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Birth characteristics and asthma symptoms in young adults: results from a population-based cohort study in Norway

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Birth characteristics and asthma symptoms in young adults: results from a population-based cohort study in Norway. C. Svanes, E. Omenaas, J.M Heuch, L.M. Irgens, A. Gulsvik. ©ERS Journals Ltd 1998.

ABSTRACT: There is evidence that the origin of obstructive lung disease may be traced back to foetal life. The associations between birth characteristics and asthma symptoms were studied in a random population sample of young Norwegian adults.

Respiratory symptoms were recorded in a population-based questionnaire survey. The records of all subjects aged 20–24 yrs were linked with the Medical Birth Registry of Norway. Of 868 subjects born in Norway, there were 690 (79%) responders. The associations between asthma symptoms and birth characteristics were analysed by logistic regression, adjusted for possible confounding factors.

Asthma symptoms in young adults were inversely associated with birth weight (odds ratio (OR)$_{wheeze}$=0.82; 95% confidence interval (CI)=0.69–0.96·500 g increase in birth weight^{-1})), and after adjustment for gestational age, birth length, parity and maternal age (OR$_{wheeze}$=0.69; 95% CI=0.50–0.95·500 g increase in birth weight^{-1}). The association did not vary according to adult smoking habits or atopic status and remained when premature and low weight births were excluded (OR$_{wheeze}$=0.73; 95% CI=0.60–0.90·500 g increase in birth weight^{-1}). The association was consistent for all asthma symptoms. Adjusted for birth weight, asthma symptoms were further associated with low gestational age, high birth length and low maternal age.

In a random sample of young adults, asthma symptoms were strongly associated with low birth weight, an association driven by the full-term births within the normal birth weight range. The findings show that the risk for adult asthma is partly established early in life and suggest that poor intrauterine growth is involved in the aetiology of asthma.

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The assumed increase in prevalence of asthma is largely unexplained. However, there is evidence that the susceptibility to obstructive lung disease may be traced back to foetal life [1]. BARKER *et al.* [2] found that level of forced expiratory volume in one second (FEV_1) in elderly males and mortality from chronic obstructive lung disease in males were both inversely associated with birth weight. The authors hypothesized that intrauterine conditions causing growth retardation might irreversibly constrain the development of the airways. A study of Israeli recruits showed an association between low birth weight and asthma in male adolescents [3], and in a study of British children aged 5–11 yrs, lung function was associated with birth weight and respiratory illness with prematurity [4]. Another study of British children showed an association between low birth weight and early childhood wheeze, while a similar association with persistent wheeze did not reach statistical significance [5]. However, the understanding of how birth factors may influence susceptibility to adult lung disease is limited, and this relationship was studied only in males.

Further understanding of a possible early origin of adult asthma could be of major importance in prevention of the disease in future generations. However, obtaining precise information about births in an unselected adult population may be difficult. The Medical Birth Registry of Norway provides a unique opportunity to study these issues as detailed information on all births in Norway has been recorded since 1967. The objective of the present study was to assess the associations between birth characteristics (birth weight, gestational age, birth length, parity and maternal age) and asthma symptoms in a random population sample of females and males aged 20–24 yrs.

Materials and methods

Study population and study design

Respiratory symptoms were assessed in a cross-sectional survey performed as a part of the European Community Respiratory Health Survey [6]. The study population comprised a random sample of 4,300 out of 82,227 people aged 20–44 yrs who lived in Bergen, Norway, on October 1, 1991. A questionnaire was mailed to the selected participants, and further copies were sent after 3 and 8 weeks if no reply was received.

Of the original population sample, 940 subjects were born in or after 1967. This part of the data set was linked with the Medical Birth Registry of Norway by the national identification number. Information on birth weight was

Table 1. – Birth characteristics of the study population, a random sample of 357 females and 333 males aged 20–24 yrs and born in Bergen, Norway

	n	Females	Males
Birth weight g	690	3395±534	3520±557
Gestational age days	670	283±14	281±16
Birth length cm	690	49.8±2.1	50.6±2.3
Parity no. of older siblings	690	1.1±1.3	1.2±1.2
Maternal age yrs	690	27±6	27±5

Values are presented as mean±SD.

not available for 72 people, of whom 71 were not born in Norway. Among the 868 subjects with data available on birth, there were 690 responders (357 females and 333 males, a 79% response rate). Mean birth weight was similar in responders (3,455 g) and nonresponders (3,461 g).

The study was approved by the regional Ethics Committee and the Norwegian Data Protection Board.

Questionnaire

The questionnaire used was the European Community Respiratory Health Survey (ECRHS) modified version of the International Union Against Tuberculosis and Lung Disease (IUATLD) questionnaire [7, 8], including eight questions commonly related to the diagnosis of asthma. The questions were translated into Norwegian and questions on smoking habits, dietary habits and height were added.

Exposure variables from the Medical Birth Registry of Norway

The Medical Birth Registry of Norway provides information on all births in Norway (with a gestational age of Š16 weeks) since 1967, including data on birth weight, birth length, gestational age, parity, parental age and complications at birth. The registry is based on a notification form completed at the time of each birth. Gestational age is based on the date of the last menstrual period. The birth characteristics of the study population are given in table 1.

Statistical analysis

The associations between birth factors and asthma symptoms were analysed by logistic regression [9], adjusting for sex, age, smoking habits and hay fever. Hay fever was included as a confounding variable, being related to both asthma and birth weight. In the analyses including all birth factors, adult height was included, since anthropometry at birth and in adulthood are related. There was no effect of paternal age; thus, this variable was not included. In final analyses, birth weight was used as a continuous variable, since various methods of categorization revealed approximately linear trends. Gestational age was dichotomized at 36 weeks. Adjustment for gestational age categorized in weeks, did not alter the effect of birth weight on asthma symptoms. A significance level of 0.05 was used and all p-values refer to two-sided tests. All analyses were carried out using Stata (Stata Corp., Texas, USA).

Results

The prevalence of asthma symptoms in a population sample of young adult males and females decreased with increasing birth weight and was higher in subjects born prematurely (table 2). An inverse association with birth weight was found for all respiratory symptoms after adjustment for possible confounding factors (table 3). This association was particularly strong for current asthma medication, which decreased by a factor of 0.59 per 500 g increase in birth weight (table 3). Subjects with an increasing number of asthma symptoms (positive answers to question (Q)1, Q1.1, Q1.2, Q2, Q3 and Q4) showed decreasing mean birth weight (fig. 1). The inverse association

Table 2. – Prevalence of wheeze, wheeze with shortness of breath (SOB) and asthma medication according to birth characteristics in a random population sample aged 20–24 yrs in Bergen, Norway

Variable	Category	n	Wheeze %	Wheeze + SOB %	Asthma medication %
Birth weight g	<3000	124	34	23	9
	3000–3499	220	26	18	4
	3500–3999	242	26	17	3
	Š4000	102	21	16	1
Gestational age days	ð252*	21	38	30	10
	>252	667	26	18	4
Birth length cm	<49	129	33	25	6
	49	112	30	16	5
	50	143	24	16	3
	51	122	25	14	3
	Š52	182	23	19	4
Parity no. of older siblings	0	246	23	14	4
	1	242	29	20	5
	2	117	32	22	5
	Š3	83	24	18	0
Maternal age yrs	<20	38	29	13	3
	20–24	230	31	22	4
	25–29	230	26	18	5
	Š30	190	21	16	3

*: 36 weeks.

Table 3. – Mean birth weight (BW; in g) in subjects with and without asthma symptoms and hay fever, and association between symptoms and birth weight in a random population sample aged 20–24 yrs in Bergen, Norway

Question	No		Yes			
	n*	BW	n*	BW	OR (95% CI) per 500 g increase in BW†	p-value of OR
Q1. Wheeze‡	505	3481	183	3380	0.82 (0.69–0.96)	0.015
Q1.1. Wheeze with breathlessness‡	558	3472	124	3381	0.82 (0.69–0.99)	0.036
Q1.2. Wheeze without a cold‡	562	3478	119	3354	0.78 (0.65–0.94)	0.008
Q2. Waking with tightness in the chest‡	580	3461	107	3424	0.94 (0.77–1.14)	0.5
Q3. Waking with breathlessness‡	650	3463	37	3298	0.73 (0.54–0.98)	0.037
Q4. Waking with cough‡	486	3474	201	3412	0.93 (0.79–1.08)	0.3
Q5. Attack of asthma‡	661	3459	27	3381	0.84 (0.60–1.18)	0.3
Q6. Current asthma medication	658	3465	28	3191	0.59 (0.42–0.83)	0.003
Q7. Hay fever	538	3439	142	3509	1.17 (0.98–1.40)	0.080

*: Each question was not answered by some subjects, thus the sums of "yes" and "no" do not equal 690. †: as estimated by logistic regression, adjusting for sex, age, hay fever and current smoking habits. ‡: symptoms during the last 12 months. OR: odds ratio; CI: confidence interval; Q: question number on questionnaire.

between birth weight and number of respiratory symptoms was highly significant (p=0.001; polytomous logistic regression analysis).

Hay fever tended to increase with increasing birth weight (table 3), being significantly more common in subjects with birth weights >4,000 g than in those with birth weights <4,000 g (odds ratio (OR)=1.7; 95% confidence interval (CI)=1.03–2.8).

When excluding complicated births (infants <36 weeks, <2,500 g or with asphyxia at delivery), adult asthma symptoms were strongly related to birth weight (OR_{wheeze}= 0.73; 95% CI=0.60–0.90 per 500 g increase in birth weight). In the 63 subjects with complicated births, no association between birth weight and adult respiratory symptoms was found (OR_{wheeze}=0 96; 95% CI=0.59–1.55 per 500 g increase in birth weight). The associations between birth weight and wheezing symptoms (Q1, Q1.1 and Q1.2) and current asthma medication were fairly similar for males and females when analysed separately, while waking with tightness in the chest, breathlessness or cough was significantly associated with low birth weight only in females (data not shown). The effect of birth weight on asthma symptoms was fairly similar for smokers and never-smokers and in subjects with and without hay fever.

The inverse association between birth weight and asthma symptoms remained significant after adjustment for other birth characteristics (table 4). The effect of birth weight was strengthened by adjustment for length at birth and within each level of birth weight asthma symptoms were more common in long infants (table 4). Adjustment for gestational age did not alter the effect of birth weight. Prematurity seemed to be independently associated with increased symptom risk, although the effect did not reach statistical significance in this relatively small population sample (table 4). Asthma symptoms were less common in offspring of older mothers, but tended to increase with increasing parity (table 4). Hay fever tended to increase with increasing birth weight and the estimate was not altered by adjustment for other birth characteristics even though the confidence intervals were wider (table 4). There was a borderline significant association between hay fever and low parity (p=0.07).

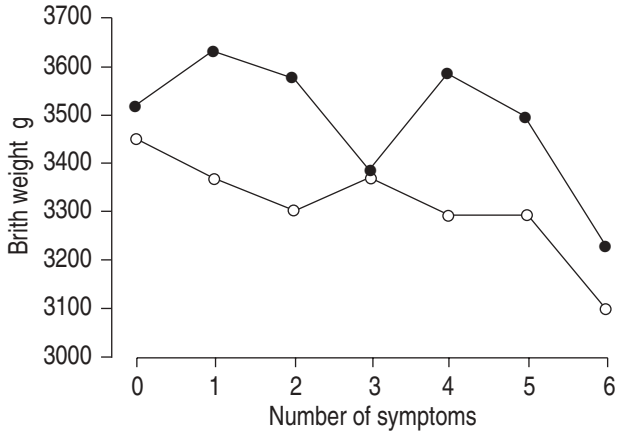

Fig. 1. – Mean birth weight in males (●) and females (○) with 0–6 respiratory symptoms at the age of 20–24 yrs.

Discussion

Asthma symptoms in a random sample of young Norwegian adults were strongly and inversely associated with birth weight. This was consistent when adjusting for gestational age, other birth characteristics and adult factors were adjusted for, and the association was similar in smokers and nonsmokers, as well as in people with and without hay fever. The association between birth weight and asthma symptoms remained when births complicated by prematurity, low birth weight or asphyxia were excluded; the association was driven by the full-term births within the normal birth weight range. Asthma symptoms were further independently related to prematurity and to low maternal age.

This is to the authors' knowledge the first study to show an association of birth weight with adult asthma in an unselected population sample. The detailed and accurate birth data and the complete record linkage could possibly explain the clear findings of this study, despite the relatively small sample size. The conclusions agree with previous studies that have shown associations of birth weight with obstructive lung disease in elderly males [2] and with asthma in children [4] and in male adolescents [3]. A study of asthma and wheezing illness in the 1958 British national cohort could not detect any effect of birth weight [10], while a recent analysis of the British 1970 cohort revealed an inverse association between birth weight (adjusted for gestational age) and asthma in young adults [11].

Table 4. – Mutually adjusted effects of birth characteristics on asthma symptoms and hay fever in a random population sample of young adults in Norway

Variable	Wheeze Q1	Wheeze + SOB Q1.1	Š3 symptoms* Q1–4	Asthma medication Q6	Hay fever Q7
Birth weight per 500 g increase	0.69 (0.50–0.95)	0.65 (0.45–0.94)	0.66 (0.46–0.95)	0.43 (0.21–0.88)	1.16 (0.84–1.61)
Gestational age ð36 weeks *versus* full-term	1.81 (0.62–5.31)	2.41 (0.76–7.60)	2.56 (0.83–7.88)	1.86 (0.23–12.0)	1.04 (0.31–3.51)
Length at birth per cm increase	1.14 (0.97–1.35)	1.20 (0.99–1.44)	1.17 (0.98–1.41)	1.25 (0.86–1.83)	1.03 (0.87–1.23)
Parity per older sibling	1.16 (0.92–1.46)	1.27 (0.98–1.65)	1.34 (1.03–1.73)	0.90 (0.53–1.53)	0.80 (0.62–1.02)
Maternal age per yr increase	0.95 (0.91–0.99)	0.96 (0.91–1.01)	0.94 (0.89–0.98)	1.02 (0.94–1.11)	1.02 (0.98–1.07)

Data are odds ratio (95% confidence interval), estimated by logistic regression adjusting for sex, age, adult height, hay fever and current smoking habits. *: yes to three or more questions Q1, Q1.1, Q1.2, Q2, Q3 and Q4. SOB: shortness of breath; Q: question number on questionnaire.

The association between birth factors and adult asthma symptoms indicates that the risk for asthma is partly established early in life. The effect of birth weight on asthma symptoms was strengthened by adjustment for birth length, and long infants within a specific birth weight group were at particularly high risk. Further, asthma symptoms were associated with low birth weight when adjusting for gestational age, and when only full-term births were considered. These observations indicate a specific role of poor foetal weight gain in the aetiology of asthma. The findings thus support the hypothesis that obstructive lung disease in adulthood could be causally related to poor intrauterine growth [2]. An effect of intrauterine growth could relate directly to poor development of the small airways [12] as well as to biochemical factors involved in poor placental function.

As well as intrauterine environment, birth weight could reflect the childhood environment and early established lifestyle patterns [13]. However, adjustment for adult height, which to some degree reflects childhood nutrition, and for smoking which is an important marker of lifestyle, did not attenuate the effect of birth weight. Further, considering the strength and consistency of the association as well as the "dose–response" relationship, it seems unlikely that birth weight should act merely as a proxy-variable for childhood and lifestyle factors.

Low socioeconomic status (SES) is related to low birth weight [13] and to obstructive lung disease [14] and could possibly confound the association between asthma and birth weight. An effect of birth weight on asthma symptoms was also found in a group with very young or unmarried mothers (OR=0.59, 95% CI=0.34–1.05). Further, the effect of birth weight was similar in short subjects (adult height <25% percentile: OR_{wheeze}=0.66, 95% CI=0.47–0.93) and in tall subjects (adult height >75% percentile: OR_{wheeze}=0.77, 95% CI=0.55–l.10). Adjustment for adult dietary habits (data not given) and adult smoking habits, both related to adult SES, did not alter the effect of birth weight on asthma. Thus, based on indirect measures of SES at birth (young or unmarried mother), in childhood (adult height) or in adulthood (current food and smoking habits), the authors believe that the association between birth weight and asthma symptoms cannot be attributed to confounding by SES. However, a poor intrauterine environment could be one of the features of low SES causing adult morbidity.

Maternal smoking is a well-known risk factor for low birth weight and may be one of the factors contributing to poor intrauterine growth and impaired development of the lungs [12]. In the present study no information was available on this variable, but in studies of children Rona *et al.* [4] found that adjustment for maternal smoking did not alter the effect of birth weight on lung function, and Lewis *et al.* [5] found independent effects of maternal smoking and low birth weight on childhood wheeze. Further, the mothers of the elderly males in the study of Barker *et al.* [2] lived at a time when smoking was rare among females. It seems likely that other factors as well as maternal smoking may adversely affect foetal lung development.

Hay fever was used as an indicator of atopy, as a very strong relationship between self-reported hay fever and atopy, defined as specific immunoglobulin (Ig)E to grass, has been reported [15]. Asthma symptoms and hay fever differed in their associations with most birth characteristics. While people with asthma tended to have low birth weights, those with hay fever tended to have high birth weights. These findings, thus, suggest that the association of low birth weight and asthma is not due to allergy. Atopy, however, was a negative confounder for the association between asthma and birth weight.

In conclusion, this study provides evidence that the risk of adult asthma is partly established early in life. The relative importance of the early life environment seems to be considerable: one can estimate that 15–20% of adult asthma symptoms can be related to birth weight in the lower tertial. (For comparison, an attributable risk of 27% has been calculated for atopy in this population [16].) The present findings specifically suggest that poor intrauterine growth may play a role in the development of adult asthma.

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