

Occupational exposure during pregnancy and the risk of hay fever in 7-year-old children

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Abstract

Objectives: The prevalence of allergic diseases including hay fever has increased in the last decades, especially in Westernised countries. The aim of this study was to analyse whether occupational exposure during pregnancy is associated with development of hay fever in 7-year-old Danish children.

Methods: A total of 42 696 women and their children from the Danish National Birth Cohort were categorised according to maternal occupational exposure. Exposure information was obtained by combining job title in pregnancy with a commonly used asthma Job Exposure Matrix. Information on hay fever in the child was obtained by an internet questionnaire at follow-up at 7 years of age.

Results: Adjusted logistic regression analyses showed no significant association between maternal occupational exposure during pregnancy and hay fever among the 7-year-old children. Stratifying for atopic status in the children did not change the results. The prevalence of hay fever was 10.0% in the atopic children compared with 3.6% in the non-atopic children. Maternal atopic disposition increased the risk of hay fever in the offspring, odds ratio (OR) 2.49 [95% confidence interval (CI) 2.26; 2.74]. Rural residence during pregnancy decreased the risk for hay fever [OR 0.74 (95% CI 0.59; 0.92)] as did parity, OR 0.72 (95% CI 0.66; 0.80) and 0.70 (95% CI 0.48; 1.00) for 2nd and 3rd child, respectively, compared with the firstborn child.

Conclusion: The results suggest that occupational exposure among pregnant women in Denmark is not a risk factor for hay fever among young children.

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Key words:

allergy – hay fever – maternal exposure – prenatal exposure delayed effects – prospective cohort study – occupational exposure

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Authorship and contributorship

Berit Hvass Christensen: Selection of data from Danish National Birth Cohort (DNBC), performing statistical analyses, writing of article text and tables. Ane Marie Thulstrup: Supervision of statistical analyses, revision of article text. Kirsten Skamstrup Hansen: Revision of text. Lars Rauff Skadhauge: Revision of text. Karin Sørig Hougaard: Revision of text. Vivi Schlünssen: Main reviser of text and tables.

Ethics

All participants from the DNBC provided written consent. The study was approved by all of the scientific ethics committees in Denmark and by the Danish Data Protection Board.

Conflict of interest

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

Introduction

During the last decades, the prevalence of allergic disease, including hay fever, has increased to above 20% in many countries (1–3). Possible risk factors and preventive factors for allergy have been investigated, i.e. chemical and allergen exposure during pregnancy (4–6), maternal and environmental tobacco smoke (ETS) during prenatal and postnatal life (7), air pollution (8, 9), medication and vaccination (10, 11), maternal diet (12), farm exposures (13, 14) and number of older siblings (15), but the increase is yet to be fully understood.

Many women are exposed to allergens and irritants at work during pregnancy, and several studies show that the immune system certainly is susceptible to programming during foetal life (16, 17). A study by LL Magnusson *et al.* (18) suggested that occupational exposure to organic solvents during pregnancy was associated with an increased risk of hay fever in late childhood.

Our hypothesis is that maternal exposure to asthmogens during pregnancy has an impact on the immune system of the foetus, which predisposes the offspring to allergic disease including hay fever later in life. The aim of the present study was to analyse whether different classes of occupational exposures during pregnancy are associated with development of hay fever in 7-year-old Danish children.

Material and methods

The study population originated from the Danish National Birth Cohort ('Better health for mother and child', DNBC) consisting of 100 418 pregnancies. The cohort is described in detail elsewhere (19). The initial data were collected from 1996–2002, and the 7-year follow-up data were collected from 2003–2010 as the children reached 7 years of age. This analysis included only one singleton pregnancy per woman and subjects with information on occupation (mother) and hay fever, asthma and dermatitis (child), giving a total study population of 42 696 women and their children. Measure on job exposure during pregnancy was obtained by combining information on job title [Danish version of International Standard Classification of Occupations (ISCO)–codes, a national version of the International Standard Classification of Occupations used as standard by Statistics Denmark] obtained from telephone interviews during pregnancy and a commonly used asthma Job Exposure Matrix (JEM) (20) based on known risk factors for occupational

asthma, slightly modified to comply with Danish working conditions. Seven exposure groups were formed: high molecular weight agents (HMW), low molecular weight agents and irritants (LMW), high and low molecular weight agents (mixed), farmers, unclassifiable, students and references (administrative and office workers). In order to make the JEM fit the Danish working environment, adjustments were made by Christensen BH and Schlünssen, V based on knowledge of exposures to asthmogens in the Danish working environment. As an example, medical doctors who were categorised in the original JEM as not having any exposure to asthmogens were converted to the mixed HMW and LMW group. Furthermore, two extra categories were created: the farmers were chosen as a special group as early-life farming exposure consistently has been found to be negatively associated to allergy. The students were considered as a special group. The seven exposure categories consisted of the following occupations and typical *allergens/irritants*: HMW agents (veterinarians, gardeners and bakers; *Grass pollen, animal dander, flour/grain*); LMW agents or irritants (cooks, cleaners, hairdressers, dentistry and all kinds of manufacturing of dust-producing materials; *aerosols, dust from manufacturing of wood/ textile/ stone/ rubber/ plastics etc*); mixed HMW and LMW agents (health-care professionals; *antibiotics, latex, cleaning agents*); farmers (*organic dust, Grass pollen, animal dander, ammonia*), students (*no occupational exposure*) and unclassifiable (subjects where the same job title contained many different environments, e.g. waiters, engineering technicians, biologists, shop managers; *diverse exposure*). Office workers, teachers and journalists were classified as the reference group (*no or low occupational exposure*). Information regarding absence from work during pregnancy was obtained from the Danish Register for Evaluation of Marginalisation (DREAM) database from the Danish Ministry of Employment (21). Women without absence from work were defined as those who did not receive compensation because of absence from work for more than 14 consecutive days at any time during the first 30 weeks of pregnancy.

Information on hay fever was obtained from an internet-based follow-up questionnaire when the children were 7 years. Hay fever was defined if the mother answered 'Yes' to the question: 'Has a doctor ever told you that your child has hay fever?'

Ever atopic dermatitis was used as a proxy for atopy among the children. Information on atopic dermatitis was collected by telephone interview when the child was 18 months old and at the follow-up questionnaire at 7 years of age. Atopic dermatitis was defined as parental

reported ever atopic dermatitis at 18 months AND yes to itchy rash in the locations known to be typical for atopic dermatitis AND/OR persistent itchy rash in the locations known to be typical for atopic dermatitis at 7 years. The mother was categorised as being atopic if she herself reported ever asthma, rhinitis or atopic dermatitis. Maternal smoking during pregnancy was defined as no use of tobacco, less than 10 cigarettes per day or more than 10 cigarettes per day. ETS at 7 years was defined as a current smoking mother and/or a current smoking father when the child was 7 years.

All analyses were performed in STATA SE11.0 (STATA corp., College Station, TX, USA). Logistic regression analysis was used to examine the associations between occupational exposure during pregnancy and hay fever adjusted for the following a priori chosen confounders: maternal atopic disposition, maternal smoking during pregnancy and use of antibiotics during pregnancy, rural residence and parity.

The analyses were stratified according to the atopic status of the children. The analyses were repeated among the subgroup of working women with no

absence from work in the first 30 weeks of their pregnancy and with additional variables on ETS at 7 years, and furry pets in the pregnant mothers' home. Unless otherwise stated, the significance level was $P < 0.05$, two-sided.

Results

Table 1 displays the demographics of the 42 696 mothers and their offspring stratified by exposure group. No substantial differences were seen according to age and body mass index for the mothers. Maternal smoking during pregnancy was highest in the LMW group (32.7%) and lowest among unclassifiable (14.8%). Rural residence and exposure to furry pets were highly variable and most common among farmers, 44% and 68%, respectively. The prevalence of atopy in the children was 18.0%, with no substantial difference between groups. The prevalence of atopy in the mothers was 21.3%, highest for students (23.8%). On average, 30.2% of the 7-year-old children were exposed to ETS, highest in the LMW group (43.5%).

Table 1. Demographics of 42 696 women and their 7-year-old children divided into exposure groups. Reference group: administrative and office workers

Exposure	HMW	LMW/irr.	Mixed	Farmer	Unclassifiable	Student	Reference
Mother							
N	415	3784	7903	335	2462	3931	23 866
Age, years, mean	29	29	30	30	31	28	31
(95% CI)	(23, 36)	(22, 37)	(23, 37)	(22, 38)	(25, 37)	(22, 35)	(24, 38)
BMI, median	23.0	23.1	22.6	22.8	22.3	22.0*	22.5
(10%; 90%)	(19.5; 31.8)	(19.4; 30.5)	(19.4; 29.0)	(19.7; 28.5)	(19.4; 27.4)	(19.1; 27.5)	(19.4; 28.3)
Smoking, %							
No tobacco use	75.4	67.3*	77.3	82.1	85.2	79.1	81.6
1–10 cigs/day	9.4	15.4*	11.8	7.8	8.1	11.0	10.3
>10 cigs/day	15.2	17.3	11.0	10.2	6.7*	10.0	8.1
Rural residence	15.4*	8.0	7.5	44.2*	6.4	4.0*	5.6
Furry pets	63.1	49.4*	41.5*	67.8*	35	29.8*	35.6
Atopy	14.9	19.8	22.1	17.0	21.6	23.8*	20.9
Parity:							
0	50.8	48.5	48.7	45.1	54.0	66.5	51.6
1–2	46.3	49.0	47.9	48.1	44.4	31.8*	46.6
3+	2.9	2.4	3.4	6.6*	1.5	1.6	1.8
At 7-year follow-up							
Mother							
Smoking	19.3	27.6*	17.6	13.7	10.9	16.2	15.1
Father							
Smoking	28.2	30.9*	22.9	18.2	18.2	21.7	20.4
Child							
Atopy	16.4	16.4	18.7	17.3	18.5	18.0	17.9
ETS exposure	37.6	43.5*	31.6	26.0	24.1	30.2	28.1

* $P < 0.05$ group vs and all other exposure groups.

HMW, high molecular weight; LMW, low molecular weight; irr., irritants; CI, confidence interval; BMI, body mass index; ETS, environmental tobacco smoke.

The prevalence of hay fever was higher among children with atopic dermatitis (10.0%) compared with children without atopic dermatitis (3.6%), $P < 0.0001$, but no significant difference between exposure groups was seen. The prevalence for children without atopic dermatitis ranged between 2.2% among farmers to 3.7% among unclassifiable, $P = 0.226$ whereas for children with atopic dermatitis, the range was 8.2% for LMW to 12.1% for farmers, $P = 0.323$ (data not shown).

Adjusted logistic regression analyses showed no significant association between maternal occupational exposures and hay fever (Table 2). Stratifying for atopic status in the children did not change the results. Rural residence decreased the risk for hay fever with odds ratio (OR) 0.74 [95% confidence interval (CI) 0.59; 0.92], as did parity where OR for hay fever in the 2nd and 3rd child were 0.72 (95% CI 0.66; 0.80) and 0.70 (95% CI 0.48; 1.00), respectively, compared with the first child. Maternal atopic disposition increased the risk of hay fever in the offspring [OR 2.49 (95% CI 2.26; 2.74)]. No significant associations were seen between maternal smoking nor the use of antibiotics, during pregnancy and hay fever.

Repeating the analysis on the subgroup of women with no work absence in the first 30 weeks of pregnancy ($n = 19\ 100$) did not change the results. Stratifying by asthma status of the child (defined as either 'wheeze in the last 12 months' or 'ever asthma') made no difference; the same was true when ETS at 7 years

and exposure to furry pet during pregnancy were included in the analysis (data not shown).

Discussion

Maternal occupational exposure during pregnancy did not increase the risk of hay fever in the children at age 7 years compared with the reference group. Not surprisingly, hay fever was more common among atopic children. Maternal atopic disposition increased the risk of hay fever in the offspring, whereas rural residence and older siblings were protective.

Only one study has previously reported on the association between maternal occupation and the development of hay fever in the offspring. In explorative analyses of maternal occupational job titles during pregnancy and hay fever among their 14- to 18-year-old children, an excess ratio of hay fever was seen when the mothers were employed in jobs with likely high risk to organic solvents during pregnancy [OR 2.8 (95% CI 1.1; 7.5)] (18). In the present study, we did not specifically focus on organic solvent exposure.

Originally, socio-economic status (SES) was considered as a confounder, but because of the close correlation between occupation and SES, we decided not to include SES in the final models to avoid over adjustment. Season of birth might influence the prevalence of hay fever. As season of birth and maternal occupation was unrelated, we did not include season as a

Table 2. Mothers' occupational exposure during pregnancy and the odds ratio (OR) of hay fever in the child at age 7 years, stratified by atopic status in the children. Reference group: administrative and office workers

	Crude OR (95% CI)		
	All children	Atopic children	Non-atopic children
High molecular	0.75 (0.45; 1.26)	0.87 (0.37; 2.03)	0.71 (0.37; 1.38)
Low molecular/ irritants	0.84 (0.71; 1.00)	0.80 (0.59; 1.09)	0.88 (0.71; 1.09)
Mixed	1.03 (0.92; 1.16)	1.06 (0.87; 1.29)	1.00 (0.86; 1.16)
Farmer	0.81 (0.46; 1.41)	1.24 (0.56; 2.74)	0.59 (0.26; 1.33)
Unclassifiable	1.00 (0.82; 1.22)	0.91 (0.66; 1.27)	1.04 (0.81; 1.32)
Student	1.03 (0.88; 1.20)	1.05 (0.81; 1.36)	1.02 (0.83; 1.24)
Reference	1	1	1
	Adjusted OR (95% CI)		
	All children	Atopic children	Non-atopic children
High molecular	0.82 (0.48; 1.41)	0.98 (0.42; 2.31)	0.74 (0.36; 1.50)
Low molecular/ irritants	0.85 (0.71; 1.02)	0.85 (0.61; 1.17)	0.88 (0.70; 1.10)
Mixed	1.05 (0.93; 1.18)	1.05 (0.86; 1.29)	1.02 (0.87; 1.19)
Farmer	1.04 (0.59; 1.84)	1.54 (0.68; 3.52)	0.78 (0.34; 1.78)
Unclassifiable	1.01 (0.83; 1.24)	0.93 (0.66; 1.32)	1.05 (0.82; 1.35)
Student	0.95 (0.81; 1.12)	0.95 (0.72; 1.26)	0.96 (0.78; 1.18)
Reference	1	1	1

CI, confidence interval.

confounder in the final analysis. *Data on breastfeeding are available in the DNBC data set, but because only between 0.2% and 1.2% of the women stated to never have breastfed, it was not possible to look at the differences between breastfeeding and non-breastfeeding mothers in this analysis.*

DNBC is a large birth cohort with prospective collection of information regarding exposures during pregnancy. However, the crude occupational exposure measures available make exposure misclassification likely and presents a limitation of the study. The exposure assessment was based on information about type of job and general probability of exposure in each type of job. We did not have access to detailed individual exposure information, and therefore, non-differential exposure misclassification is highly probable.

Another limitation is the lack of objective measures for atopy, e.g. a positive skin prick test or analysis of specific Immunoglobulin E (IgE). We have used ever atopic dermatitis as a proxy for atopy, as this condition is tightly linked with being sensitised, but misclassification is inherently present. Although in this study, atopic status did not seem to considerably affect the association between occupational exposure and hay fever.

We have defined atopic dermatitis as a combination of parental reported atopic dermatitis and eczema in locations typical for atopic dermatitis. These questions have been validated against a clinical investigation for atopic dermatitis, and it was concluded that they can be used to define atopic dermatitis in large-scale epidemiologic studies (22). We are aware that our definition is not totally identical to the one suggested by Benn *et al.*, i.e. we also included eczema at 7 years and used a slightly different combination of questions, which probably increased the sensitivity at the expense of a decreased specificity.

We are aware that hay fever is not identical with allergic rhinitis. There is no firm separation in the Danish language between allergic rhinitis and hay fever, and hay fever may not include children with perennial rhinitis, so even though we expect hay fever and allergic rhinitis to be closely correlated, our results are only true for hay fever.

We are aware that hay fever often appears later in childhood, and therefore, the full effect of potential occupational exposure has yet to be seen. Our study confirms earlier described associations between hay fever, atopy and atopic disposition (23), and between number of older siblings and rural residence (24) supporting that the data are capable of displaying expected associations. Our study was based on a large population-based cohort of women and their children,

and the women had a variety of occupational job titles, making exposure contrast possible, although there may be some exposure misclassification.

The mothers were asked about current occupation at the 1st telephone interview around week 12–16 of gestation. Our main focus is exposure during pregnancy. It could be very interesting to investigate the effect of mother's occupation before pregnancy in more details, but this was not possible in this study, but we assume only a minority changed occupation just prior to getting pregnant. In later data-analyses looking at post-natal exposure, it was found that only 8558 out of 42 696 participating women changed occupational exposure from early pregnancy until 18 months after giving birth, and that most of these women were students at the 1st questionnaire (unpublished data), suggesting that most of the mothers maintain the same kind of job for a longer time.

In conclusion, our results suggest that occupational exposure among pregnant women in Denmark is probably not a risk factor for hay fever among young children, although small risks in the entire group or high risks in small subgroups may not be detected by the study.

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