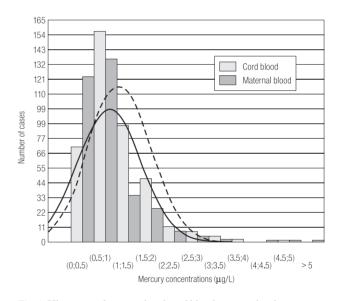


Fig. 1. Histogram of maternal and cord blood mercury levels.

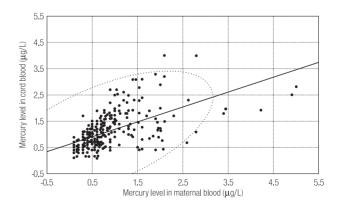


Fig. 2. Scatter plot of mercury in maternal and cord blood.

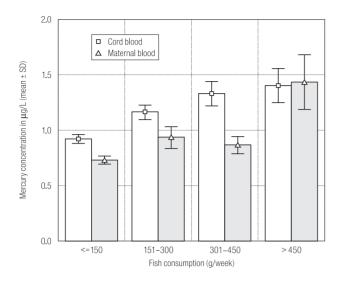


Fig. 3. Maternal and cord mercury levels related to fish consumption.

The mean cord blood Hg level in newborns of mothers who reported fish consumption in the third trimester was significantly higher (1.12; 95%CI: 1.05–1.20) in comparison to newborns born to mothers who did not eat fish in the last trimester of pregnancy (0.66; 95%CI: 0.55-0.77). The corresponding Hg levels in the maternal blood were 0.88 µg/L (95%CI: 0.80–0.96) and 0.47 µg/L (95%CI: 0.45–0.72). Fish consumed during the last pregnancy trimester correlated stronger with umbilical cord Hg concentrations ($r_s = 0.32$; 95%CI: 0.22–0.40) than with maternal blood Hg at delivery ($r_s = 0.23$; 95%CI: 0.14–0.33). Figure 3 presents the scatter plot with regression line and 95% prediction intervals for fish consumption and cord blood Hg concentrations. One can estimate that up to 10% of variability (95%CI: 5.0-16.2) in cord blood Hg may be explained by the amount of fish consumption in the third pregnancy trimester. The corresponding estimates of variability in maternal blood Hg explained by fish consumption would amount to 5.3% (95%CI: 2.0-10.9).

Table 2 presents the correlation coefficients between the Hg level in cord and maternal blood at delivery and the mean weekly fish intake (g/week) of different types of fish servings in various trimesters of pregnancy. The total amount of fish intake in the last trimester of pregnancy correlated better with cord blood Hg ($r_s = 0.32$) than with maternal blood Hg at delivery ($r_s = 0.25$). The corresponding correlation coefficients for the first two pregnancy trimesters were $r_s = 0.24$ and $r_s = 0.11$.

 Table 2. Correlation between the fish consumption pattern (g/week)

 during different trimesters of pregnancy and mercury (Hg) level in

 cord and maternal blood at delivery (the Spearman nonparametric

 correlation coefficient)

Cord blood Hg	Maternal blood Hg				
First and second trimester					
0.224**	0.089				
0.147*	0.040				
0.082	0.072				
0.241**	0.107				
Third trimester					
0.217**	0.154*				
0.306**	0.275**				
0.066	0.065				
0.321**	0.252**				
	Contract 0.224** 0.147* 0.082 0.241** Third trimester 0.217** 0.306** 0.066				

* Significant at p < 0.01; ** Significant at p < 0.001.

DISCUSSION

On the basis of our study we can claim that fish consumption (g/week) in Poland is rather moderate and amounts to 140 g/week on average in the first two trimesters and to about 180 g/week in the third trimester. As expected, intake of fish drops by about 50% at the end of pregnancy relative to its average, individual consumption throughout pregnancy. About 90% of newborns showed Hg concentration below 2 μ g/L, while 90% of mothers showed blood Hg level below 1.6 μ g/L. Similar results on Hg levels in cord and maternal blood were reported from communities in Sweden [16,17]. In 2001, the CDC reported Hg levels in blood in a representative sample of the US population [18]. The geometric mean blood Hg levels were 0.3 μ g/L for children 1–5 years old and 1.2 μ g/L for women 16–49 years old.

Neither Hg level in maternal blood (0.83 μ g/L) nor cord blood Hg concentrations (1.09 μ g/L) observed in our study were high, considering that cord blood Hg level above 5.8 μ g/L is assumed to be associated with loss of IQ in prenatally exposed children [19]. Methylmercury concentration in scalp hair during pregnancy is considered a reliable indicator for predicting the probability of psychomotor retardation in the child. The US Environemntal Protecton Agency (EPA) has established the reference dose of 1.0 mg total Hg/kg/ dry weight in hair as indicative of mercury exposure and at this level, women of child-bearing age are advised to stop consumption of fish that may have elevated Hg levels [20]. The mentioned criteria should be considered as preliminary until additional information can be obtained from cohort studies actually in progress. Our analysis has recently shown the increased prevalence of delayed cognitive and psychomotor functions in oneyear-old infants who had much lower Hg content in cord blood [21]. However, the risks of exposure to MeHg from fish have to be balanced with health benefits of fish eating. Fish is a source of high-quality protein as well as of unsaturated fatty acids and other beneficial nutrients.

Like in other studies, we found the significant relationship between fish intake and mercury concentration in cord and maternal blood at delivery. In our study, the maternal blood Hg level was higher by 0.30 µg/L on average among fish eaters compared to those who denied fish consumption in pregnancy (0.88 µg/L vs. 0.58 µg/L). We also found much higher cord blood Hg level (by $0.46 \,\mu\text{g/L}$) in newborns born to fish eaters compared to non-eaters (1.12 µg/L vs. 0.66 µg/L). Using linear regression models, we estimated that in the total study group, the cord blood mercury level increased by 0.14 µg/L on average with each 100 g of fish intake/week during pregnancy, and only by $0.09 \mu g/L$ in maternal blood. We also estimated that the fish consumption in pregnancy accounts for 10% of variability in cord blood Hg level. Therefore, up to 90% of variability in cord blood Hg concentrations results from other sources of exposure, which may among others be dental amalgam fillings in mothers. Health effects of Hg amalgam fillings (containing 50% of Hg), producing higher mercury level in maternal and cord blood or placenta, have been a matter of concern for years [22–25]. Another source of Hg exposure may be the use of skin-lightening creams and teething powders in pregnancy [26]. A good portion of variability in blood Hg levels at delivery may be explained, however, by the influence of maternal blood MeHg even before pregnancy [27–29].

We confirmed the higher ratio of Hg concentrations in cord blood compared to that found in maternal blood. The explanation of these findings is not straightforward. The described differences could not result from the laboratory bias since maternal and cord blood samples were collected, stored and analyzed in the same manner by the same laboratory, and the samples were blinded for the lab personnel. Other reports from various populations also indicated that the gradient of mercury between cord and maternal blood at the time of delivery was greater than 1.0 [30–33]. In our study, the median ratio of Hg levels in cord blood and maternal blood was 1.7 (95%CI: 1.50–1.89), and our estimates were very close to those published by EPA in 2003, which have been based on a comprehensive review of 21 studies worldwide [34]. A significantly lower Hg concentration in maternal blood at delivery should be taken into consideration if the exposure assessment risk analysis for population at large is to be based on maternal blood data at delivery. The increased Hg concentrations in cord blood relative to

maternal blood is usually attributed to the binding of MeHg to fetal hemoglobin. A higher concentration of MeHg in the cord blood may also result from a larger hematocrit and a higher hemoglobin concentration in newborns. Fetal-specific serum albumin proteins, such as alpha-fetoprotein may also lead to greater inherent affinity of fetal blood for MeHg compared with maternal blood [35]. To date however, the different binding of MeHg to fetal and adult proteins does not appear to have been investigated.

CONCLUSIONS

Our study shows that babies in Poland are exposed to moderate levels of mercury prior to birth. Although the fish-eating pattern was found to be significantly related to both maternal and cord blood levels, only about 10% of variability in cord blood Hg level was explained by this factor. The findings also suggest that the level of cord blood mercury should not be used for describing the inter-individual differences in maternal exposure to Hg compounds unless a proper correction factor is introduced.

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REFERENCES

- 1. Fewtrell MF, Abbot RA, Kennedy K, Singhal A, Morley R, Caine E, et al. *Randomized, double-blind trial of long-chain polyunsaturated fatty acid supplementation with fish oil and borage oil in preterm in-fants*. J Pediatr 2004;144:471–9.
- O'Connor DL, Auestad N, Jacobs J, Margeson D, Hall R, Fitzgerald K, et al. Growth and development in preterm infants fed log-chained polyunsaturated fatty acids: a prospective, randomized controlled trial. Pediatrics 2001;108:359–71.
- Kjellström, T, Kennedy P, Wallis S, Stewart A, Friberg L, Lind B, et al. *Physical and mental development of children with prenatal exposure to mercury from fish. Stage 1. Preliminary tests at age 6* [Report 3642]. Stockholm, Sweden: National Swedish Environmental Protection Board; 1989.
- Chang LW, Reuhl KR, Spyker JM. Ultra structural study of the latent effects of methyl mercury on the nervous system after prenatal exposures. Environ Res 1997;13:171–85.
- Evaluation of Carcinogenic Risk to Humans. Mercury and Mercury Compounds. Monographs, Vol. 58. Lyon: International Agency for Research on Cancer; 1994.
- Methylmercury. Environmental Health Criteria, No. 101. Geneva: World Health Organization; 1990.
- Amin-Zaki L, Elhassani S, Majeed MA, Clarkson TW, Doherty RA, Greenwood M. *Intrauterine methylmercury poisoning in Iraq*. Pediatrics 1974;54:587–95.
- Amin-Zaki L, Majeed MA, Elhassani SB, Clarkson TW, Greenwood MR, Doherty RA. *Prenatal methylmercury poisoning. Clinical observations over five years*. Am J Dis Child 1979;133:172–7.
- Takizawa Y, Kitamura S. Estimation of the incidence of mercury exposure in the Minamata and Niigata areas using mathematical model from Iraqi poisonings. In: Takizawa Y, Osame M, editors. Understanding Minamata Disease: Methylmercury Poisoning in Minamata and Niigata. Tokyo, Japan: Japan Public Health Association; 2001. p. 27–32.
- Meyers GJ, Marsh DO, Davidson PW, Cox C, Shamlaye CF, Tanner MA, et al. Main neurodevelopment study in Seychellois children following in utero exposure to methylmercury from a maternal fish diet: outcome at six months. Neurotoxicology 1995;16:653–64.
- Grandjean P, Weihe P, White RF, Debes F, Araki S, Yokoyama K, et al. Cognitive deficit in 7-year-old children with prenatal exposure to methymercury. Neurotoxicol Teratol 1997;19:417–28.
- 12. Davidson PW, Myers GJ, Cox C, Axtell C, Shamlaye C, Sloane-Reeves J, et al. *Effects of prenatal and postnatal methylmercury exposure from fish consumption on neurodevelopment: outcomes at*

66 months of age in the Seychelles child development study. JAMA 1998;280:701–7.

- Meyers GJ, Marsh DO, Davidson PW, Cox C, Shamlaye CF, Palumbo D, et al. *Prenatal methylmercury exposure from ocean fish consumption in the Seychelles child development study.* Lancet 2003;361:1686–92.
- Kohler U, Kreuter F. *Data analysis using STATA*. Texas: Stata Press Publication, College Station; 2005.
- 15. STATA software for windows, release 9. Texas: StaCorp; 2005.
- Bjonberg KA, Vahter M, Petersson-Grawe K, Glynn A, Cnattingias S, Darnerud PO, et al. *Methyl mercury and inorganic mercury in Swedish pregnant women and in cord blood: influence of fish consumption.* Environ Health Perspect 2003;111:637–41.
- 17. Lindqvist OK, Johansson M, Astrup A, Anderson L, Bringmark G, Hovsenius L, et al. *Mercury in the Swedish environment: recent research on cause, consequences and connective methods.* Water Air Soil Pollut 1991;55:1–261.
- Center for Disease Control and Prevention. Blood and hair mercury levels in young children and women of child bearing age in United States, 1999. Morb Mortal Wkly Rep 2001;50:140–3.
- National research Council (NRC). Toxicological effects of methylmercury. Washington (DC). National Academy Press; 2000.
- 20. Maas RP, Patch SC, Sergent KR. A Statistical Analysis of Factors Associated with Elevated Hair Mercury Levels in the US Population: An Interim Progress Report. Tech Rep 04-136. Ashville: Environmental Quality Institute, University of North Carolina, 2004.
- Jędrychowski W, Jankowski J, Flak E, Skarupa A, Mróz E, Sochacka-Tatara E, et al. *Effects of prenatal exposure to mercury on cognitive* and psychomotor function in one-year-old infants: Epidemiological cohort study in Poland. Ann Epidemiol 2006;16:439–47.
- 22. Skare I, Engqvist A. Human exposure to mercury and silver released from dental amalgam restorations. Arch Environ Health 1994;49:384–94.
- Langworth, S, Kolbeck KG, Akesson A. Mercury exposure from dental fillings. II. Release and absorption. Swed Dent J 1988;12:71–2.
- Olsson S, Bergman M. Daily dose calculations from measurements of intra-oral mercury vapor. J Dent Res 1992;71:414–23.
- Lorscheider FL, Vimy MJ, Summers AO, Zwiers H. The dental amalgam mercury controversy – inorganic mercury and the CNS; genetic linkage of mercury and antibiotic resistances in intestinal bacteria. Toxicology 1995;97:19–22.
- Hursh JB, Clarkson TW, Miles EF, Goldsmith LA. Percutaneous absorption of mercury vapor by man. Arch Environ Health 1989;44:120–7.

- Johnson DC, Braman RS. Distribution of atmospheric mercury species near ground. Environ Science Technol 1974;8:1003–9.
- Matheson DH. Mercury in the atmosphere and in precipitation. In: Nriagu JO, editor. The Biogeochemistry of Mercury in the Environment. Amsterdam: Elsevier; 1979. p. 113–29.
- 29. Beusterien KM, Etzel RA, Agocs MM, Egeland GM, Socie EM, Rouse MA, et al. *Indoor air mercury concentrations following application of interior latex paint.* Arch Environ Contam Toxicol 1991;21:62–4.
- Dennis CAR, Fehr F. The relationship between mercury levels in maternal and cord blood. Sci Total Environ 1975;3:275–7.
- Fujita M, Tokabatake E. Mercury levels in human maternal and neonatal blood, hair, and milk. Bull Environ Contam Toxicol 1977;18:205–9.

- Kuhnert PM, Kuhnert BR, Erhard P. Comparison of mercury levels in maternal blood, fetal cord blood and placental tissues. J Obstet Gynecol 1981;139:209–13.
- 33. Brune D, Nordberg DF, Vesterberg O, Gehardson I, Wester PO. A review of normal concentration of mercury in human blood. Sci Total Environ 1991;100:235–82.
- 34. Stern AH, Smith AE. An assessment of the cord blood: maternal blood methylmercury ratio: implications for risk assessment. Environ Health Perspect 2003;111:1465–70.
- Deutsch HF. Chemistry and biology of alpha-fetoprotein. Adv Cancer Res 1991;56:253–312.