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Higher Fish Consumption in Pregnancy May Confer Protection against the Harmful Effect of Prenatal Exposure to Fine Particulate Matter

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Key Words
Air pollutants · Prenatal exposure · Fish consumption · Birth size · Cohort study

Abstract
Background/Aim: The objective of this study was to assess a hypothesized beneficial effect of fish consumption during the last trimester of pregnancy on adverse birth outcomes resulting from prenatal exposure to fine air particulate matter. ***Methods:*** The cohort consisted of 481 nonsmoking women with singleton pregnancies, of 18–35 years of age, who gave birth at term. All recruited women were asked about their usual diet over the period of pregnancy. Measurements of particulate matter less than 2.5 μm in size ($PM_{2.5}$) were carried out by personal air monitoring over 48 h during the second trimester of pregnancy. The effect of $PM_{2.5}$ and fish intake during gestation on the birth weight of the babies was estimated from multivariable linear regression models, which beside the main independent variables considered a set of potential confounding factors such as the size of the mother (height, prepregnancy weight), maternal education, parity, the gender of the child, gestational age and the season of birth. ***Results:*** The study showed that the adjusted birth weight was significantly lower in newborns whose mothers were exposed to particulate matter greater than 46.3 $\mu g/m^3$ (β coefficient = –97.02, $p = 0.032$). Regression analysis stratified by the level of maternal fish consumption (in tertiles) showed that the deficit in birth weight amounted to 133.26 g ($p = 0.052$) in newborns whose mothers reported low fish intake (<91 g/week). The birth weight deficit in newborns whose mothers reported medium (91–205 g/week) or higher fish intake (>205 g/week) was insignificant. The interaction term between $PM_{2.5}$ and fish intake levels was also insignificant (β = –107,35, $p = 0.215$). Neither gestational age nor birth weight correlated with maternal fish consumption. ***Conclusions:*** The results suggest that a higher consumption of fish by women during pregnancy may reduce the risk of adverse effects of prenatal exposure to toxicants and highlight the fact that a full assessment of adverse birth outcomes resulting from prenatal exposure to ambient hazards should consider maternal nutrition during pregnancy.

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Introduction

Newborns and young children are especially vulnerable to the toxic effects of ambient pollutants such as polycyclic aromatic hydrocarbons (PAHs), nitrosamines, pesticides, polychlorinated biphenyls, metals and radiation [1–4]. Moreover, there is a large body of data showing that, in addition to parental smoking and environmental tobacco smoke [5–11], outdoor and indoor air pollutants may increase the risk of adverse birth outcomes, including lower birth weight, premature births and intrauterine growth retardation [12–20].

While a vast number of published papers have documented the detrimental effects of ambient pollutants on birth outcomes, there is a scarcity of data on the potential protective effects of maternal nutrition in pregnancy against the health hazards for newborns resulting from prenatal exposure to pollutants. It has long been known from human studies that pregnancy outcomes are related to maternal nutrition [21–29], and maternal fish intake during pregnancy attracted much attention because fish is a rich source of proteins, vitamins, iron and long-chain unsaturated fatty acids, which are necessary for healthy fetal development [30–33].

The objective of this analysis was to assess a hypothesized protective effect of maternal fish consumption in pregnancy against the birth weight deficit resulting from prenatal exposure to fine air particulate matter, which was confirmed by our earlier findings [19, 20]. This is a hot topic for public health, since air pollution abatement programs have proven to be insufficient or inadequate in many settings.

Subjects and Methods

Subjects

The design of this prospective cohort study and the detailed selection of the population have been described previously [34]. Briefly, this is part of an ongoing comparative longitudinal investigation of the health impact of prenatal exposure to outdoor/indoor air pollution on infants and children being conducted in New York City and Krakow. The Ethical Committee of the Jagiellonian University approved the study.

The data under present analysis came from 481 women who gave birth at term (>36 weeks of gestation) between January 2001 and February 2004. Women attending ambulatory prenatal clinics in the first and second trimesters of pregnancy were eligible for the study. The enrolment included only nonsmoking women with singleton pregnancies, aged 18–35 years, who were free from chronic diseases such as diabetes and hypertension. Upon enrolment, a detailed questionnaire was administered to each subject at the entry to the study to solicit information on demographic data, home characteristics, date of the last menstrual period, medical and reproductive history, occupational hazards, alcohol consumption and nutritional habits. After the participating women had given birth, maternal and hospital records were reviewed and birth weight was recorded for all infants. The gestational age at birth was defined as the interval between the first day of the mother's last menstrual period and the date of birth.

Dosimetry of Prenatal Personal Exposure to Fine Particles

During the second trimester, a member of the air monitoring staff instructed the woman in the use of the personal monitor, which is lightweight, quiet and worn in a backpack. The woman was asked to wear the monitor during the daytime for 2 consecutive days and to place the monitor near the bed at night. During the morning of the second day, the member of the air monitoring staff and an interviewer visited the woman's home to change the battery pack and administer the full questionnaire. They also checked to see that the monitor had been running continuously and that there had been no technical or operating failures. A staff member returned to the woman's home on the morning of the third day to pick up the equipment.

A Personal Environmental Monitoring Sampler, designed by the Department of Environmental Health, School of Public Health at Harvard University, was used to measure the mass of the particles with a size of ≤ 2.5 μm ($PM_{2.5}$) at a flow rate of 4.0 liters/min. Flow rates were calibrated (with filters in place) using a bubble meter prior to the monitoring and were checked again with the change of the battery pack on the second day and at the conclusion of the monitoring. Pumps operated continuously at 2 l/min over the 48-hour period. Particles were collected on a Teflon membrane filter (37-mm Teflon™; Gelman Sciences). The combination of the low pressure drop (permitting use of a low-power sampling pump), low hygroscopicity (minimizing bound water interference in mass measurements) and low trace element background (improving analytical sensitivity) of these filters makes them highly appropriate for personal particle sampling.

Dietary Assessment

Dietary assessment was carried out in a face-to-face interview with each participating woman at the entry to the study, using a semiquantitative food frequency questionnaire (FFQ). Interviews on selected food items were completed twice during the gestation period (in the second and third trimester of pregnancy). In the course of the food interviews, detailed information on the frequency of consumption of smoked, fried, roasted and grilled fish servings was collected. Maternal fish intake was categorized as follows: never, less than once a month, once a week, 1–2 times a week, 3–4 times a week or every day. We assumed that each fish meal averaged 150 g to estimate the median grams of fish eaten per week.

Statistical Methods

The descriptive part of the analysis preceded the main statistical evaluation of the data, which aimed to explain the relationship between birth weight (dependent variable) and the 2 main independent variables (maternal personal exposure to fine particles in pregnancy and maternal fish consumption). Beside the main independent variables, the first regression model included maternal age, maternal size (height, prepregnancy weight), maternal education, parity, gestational age, the gender of the child and the sea-

Table 1. Characteristics of the study group according to the level of fish consumption (in tertiles) over the last trimester of pregnancy

	Total (n = 481)	Fish consumption during the third trimester			
		<91 g/week (n = 181)	91–205 g/week (n = 174)	>205 g/week (n = 126)	p
Maternal age, years	27.56 ± 3.588	27.27 ± 3.743	27.82 ± 3.400	27.62 ± 3.613	0.3365
Maternal education, years of schooling	15.56 ± 2.750	15.49 ± 2.776	15.67 ± 2.652	15.52 ± 2.861	0.8094
Mother's height, cm	165.05 ± 5.490	165.40 ± 5.883	164.84 ± 5.275	164.83 ± 5.206	0.5515
Mother's prepregnancy weight, kg	58.23 ± 8.491	57.65 ± 7.522	59.11 ± 9.765	57.83 ± 7.853	0.2240
Parity					
1	305 (63.4)	118 (65.2)	112 (64.4)	75 (59.5)	
≥2	176 (36.6)	63 (34.8)	62 (35.6)	51 (40.5)	0.5664
Gender of baby					
Boys	245 (50.9)	85 (47.0)	92 (52.9)	68 (54.0)	0.3928
Girls	236 (49.1)	96 (53.0)	82 (47.1)	58 (46.0)	
Gestational age, weeks	39.54 ± 1.140	39.59 ± 1.164	39.45 ± 1.120	39.58 ± 1.134	0.4723
Birth weight, g	3,445.6 ± 435.02	3,454.9 ± 425.34	3,429.1 ± 417.96	3,455.1 ± 473.09	0.8230
ETS					
No	352 (73.2)	124 (68.5)	133 (76.4)	95 (75.4)	0.1951
Yes	129 (26.8)	57 (31.5)	41 (23.6)	31 (24.6)	
$PM_{2.5}$, μg/m^3					
<27.0	161 (33.5)	69 (38.1)	51 (29.3)	41 (32.5)	
27.0–46.29	162 (33.7)	51 (28.2)	72 (41.4)	39 (33.7)	0.0816
>46.29	158 (32.8)	61 (33.7)	51 (29.3)	46 (32.8)	
Season of birth					
Spring	144 (29.9)	49 (27.1)	49 (28.2)	46 (36.5)	
Summer	114 (23.7)	50 (27.6)	38 (21.8)	26 (20.6)	0.2209
Autumn	119 (24.7)	39 (21.5)	46 (26.4)	34 (27.0)	
Winter	104 (21.6)	43 (23.8)	41 (23.6)	20 (15.9)	

Values are means ± SD or numbers of subjects (percentages in parentheses). ETS = Environmental tobacco smoke.

son of birth. The season of birth was introduced in the regression models as a dummy variable, with summer defined as the reference level. As the distributions of the air pollutants and fish consumption were markedly skewed, the variables were introduced in regression models as ordered categorical variables (divided by tertiles of given distributions). In the subsequent model, we included the interaction term ($PM_{2.5}$ levels × fish intake below the first tertile). In order to asses the magnitude of the birth weight deficit at various $PM_{2.5}$ and fish consumption levels, stratified regression models for each strata of fish intake (in tertiles) were performed. In all statistical analyses, the significance level was assumed as $p \leq 0.05$.

Results

Table 1 describes the characteristics of women and newborns in the total study sample and in subgroups defined by the level of fish consumption (in tertiles). The characteristics of mothers and newborns were similar across the subgroups with different levels of fish intake. The mean birth weight and gestational age for the babies under study were 3,445.6 g (95% confidence interval 3,405.9–3,484.1 g) and 39.5 weeks (95% confidence interval 39.2–39.5 weeks), respectively. Neither gestational age ($r = 0.020$, $p = 0.687$) nor birth weight ($r = 0.002$, $p = 0.968$) correlated with the fish consumption over the period of pregnancy. Analysis of personal air samples collected from pregnant women in the second trimester showed that median prenatal $PM_{2.5}$ exposure averaged 35.3 μg/m^3, with a wide range of concentrations (10.4–249.9 μg/m^3).

Table 2 presents the β regression coefficients for birth weight and $PM_{2.5}$, estimated from statistical regression models, which accounted for potential confounders. Regression coefficients from model A, which did not include the interaction term ($PM_{2.5}$ × fish intake level), showed that the birth weight deficit among infants ex-

Table 2. Effect of prenatal exposure to fine particulate matter and maternal fish consumption on the birth weight of babies estimated from the multivariable linear regression model A (without interaction)

Predictors	Coefficient	p-level	95% confidence interval	
Maternal age	–1.50	0.792	–12.63	9.63
Maternal education[a]	8.80	0.194	–4.48	22.08
Maternal height	12.20	0.000	–5.58	18.82
Maternal prepregnancy weight	11.29	0.000	6.98	15.59
Gestational age	139.33	0.000	109.80	168.85
Parity[b]	113.12	0.001	49.19	177.05
Female child	–181.01	0.000	–248.43	–113.59
Fish consumption level[c]	18.56	0.602	–51.31	88.43
Prenatal exposure to fine particulate matter (in tertiles)				
$PM_{2.5}$ <27.0 μg/m^3	1.00			
$PM_{2.5}$ 27.0–46.29 μg/m^3	–1.01	0.981	–83.19	81.17
$PM_{2.5}$ >46.29 μg/m^3	–97.02	0.032	–185.67	–8.37
Intercept	–4,767.99	0.000	–6,385.04	–3,150.95

Additionally included in the regression model: season of birth. n = 481.
[a] Years of schooling.
[b] 1 = First, 2 = second, 3 = third or more.
[c] 1 = Low level (<91 g/week), 0 = >90 g/week.

posed to higher $PM_{2.5}$ concentrations (>46.3 μg/m^3) amounted to 97.02 g (p = 0.032). The regression model B (table 3), which considered the full set of covariates together with the interaction term, demonstrated that the interaction between prenatal $PM_{2.5}$ exposure and fish intake level was insignificant (β = –107.35, p = 0.215).

Table 4 shows the regression coefficients for $PM_{2.5}$ and birth weight estimated from regression analysis stratified by the tertiles of fish intake and adjusted for all covariates considered in the previous models. The estimated birth weight deficit of newborns whose mothers reported low fish intake (<91 g/week) and were exposed prenatally to higher $PM_{2.5}$ concentrations (>46.3 μg/m^3) amounted to –133.26 g (p = 0.052). The regression coefficients for birth weight and $PM_{2.5}$ in newborns whose mothers reported medium (91–205 g/week) or higher fish consumption (>205 g/week) were insignificant; the corresponding regression coefficients were –93.38 (p = 0.247) and –23.69 (p = 0.811).

Discussion

Since the results showed that the negative impact of fine particulate matter on birth weight was only significant in infants born to mothers who reported low fish consumption in pregnancy, this may suggest that a higher maternal fish intake confers protection against the harmful effect of prenatal exposure to ambient toxicants. We estimated that in infants whose mothers reported low fish consumption (<91 g/week), the average birth weight deficit attributable to higher prenatal exposure to fine particulate matter (>46.3 μg/m^3) amounted to 133 g. However, the interaction term between low fish consumption and prenatal exposure to fine particulate matter was insignificant.

The biological mechanisms whereby $PM_{2.5}$ might cause adverse pregnancy outcomes are still unclear. $PM_{2.5}$ is a proxy measure of a wide range of toxic agents present in the environment, which mainly occur through combustion processes that generate other toxic agents as well. Usually, the ambient fine particle fraction contains constituents of soots including PAHs, tobacco and wood smoke, organic compounds, sulfates and metals [35]. All these substances may potentially affect intrauterine fetal growth.

Our observation suggesting a protective effect of higher fish consumption against harmful ambient hazards in fetal development is consistent with the actual body of knowledge on the importance of n-fatty acids in health and disease [36]. The intake of fish or fish oils has long been hypothesized to prevent certain chronic conditions

Table 3. Effect of prenatal exposure to fine particulate matter and maternal fish consumption on the birth weight of babies estimated from the multivariable linear regression model B (with interaction between particulate matter and fish consumption)

Predictors	Coefficient	p-level	95% confidence interval	
Maternal age	–1.97	0.729	–13.12678	9.190845
Maternal education[a]	9.26	0.172	–4.05	22.57
Maternal height	12.39	0.000	5.75	19.03
Maternal prepregnancy weight	11.27	0.000	6.96	15.58
Gestational age	138.67	0.000	108.98	168.37
Parity[b]	115.38	0.000	51.24	179.51
Female child	–176.58	0.000	–244.47	–108.68
Fish consumption level[c]	64.32	0.282	–53.03	181.67
Prenatal exposure to fine particulate matter (in tertiles)				
$PM_{2.5}$ <27.0 μg/m^3	1.00			
$PM_{2.5}$ 27.0–46.29 μg/m^3	15.18	0.774	–88.88	119.24
$PM_{2.5}$ >46.29 μg/m^3	–51.15	0.381	–165.75	63.45
Interaction term ($PM_{2.5}$ medium level × low fish consumption)	–32.68	0.708	–203.93	138.56
Interaction term ($PM_{2.5}$ higher level × low fish consumption)	–107.35	0.215	–277.09	62.39
Intercept	–4,789.73	0.000	–6,410.45	–3,169.01

Additionally included in the regression model: season of birth. n = 481.
[a] Years of schooling.
[b] 1 = First, 2 = second, 3 = third or more.
[c] 1 = Low level (<91 g/week), 0 = >90 g/week.

such as cardiovascular events [37, 38] or colorectal cancer [39, 40]; however, the mechanisms by which it might affect health status are still under debate. Recent evidence suggests that fish and n-3 fatty acid consumption may attenuate inflammation and oxidative stress in humans [41–43]. Since fish micronutrients are assumed to possess antioxidant activity, they may protect tissues and cells by reacting with oxygen free radicals generated by metabolites of PAHs or other ambient toxicants present in fine particulate matter and counteract oxidative DNA damage [44–47]. Animal studies have already shown that reactive oxygen species and oxidative stress are associated with poor fetal growth [48, 49]. Evidence from studies of pregnant women also suggests that oxidative stress plays a role in low birth weight [50, 51]. However, when considering the potential effects of fish micronutrients on birth outcomes, we have to be aware that fish intake may only be a marker for other underlying factors affecting birth outcomes.

Over the past decade there has been a considerable increase in fish consumption, which has mainly been attributed to general knowledge about the nutritional value of fish. However, the effect of maternal fish intake during pregnancy is actually a very sensitive issue since many types of fish are a major source of exposure to methylmercury [52–55]. As the toxic effect of methylmercury in humans may depend on the balance between n-3 fatty acids and methylmercury in the fish consumed, the US Food and Drug Administration has advised pregnant women and women who may be pregnant not to eat swordfish, king mackerel, tilefish, shark or fish from locally contaminated areas [56].

Our study has some limitations and among them we have to mention the fact that the women in our study sample differ from the broader population of women in Poland since we excluded women with conditions that strongly affect fetal growth, such as cigarette smoking, multiple pregnancy or pre-existing diabetes or hypertension. Our data on fish consumption were based on the FFQ method, which is useful for ranking individuals but does not help to assess the absolute intake of various nutrients. The FFQ method is also sensitive to systematic errors in reporting, and therefore our results must be interpreted cautiously. Moreover, in our study we did not collect information on the exact amount and type of fish consumed by the study participants.

Table 4. Effect of personal prenatal exposure to $PM_{2.5}$ (in tertiles) on the birth weight of newborns adjusted for potential confounders according to the level of fish consumption during pregnancy (in tertiles)

Predictors	Coefficient	p-level	95% confidence interval	
Low fish intake (<91 g/week)				
Maternal age	–1.60	0.867	–20.54	17.33
Maternal education	17.26	0.121	–4.61	39.14
Maternal height	10.79	0.051	–0.06	21.64
Maternal prepregnancy weight	7.61	0.070	–0.631	15.84
Parity	74.19	0.175	–33.45	181.84
Gestational age	168.29	0.000	138.29	198.29
Female child	–186.21	0.001	–296.40	–76.02
$PM_{2.5}$ <27.0 μg/m^3	1.00			
$PM_{2.5}$ 27.0–46.29 μg/m^3	–39.04	0.567	–173.23	95.15
$PM_{2.5}$ >46.29 μg/m^3	–133.26	0.052	–267.41	0.89
Intercept	–5,507.14	0.00	–7,677.71	–3,336.58
Medium fish intake (91–205 g/week)				
Maternal age	1.98	0.827	–15.81	19.76
Maternal education	–2.68	0.812	–24.88	19.53
Maternal height	11.43	0.039	0.59	22.26
Maternal prepregnancy weight	14.07	0.000	8.17	19.97
Parity	98.10	0.050	–0.01	196.21
Gestational age	164.32	0.000	128.56	200.10
Female child	–177.67	0.002	–288.04	–67.31
$PM_{2.5}$ <27.0 μg/m^3	1.00			
$PM_{2.5}$ 27.0–46.29 μg/m^3	3.94	0.953	–128.69	136.57
$PM_{2.5}$ >46.29 μg/m^3	–93.38	0.247	–252.16	65.40
Intercept	–5,702.08	0.000	–7,990.48	–3,413.68
High fish intake (>205 g/week)				
Maternal age	–11.59	0.357	–36.41	13.23
Maternal education	12.72	0.385	–16.19	41.64
Maternal height	11.28	0.144	–3.89	26.46
Maternal prepregnancy weight	13.03	0.016	2.45	23.62
Parity	137.88	0.066	–9.17	284.93
Gestational age	200.41	0.000	139.98	260.83
Female child	–151.46	0.046	–299.90	–3.03
$PM_{2.5}$ <27.0 μg/m^3	1.00			
$PM_{2.5}$ 27.0–46.29 μg/m^3	90.02	0.335	–94.02	274.05
$PM_{2.5}$ >46.29 μg/m^3	–23.69	0.811	–219.96	172.57
Intercept	–7,095.60	0.000	–1,0674.68	–3,516.51

On the other hand, we must mention the strength of our study, which comes from the fact that the most important confounders for neonatal birth weight, such as tobacco smoking by mothers during pregnancy or the presence of chronic diseases, were removed through the entry criteria. Other factors that are thought to affect the probability of delivery of newborns with lower growth, such as maternal height or prepregnancy weight, gestational age, the gender of the child and the season of birth were also accounted for. To avoid other important potential methodological limitations of previous papers regarding the characterization of exposure to environmental toxicants, our study included the assessment of total personal individual exposure to fine particulate pollutants from all potential sources, both indoors and outdoors.

Personal monitoring of exposure to fine particles among pregnant women in our study was performed over a short period of 48 h in the second trimester of pregnancy. To evaluate the correlation between the levels of $PM_{2.5}$ measured over 48 h in the second trimester of pregnancy with those in the last trimester, a series of repeated measurements in both trimesters was carried out in a subsample of 85 pregnant women. The correlation coefficient of log transformed $PM_{2.5}$ measurements in the

second and the third trimesters of pregnancy appeared to be significant ($r = 0.360$, $p = 0.0007$). This gives us a certain degree of confidence that the measurements of the total personal level of exposure to fine particles taken in the second trimester may be representative for the period of pregnancy as a whole.

Since birth outcomes such as weight at birth alone are inadequate summary measures of the health effects of fetal exposure, future studies should use more refined assessment methods for development not only in terms of anthropometric features but also in terms of the neurodevelopmental performance of infants. The planned longer-term follow-up of our cohort should enable us to determine the sequelae of prenatal exposure to environmental toxicants together with eventual protective effects of maternal nutrition.

In conclusion, our results suggest that a higher consumption of fish by women during pregnancy may reduce the risk of adverse health effects of prenatal exposure to toxicants and highlight the fact that a full assessment of adverse birth outcomes resulting from prenatal exposure to ambient hazards should consider maternal nutrition during pregnancy as well. The results should be a strong incentive for other studies aimed at showing the important role of maternal nutrition during gestation in preventing detrimental health effects of prenatal exposure to various toxicants.

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