Birth weight and gestational age among children of Danish pharmacy assistants

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Abstract

Study objective—The aim was to investigate whether specific types of work or exposures among pharmacy assistants were correlated with changes in birth weight or gestational age.

Design—The study was a nationwide historical cohort with open entry of all female members of the union of pharmacy assistants during 1979 to 1984.

Participants—The cohort comprised 4939 pharmacy assistants under 40 years of age. The questionnaire was answered by 93%.

Measurements and main results—Information on birth weight and gestational age was obtained by linkage to the national birth register. Exposure information on type of work and exposure to pharmaceutical and chemical products during pregnancy was self reported. Only small and non-significant differences in birth weight and gestational age were found between the compared groups. Mean birth weight was 50 g above the national mean and gestational age was longer ($p < 0.0005$).

Conclusions—Compared to the Danish population, children of pharmacy assistants are at low risk for experiencing low birth weight and preterm birth. Social status and less smoking during pregnancy among pharmacy assistants might explain the slightly greater mean birthweight and gestational age in this sector of the population.

Birth weight is an important predictor of perinatal mortality and childhood growth and development. In some countries birth weight is noted with reasonable precision and is available from birth registers. Fetal growth, and thus birth weight, is to some extent determined by environmental factors, although genetic and hormonal factors are of greater importance. Birth weight is known to vary with race, maternal height, educational level, previous miscarriage, premature birth, age, and parity.¹⁻³

Among environmental factors, although maternal smoking has been shown consistently to reduce birth weight in a dose-response fashion,²⁻⁵ and heavy alcohol consumption during pregnancy lowers birth weight,^{6,7} information about the effect of occupational exposures is sparse.

The analyses presented here are part of a larger study covering several types of reproductive failures among Danish pharmacy assistants. Previously, women working in the pharmaceutical industry or at pharmacies have

been reported to experience an increased risk of infertility,⁸ prolonged time to pregnancy,⁹ spontaneous abortions,¹⁰⁻¹² and congenital malformations among their offspring.¹¹ This study is explorative and descriptive and the aim was to investigate whether specific types of work task or exposures among pharmacy assistants were correlated with birth weight or gestational length. More information on the study has been published.^{9,10}

Methods

The study is a nationwide historical cohort study with open entry consisting of all female members of the national union of the pharmacy assistants. The study group consists of all gainfully employed members of the union during January 1st 1979 to December 31st 1984, less than 40 years of age on December 31st, 1978. Data on type of pharmacy, occupation, and exposure to drugs and chemicals are self reported. The questionnaire was mailed to 4939 pharmacy assistants in 1985 and 4585 responded (93%).

Data on birth weight and gestational length were obtained by linkage to the national register on birth certificates (The Danish Medical Birth Register) by means of the personal identity number. Data on births are considered complete as there is complete clearing between the Medical Birth Register and the civil registration system.^{13,14} However, four percent of the births found in the register were not reported in the questionnaires by the participating women.

Birth weight was measured at the time of delivery by the midwife and noted in 10 g intervals. Gestational age was measured in full weeks from the first day of last menstruation period, and was usually corrected by ultrasound scanning when dates were uncertain. Even so, gestational age was recorded as uncertain in five percent.

Low birth weight is defined as birth weight less than 2500 g and early birth as births before 38 full weeks of gestation (the WHO definition of preterm birth, less than 37 weeks of gestation, was not used for numerical reasons).

Only women who worked during pregnancy for more than one week (94% of all) are included in the analyses (1882 single births). The unit of analysis in the present context is a birth (not the woman) and the majority of women (78%) only had one birth during the study period (average 1.3 births per woman).

Analysis of variance (ANOVA)¹⁵ was used, together with the unconditionally logistic regression model. Mother's age, parity, smoking, and alcohol consumption were considered as

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Table I Basic characteristics of the study base

	No of births	%
Age (years)		
15–24	373	20
25–34	1463	78
35–45	46	2
Parity		
0	936	50
1	800	43
2+	146	8
Smoking (cigarettes per day)		
Non-smokers	1255	67
1–9	293	16
10–14	226	12
15–	108	6
Alcohol (drinks per week)		
0	616	33
1–4	1142	61
5–9	79	4
10–	5	0
No information	40	2
All	1882	

possible confounding variables (table I). All indicated confidence limits are 95% limits.

Results

BIRTH WEIGHT

The mean birth weight among the pharmacy assistants was 3450 g compared with the Danish population mean of 3400 g. Low birth weight was found among 3.1% and preterm birth (before 37th week of gestation) among 3.0% of pharmacy assistants compared to 5.0% and 4.5%

Table II Birth weight: deviations from grand mean according to type of work. Analysis of variance* adjusted for mother's age and smoking habits (model 1) and additionally gestational age (model 2)

	Deviations from grand mean	
	Model 1	Model 2
Type of pharmacy		
Rural pharmacy	+13.7	+17.3
Urban pharmacy	–9.1	–9.9
Hospital-, production pharmacy and pharmaceutical industry	+37.2	–25.3
Other type of workplace	–35.0	–11.4
Grand mean (grams)	3448	3450
p value (main effect)	0.65	0.68
Type of work		
Reference work	–1.2	–7.2
Production	+2.9	+29.4
Dispensary	+9.3	–7.7
Identification	–45.3	–24.7
Other	–46.3	–22.0
Grand mean (grams)	3448	3450
p value (main effect)	0.91	0.70

* Controlled for mother's age (<25, ≥25 years), smoking (0, 1–10, >10 cigarettes/day), and gestational age in weeks as a covariate

Table III Birth weight according to self reported exposure during pregnancy (daily or weekly exposure). Analysis of variance*

Exposure	No of births	Mean b w	95% CI +/–	Deviation from ref means	P value (main effect)
Reference	709	3470	39	–	–
Antibiotics	538	3440	43	–9	0.60
Heart medicines	40	3560	136	111	0.16
Cancer drugs	8	3280	302	–216	0.24
Anticoagulants	18	3520	214	37	0.76
Sex hormones	37	3610	163	142	0.09
Other hormones	112	3460	87	2	0.96
Antidiabetics	20	3440	246	2	0.99
Psychopharmaceuticals	58	3510	126	57	0.39
Pain killers	254	3490	60	25	0.37
Antiepileptics	110	3520	92	56	0.30
Antirheumatics	43	3420	151	–42	0.59
Solvents	264	3490	65	20	0.47
Pesticides	61	3520	110	25	0.70
Heavy metals	48	3580	135	91	0.21
Preservatives	354	3440	53	–11	0.63
All	1882				

* Controlled for mother's age (<25 years, ≥25 years), parity (0, 1, 2+), alcohol consumption (0–4 drinks/week, ≥5 drinks/week), tobacco consumption (0, 1–10, >10 cigarettes/day)
BW = birth weight; CI = confidence interval

respectively among singleton births in Denmark in 1981.¹⁴ The sex ratio was comparable with the national figures.

Birth weight according to type of pharmacy and occupation did not differ among the compared groups. The analysis of variance as seen in table II only showed small and non-significant differences before or after adjustment for mother's age and smoking habits. Additional adjustment for gestational age did not alter these findings. Birth weight according to self reported exposure is shown in table III. The analysis of variance was performed adjusted for age, parity, smoking, and alcohol consumption. Women exposed to cytostatics daily or weekly had an average birth weight that was 200 g lower than the overall average. Average birth weight was 100 g lower among women exposed to cytostatics monthly. However, none of the differences were statistically significant.

The frequency of low birth weight did not differ significantly according to type of pharmacy, occupation, or exposure to drugs or chemicals (not shown). Women working with bottling of pharmaceuticals and women with "other types of jobs" showed an increased but statistically non-significant odds ratio for low birth weight.

GESTATIONAL AGE

Birth before 38 weeks of gestation was analysed according to type of work. Women working on the identification of pharmaceuticals had an increased odds ratio for early birth, but it was not statistically significant.

Logistic regression analyses were performed using birth before 38 weeks of gestation as the outcome variable and exposure to a number of different products or chemicals as predictors (table IV). Among eight women who recorded daily or weekly exposure to cytostatics during pregnancy, two gave birth before the 38th week of gestation (35th and 36th week respectively). However, this excess was not statistically significant as indicated by the wide confidence limit (95% CI = 0.9–31.6). Length of pregnancy was very close to 40 weeks on average for all pharmacy assistants (39.8 weeks). No differences were found according to type of pharmacy or occupation (data not shown).

Discussion

Comparing birth weight and gestational length among groups of pharmacy assistants according to type of work or exposure did not reveal major differences which might indicate occupational hazards. It seems unlikely that a large number of pharmacy assistants were exposed to chemical agents in doses which have a major impact on fetal growth or on duration of gestation. However, a number of limitations of the study should be considered. Working conditions among pharmacy assistants may be too similar to allow identification of any single risk group; or exposure data may be too crude and imprecise. The relatively small number of women in the study yielded rather limited scientific information for some of the specific work tasks or exposures, as indicated by the broad confidence limits.

Table IV Early birth according to self reported exposure during pregnancy (daily or weekly). Logistic regression analysis adjusted for mother's age, parity, and alcohol/tobacco consumption. Where data are too few, unadjusted odds ratios (OR) are given

	No of births	No of early births	OR unadjusted	95% confidence limits
Reference	714	35	1.0	—
Antibiotics	542	23	0.67*	0.41 – 1.12
Heart medicines	40	2	1.02	0.2 – 3.8
Cancer drugs	8	2	6.50	0.9 – 31.6
Anticoagulants	18	2	2.43	0.4 – 9.7
Sex hormones	37	3	1.72	0.4 – 5.3
Other hormones	112	6	1.09	0.4 – 2.6
Antidiabetics	20	3	3.40	0.8 – 11.3
Psychopharmaceuticals	58	4	1.44	0.4 – 3.9
Pain killers	255	8	0.63	0.3 – 1.3
Antiepileptics	110	5	0.92	0.3 – 2.3
Antirheumatics	43	3	1.46	0.3 – 4.5
Solvents	268	10	0.58*	0.29 – 1.19
Pesticides	62	2	0.65	0.0 – 2.4
Heavy metals	48	2	0.84	0.0 – 3.1
Preservatives	357	17	0.78*	0.44 – 1.37
All	1882	99		

* Logistic regression controlled for the same variables as in table III

Controlling for confounding is only partly possible since the majority of causes of growth retardation and preterm birth are unknown. Age, parity, social characteristics, smoking, and drinking habits are known to influence these pregnancy outcomes.¹⁻⁷

Mean birth weight among children of pharmacy assistants was 50 g higher than the average Danish birth weight, and the proportions of newborns with low birth weight and preterm birth were lower. This is probably due to the relatively high social standard and less frequent smoking among pharmacy assistants. In this study 35% of the women smoked during pregnancy compared to 39% in a sample of Danish Women.¹⁶ Gestational age among children of pharmacy assistants was longer compared with gestational age for all children born in Denmark during the years 1979 to 1983 ($\chi^2 = 25.95$, $p < 0.0005$, $df = 6$).¹⁷ The difference in mean birth weight may be explained by the increased duration of pregnancies among pharmacy assistants.

In the statistical analysis pregnancies are treated as independent events, and repeated pregnancies in the study period among the participating women are not taken into consideration in the analysis. However, most women contributed only one birth (on average 1.3) and the impact of this problem on the estimates is considered to be minor.¹⁸

Unfortunately, the study provided little information on pharmacy assistants exposed to cytostatics. However, some cytostatics have been shown to be teratogenic in animal studies and in women who have taken cytostatic drugs during

pregnancy.¹⁹ Additionally, exposure to cytostatic drugs among nurses has been reported to increase the risk of spontaneous abortion²⁰ and congenital malformation in the offspring.²¹

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