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Effect of sex of fetus on asthma during pregnancy: blind prospective study

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The course of asthma during pregnancy is variable and may remain unchanged, worsen, or improve, returning to the pre-pregnancy state within three months after parturition.¹ Some patients experience the same changes in each pregnancy, but nearly half do not, suggesting some intrinsic or extrinsic factor unique to each pregnancy such as the sex of the fetus.¹ We observed that the condition of patients with moderate to severe asthma generally deteriorated when they were pregnant with girls but not boys, raising the intriguing possibility that the sex of the fetus might influence the course of asthma during pregnancy. We investigated this possibility in a blind prospective study.

Subjects, methods, and results

All women aged 25-34 who were receiving regular drug treatment for asthma and were in the second trimester of pregnancy (12-21 weeks' gestation) were approached directly to participate in the study. Twenty eight women were recruited from three hospital and

four general practice antenatal clinics and six from an asthma clinic. Twelve had not taken inhaled steroids (beclomethasone or budesonide) regularly before pregnancy, 16 took 200-500 µg daily, and six more than 500 µg daily. None was taking oral steroids. None knew the sex of their baby before delivery. The study took the form of a questionnaire on symptoms of asthma, cough, shortness of breath, nocturnal waking due to asthma, drug treatment (frequency and amount), and visits to a doctor for asthma before and since the beginning of pregnancy, a minimum period of 12 weeks. Subjects were also asked to keep daily diary cards and peak expiratory flow readings throughout pregnancy. All 34 subjects completed the questionnaire; only 15 agreed to keep daily records and only 6 successfully completed these. We have therefore based our analysis on the questionnaire alone. Subjects were contacted again after parturition to ascertain the sex of the baby.

Eighteen women had boys and 16 girls. There was no difference in age range of mothers, gestation at time

of questionnaire, or severity of asthma before pregnancy between the two groups. Roughly equal numbers of mothers of boys and mothers of girls reported no change in asthmatic symptoms. However, 4 of the 18 mothers of boys reported an overall deterioration in symptoms and 8 an improvement, while 8 of the 16 mothers of girls reported an overall deterioration and none an improvement. The table shows responses to questions on individual symptoms with the results of analysis using a $2 \times 2 \chi^2$ test comparing proportions of subjects with deteriorating symptoms with proportions of those who improved or showed no change for mothers of boys and girls. For most questions there was a trend for greater proportions of mothers of girls to report increased symptoms and for greater proportions of mothers of boys to report an improvement in their asthma. Significant differences were found in shortness of breath, nocturnal waking, and general symptoms of asthma.

Comment

This study suggests that asthmatic women pregnant with girls are more likely than those pregnant with boys to have increased symptoms of asthma during pregnancy. Any psychological basis for this difference is unlikely as none knew the sex of her baby before delivery. All patients were questioned early in the second trimester, making it unlikely that the results were influenced by the tendency for asthma to improve late in pregnancy.^{2,3} Minute hormonal differences may be implicated. Acute exacerbations of asthma increased fourfold in women from day 26 to day 4 of the menstrual cycle,⁴ and injection of progesterone can reduce premenstrual asthma.⁵ Male fetuses produce a surge of androgens at weeks 12-16, when most of our patients completed the questionnaire.

Our limited study suggests a relation between fetal sex and the potential development of unstable asthma

Results of questionnaire survey of 34 women during second trimester of pregnancy according to sex of baby delivered. Values are numbers of women in each group

	Worse		Same		Better		χ^2 (95% CI)*
	Boys	Girls	Boys	Girls	Boys	Girls	
Cough	5	7	7	8	6	1	3.87 (-48% to 16%)†
Shortness of breath	5	13	7	3	6	0	9.72 (-83% to -23%)‡
Nocturnal waking	6	10	5	5	7	1	5.37 (-8% to 62%)¶
General state of asthma	5	9	5	6	8	1	6.3 (-4% to 60%)¶
Amount of drug treatment	8	7	4	5	6	4	0.28 (-33% to 34%)
Frequency of drug treatment	6	7	7	8	5	1	2.7 (-22% to 44%)
Visits to doctor	3	5	10	11	5	0	3.84 (-15% to 43%)†

*Comparison of proportion of women who were worse with proportion who were not worse for boys and girls; 95% confidence interval given for difference in proportions.

†P=0.05.

‡P<0.01.

¶P<0.05.

in pregnancy, a clinically important observation for all concerned with antenatal care. This intriguing finding should stimulate further investigation.

We thank the general practitioners and obstetricians who gave us access to antenatal clinics.

Contributors: All the authors participated in designing the study. NB prepared the questionnaire, interviewed patients, and collected the data. GMC critically revised the manuscript. HJM analysed the data, wrote the paper, and had the original idea for the study and is guarantor for the study.

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A compliment

Having your research ideas stolen

It was my first research project after completing my PhD, and it required the collaboration of one large and 20 small centres. My professor and I had contacted the large centre, which will remain nameless. The director expressed interest in the study and invited us to visit and present our proposal. The potential local collaborators were eager for information: we discussed in great detail the hypothesis, the design, the sample size estimate, the questionnaires, the methods for data collection, the plan of analysis. At the end of the day came the decision: they were going to do the study without us.

It didn't turn out to be such a bad thing after all. They published their study. We published ours—based on the remaining 20 small centres—confirming their findings. Human knowledge increased a bit.

But on the way back from the meeting I struggled to come to terms with having the idea stolen. My professor seemed amused and not particularly affected. Why? "Laura, you had an idea that was good enough to steal. You will have many more ideas. It is better to be one of those whose ideas are stolen than one of those who steal ideas."

That dealt with my concern and enabled me to join in one of the most rewarding activities of science, talking shop. Discussing

intriguing questions, hearing your colleagues' reaction to a new hypothesis, pointing out to students the questions that are just waiting to be answered. Of course, with time we all realise that scientific insights do not really belong to individual people, but are part of the white rapids of human knowledge. And then whose idea it was in the first place matters even less.

So the next time that you share an idea with someone and then see it in their grant proposal feel proud: it was an idea good enough to steal.

Laura C Rodrigues, senior lecturer in infectious disease epidemiology, University of London

We welcome articles up to 600 words on topics such as *A memorable patient, A paper that changed my practice, My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk. Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for "Endpieces," consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.