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THE COURSE AND OUTCOME OF PREGNANCY IN WOMEN WITH BRONCHIAL ASTHMA

By

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The offspring of patients with bronchial asthma has been for a long time the subject of study with respect to inheritance of the trait. It has been well established that the atopic tendency, in general, is inherited (19). For allergic children, allergy was observed to be more frequent in mothers than in fathers, and more of their siblings were affected when the mother rather than the father was allergic (1).

Apart from the question of inheritance of the general atopic tendency, the literature does not provide consistent information on the reciprocal effects of pregnancy and bronchial asthma. The asthmatic condition may ameliorate, deteriorate or remain unchanged during pregnancy (2, 9, 15, 17). With respect to the course and outcome of pregnancy in asthmatic women, high foetal and neonatal mortalities have been reported, particularly in severe cases of the disease (6, 11). Baird (2) believes that anoxia associated with severe asthma can lead to foetal death or premature labour. Schaefer and Silverman (17), on the other hand, did not observe deleterious effects on pregnancy and could state: "The pregnant

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woman can be reassured that her asthma will have no bearing on her pregnancy or on the outcome of her delivery".

The opportunity to study the subject in some detail was offered by material on 381 pregnancies in women with bronchial asthma made available through the Medical Birth Registry of Norway.

MATERIAL & METHODS

The Medical Birth Registry of Norway was established in 1970 for the central processing and analysis of the information provided through a national scheme of medical registration of births. The scheme was introduced in 1967 by the National Health Services (14) and is based on compulsory notification of the birth of every foetus of 16 weeks or more of gestation. Midwives and physicians are requested to complete a special form and to send it to the County Health Officer. The notification should include, in addition to the usual civic data about parents, information about the mother's health before and during pregnancy, as well as about labour and the condition of the newborn. For details on the registration scheme and the information provided by it, the reader is referred to a report issued by the Institute (4). Of the research programmes utilizing the material of this scheme, one is concerned with maternal diseases affecting the course and outcome of pregnancy. A previous paper has dealt with epilepsy (3).

The present series of pregnancies in women with bronchial asthma is derived from the registrations during the years 1967 and 1968. Out of 134 368 pregnancies registered during these two years, there were 381 in women reporting bronchial asthma that had its onset either before or during the pregnancy. The number of births in this group was 383. A comparison is made with a control group of 112 530 pregnancies in women reporting no disease before or during the pregnancy; the number of births in this group was 113 511.

The comparison includes the following variables: Complications during pregnancy, conduct of labour, gestation period, birth weight, frequency of malformation, disease or birth injury, stillbirths, and infant deaths. In the comparison of complications occurring during pregnancy, the criterion for inclusion in the control group was that the woman had reported no disease before pregnancy. This gave a control group for this particular comparison of 125 423 pregnancies. The study of infant mortality rate is made possible through the linkage of the material of the Medical Birth Registry to that of the official registration of deaths from the Central Bureau of Statistics of Norway.

The data were analysed by the following statistical methods:

- The chi-square test with 1 degree of freedom for comparing frequencies.
- The one-sided t-test for comparing two sample means; with degrees of freedom equal to $n_1 + n_2 - 2$.

- Adjustment of the mean birth weight by birth order and by gestation period using the direct method. The corresponding distributions of the birth population of Norway during the years 1967-68 were used as standards.
- Adjustment of the neonatal mortality rate by birth weight using the indirect method. The birth-weight-specific neonatal mortality rates of the birth population of Norway during the years 1967-68 were used as standard.

An observed difference between the two groups is considered statistically significant if p is less than 0.05.

FINDINGS

Pregnancy and labour

During pregnancy, hyperemesis, haemorrhage and toxæmia were found to be significantly more frequent in the asthmatics than in women with no recorded disease before pregnancy (Table 1).

TABLE 1

Frequency of Complications During Pregnancy in Women with Bronchial Asthma and in Women with No Recorded Disease Before Pregnancy.

Recorded disease	Total pregnancies	Hyperemesis gravidarum		Vaginal haemorrhage		Toxaemia of pregnancy	
		No.	%	No.	%	No.	%
Bronchial asthma	381	8	2.1	18	4.7	40	10.5
None before pregnancy	125 423	1041	0.8	2775	2.2	5856	4.7
Statistical decision		Significant $p < 0.01$		Significant $p < 0.001$		Significant $p < 0.001$	

The percentage of induced labour was significantly higher in asthmatic women (14.2) than in controls (9.1). Complicated labour was also significantly more frequent among the asthmatics; 14.4 % compared to 9.6 %.

Interventions during labour were slightly more frequent in asthmatic women (9.9 %) than in controls (7.7 %). All main types of intervention were somewhat, but not signifi-

cantly, more frequent in the asthmatics; artificial rupture of the membranes in 2.6 % vs. 1.4 %, forceps or vacuum extraction in 2.9 % vs. 2.4 %, caesarean section in 1.8 % vs. 1.1 %, and other interventions in 5.0 % vs. 3.8 %.

Total births

The percentage of male births in asthmatic mothers (51.7 %) was almost the same as that in controls (51.5 %). Multiple birth was observed in 2 pregnancies in the asthmatics; i.e. 0.52 %, compared to 0.87 % in the controls.

Births with malformation, disease or birth injury were slightly, but not significantly, more frequent in asthmatic mothers (5.0 %) than in controls (3.9 %).

As regards mortality (Table 2), births in asthmatic mothers had higher stillbirth rate, perinatal mortality rate and infant mortality rate than the controls. The difference, however, is significant only with respect to the neonatal mortality rate; 18.5 compared to 8.0. Adjustment of the neonatal mortality rates by birth weight reduced the difference by about 60 %.

TABLE 2

Mortality Rates for Births in Women with Bronchial Asthma and in Women with No Recorded Disease Before or During Pregnancy.

Recorded disease of mother	Total births	Live births	Mortality rates per 1000*				
			Still-birth	Peri-natal	Neo-natal	Post-neonatal	Infant
Br. asthma	383	378	13.1 (5)	26.1 (10)	18.5 (7)	2.6 (1)	21.1 (8)
None	113 511	112 328	7.8 (883)	14.6 (1657)	8.0 (898)	3.4 (382)	11.4 (1280)
Statistical decision			Not sign.	Not sign.	Sign. $p < 0.05$	Not sign.	Not sign.

* Foetal deaths of less than 28 weeks of gestation are excluded in calculating the stillbirth and perinatal mortality rates. Figures in parentheses are the actual numbers of deaths.

TABLE 3

Gestation Period and Birth Weight of Live Births in Women with Bronchial Asthma and in Women with No Recorded Disease Before or During Pregnancy.

	Disease of mother		Statistical decision
	Asthma	None	
Total number of live births	378	112 328	
Number with recorded gestation period	365	108 622	
Mean gestation period in weeks	39.5	39.9	Not sign.
Prematurely-born infants (Gestation period < 37 weeks)	7.4 %	5.0 %	$p < 0.01$
Number with recorded birth weight	378	112 000	
Infants of low birth weight (2500 grams or less)	7.1 %	3.7 %	$p < 0.001$
Mean birth weight in grams	3399.9 (diff. = 96.8)	3496.7	$p < 0.001$
Birth-order-adjusted mean birth weight	3399.2 (diff. = 90.6)	3489.8	
Gestation-period-adjusted mean birth weight	3406.4 (diff. = 74.2)	3480.6	

Live births

Table 3 presents figures on gestation period and birth weight of live births in asthmatic mothers and in controls. Infants of asthmatic mothers had a mean gestation period of 39.5 weeks, which is close to the 39.9 weeks for the controls. However, prematurely-born infants (gestation period less than 37 weeks) were significantly more frequent in the asthmatics; 7.4 % compared to 5.0 %. The percentage of infants of low birth weight (2500 grams or less) was significantly higher in asthmatic mothers (7.1) than in the controls (3.7). The mean birth weight of infants of asthmatic mothers was 3399.9 grams, and of the controls was 3496.7 grams; a difference of 96.8 grams which is statistically significant. Such a

difference calls for further analysis of birth weight, particularly with respect to the influence of mother's age, region of residence, parity and gestation period. With respect to age, asthmatic women were comparable to the controls. Mother's region of residence was not found to have an effect on birth weight; therefore, a possible variation in the region of residence between the two groups cannot be responsible for the difference in the weight of their newborns. As regards parity, the mean birth weight for each birth order was lower for infants of asthmatic mothers. Adjustment by birth order did not therefore give any appreciable reduction in the difference between the mean birth weights. On the other hand, adjustment by gestation period reduced the difference by about one-fourth.

Hypoxia at birth was observed in 1.6 % of the newborns of asthmatic mothers and in 0.7 % of the newborns of controls; a difference which is statistically significant.

DISCUSSION

It is quite striking that antepartum complications in women with bronchial asthma were more than twice as frequent as in women with no recorded disease before pregnancy.

It may be claimed that this difference could be due to a tendency of midwives and physicians to be more cautious in inquiring about the health of women who report antepartum complications, or about complications in those reporting bronchial asthma. However, this possibility of bias is probably reduced by the use of a standard registration form. The possible role of prolonged anti-asthmatic medication in predisposing to these complications will have to be taken into consideration. However, the material of the Medical Birth Registry does not provide information on this item and specific inquiries will be needed in this respect. An association between bronchial asthma and hyperemesis gravidarum may result, however, from an element of emotion which can be an underlying factor in both conditions.

The more frequent occurrence of complications during labour in the asthmatics coincides well with the fact that interventions during labour were more frequent in these women. Intervention or induction of labour may be resorted to in the management of certain antepartum complications and in order to avoid prolonged distress of the asthmatic mother.

Analysis of the various factors known to influence birth weight could only partly explain the low mean birth weight of infants of asthmatic mothers. Thus, an element of retarded intrauterine growth of the foetus must be reckoned with. Certain factors in the asthmatic mothers could be responsible for hindering normal growth of the foetus. First, the more frequent complications during pregnancy. Secondly, the presumably low blood oxygenation which is directly reflected in the foetal circulation. Such a direct correspondance between the maternal and the foetal blood oxygenation has been observed by McClure (12). Thirdly, an elevated serum concentration of 5-HT (5-hydroxytryptamine or serotonin). A considerably higher than normal concentration of this substance in allergic persons was found by Machaffie et al. (13). Since 5-HT causes vasoconstriction of the placental, uterine and umbilical vessels (7), a deficient foetal circulation may result. This is even exaggerated in cases of toxæmia, where the 5-HT content of the placenta has been demonstrated to be increased (8, 18). The deleterious effect of 5-HT on the foetus has been experimentally demonstrated (5, 16, 20).

The high frequency of hypoxia in the newborns of asthmatic mothers could be a reflection of the mother's hypoxia. However, there is also a possibility of a pathologic pulmonary conditions in such newborns. This possibility is supported by the observation of Goldberg et al. (10) that pregnant rats kept under chronic hypoxia gave birth to offspring having thick media of the small pulmonary arteries.

An excess mortality of births in asthmatic mothers was observed during the late foetal period and the first four weeks of life. This excess is probably the consequence of the high frequencies of complications during pregnancy and labour, of

premature labour, of low birth weight and of hypoxia in the newborn.

It can be concluded that pregnant asthmatics as well as their infants are high risk groups. Alert antenatal, natal and neonatal care is essential for early detection and prompt management of any emerging complications. Oxygenation of the asthmatic mother during labour would probably lower the occurrence of hypoxia in the newborn. The role of antiasthmatic medication in the causation of antepartum complications and in the retardation of intrauterine growth of the foetus, suggested by the present findings, warrants further studies.

SUMMARY

The material of the national scheme of medical registration of births in Norway, 1967-68, has been utilized in a study of the course and outcome of pregnancy in women with bronchial asthma. A series of 381 pregnancies in asthmatic women is compared to 112 530 pregnancies in women reporting no disease.

The comparison revealed that asthmatic women experience more frequent complications during pregnancy and labour, and that their newborns are more frequently prematurely born, of low birth weight, hypoxic and had a higher neonatal mortality rate. These findings indicate that pregnant asthmatics and their newborns should be considered high risk groups calling for special attention and care.

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