Relationship between birth weight and adult lung function: controlling for maternal factors

C A Edwards, L M Osman, D J Godden, D M Campbell, J G Douglas

Background: There is conflicting evidence on the ‘fetal origins hypothesis’ of association between birth weight and adult lung function. This may be due to failure to control for confounding maternal factors influencing birth weight. In the present study access to birth details for adults aged 45–50 years who were documented as children to have asthma, wheezy bronchitis, or no respiratory symptoms provided an opportunity to investigate this association, controlling for maternal factors.

Methods: In 2001 the cohort was assessed for current lung function, smoking status, and respiratory symptoms. Birth details obtained from the Aberdeen Maternity and Neonatal Databank recorded birth weight, gestation, parity, and mother’s age and height.

Results: 381 subjects aged 45–50 years had birth details available. A significant linear trend (p=0.01) was observed between birth weight and current forced expiratory volume in 1 second (FEV₁) and forced vital capacity (FVC) values (adjusted for height, age, sex, weight, deprivation category [Depcat], childhood group, and smoking status). This trend remained significant after adjusting birth weight for gestation, parity, sex, mother’s height and weight (p=0.01). The relationship between birth weight and FEV₁ and FVC remained significant when adjusted for smoking history. There was no association between birth weight and current wheezing symptoms.

Conclusion: There is a positive linear trend between birth weight, adjusted for maternal factors, and lung function in adulthood. The strength of this association supports the ‘fetal origins hypothesis’ that impairment of fetal growth is a significant influence on adult lung function.

However, maternal factors can be difficult to access for midlife studies. In Aberdeen a database maintained since 1950 has given the opportunity to test the ‘fetal origins hypothesis’ while controlling for these maternal factors. The aim of this study was to investigate whether there is a relationship between birth weight and midlife adult lung function and current wheeze, after controlling for maternal factors that influence birth weight. The analysis also took account of adult factors that affect current lung function such as smoking history, sex, age, height, and weight.

METHODS

Study population
In 1964 a random community survey of one in five children (n=2511) who attended school in Aberdeen reported that 288 children had wheeze, clinically defined as either asthma or wheezy bronchitis, and 2223 had no respiratory symptoms. In 1989 and 1994 follow up studies of the cohort included all traceable subjects who had had no respiratory symptoms as children to have asthma, wheezy bronchitis, or no respiratory symptoms. In 1989 and 1994 follow up studies of the cohort included a postal survey of all traceable subjects from the original 2511 children and interviews with 605 of them that included all traceable subjects who had had wheeze as a child, together with a random sample of non-wheezy children.

In 2001 we followed up the 605 subjects who had been interviewed in 1989 and 1994. Of these, 78 had been diagnosed with childhood asthma, 111 with childhood wheezy bronchitis, 100 with adult onset wheeze, and 316 were controls who had had no respiratory symptoms as children. The addresses of these subjects were initially checked by Data Discoveries Ltd (Edinburgh) who confirmed the addresses and supplied possible new ones. The remainder were checked on the Patient Administration System (PAS) at Aberdeen Royal Infirmary for a current address. Finally,
Study protocol

One researcher (CE) interviewed all subjects who agreed to participate between August 2000 and July 2001, either at the Chest Clinic in Aberdeen Royal Infirmary or in their own home. The interview included a modified version of the Medical Research Council’s 1986 Respiratory Symptoms Questionnaire and questions on current wheeze (past 12 months) and smoking. At the time of the interview FEV1 and FVC were measured using a portable spirometer (Vitalograph Compact II, Vitalograph, Buckingham, UK) which was calibrated daily. The spirometric measurements were performed with subjects in a sitting position without the use of nose clips. Three values were obtained and the highest FEV1 and FVC were used. Subjects prescribed a bronchodilator were requested not to use it for 6 hours before the tests were performed. Fifty one subjects had been prescribed bronchodilators, of whom five had used the bronchodilator within 6 hours of the tests being performed.

The study was approved by the Grampian Research Ethics Committee.
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et al by Shaheen between middle age lung function and birth weight reported hypothesis, and contrasts with the lack of relationship birth weight in middle age supports the fetal origins in middle age. The relationship between lung function and years, controlling for maternal and adult factors, but did not birth weight predicts lower lung function at mean age 47 uterus may affect fetal growth and have lasting effects on lung

DISCUSSION Barker et al hypothesised that an adverse environment in utero may affect fetal growth and have lasting effects on lung function in adulthood and old age. Our study found that low birth weight predicts lower lung function at mean age 47 years, controlling for maternal and adult factors, but did not find a relationship between birth weight and current wheeze in middle age. The relationship between lung function and birth weight in middle age supports the fetal origins hypothesis, and contrasts with the lack of relationship between middle age lung function and birth weight reported by Shaheen et al and Lopuha¨a et al. The failure of these two groups to detect a relationship may reflect lesser variability in the samples they studied. In particular, the sample studied by Lopuha¨a et al was made up of adults who had all been born after their mothers had experienced famine in pregnancy. The population in our study is likely to include a wider range of lung function, from adults who have wheezed since childhood to controls who had no symptoms as children or as adults. This spectrum is more likely to provide sensitivity to detect a relationship between lung function and birth weight. However, because of the sampling process used in this study, specific lung function results cannot be generalised to the general population.

This study controlled for the adult factors that affect current lung function: age, sex, and height; adult weight was also adjusted for. It is of interest that the adjustment for adult weight had little effect on the relationship between birth weight and adult lung function. This would suggest that, although babies who are classified as underweight after adjustment for maternal factors may “catch up” with their peers in later life, their experience of poor fetal growth continues to be reflected in lower adult lung function.

However, this study did not find a relationship between birth weight and adult wheeze. We do not believe that this was due to lack of validity of the wheeze assessment. Our wheeze measurement was of the form: “Have you had wheezing or whistling in your chest at any time during the past 12 months and have you at any time in the last 12 months been woken at night by an attack of shortness of breath?” Wheeze at any time over the previous 12 months is the standard used by other studies investigating the relationship between current wheeze and epidemiological factors.

Previous studies have shown an association between birth weight and early adulthood symptoms. Shaheen et al found that the prevalence of wheeze in adults aged 26 years fell with increasing birth weight.20 Svanes et al found that, in subjects aged 20–24 years, asthma symptoms were inversely associated with birth weight.21 The findings of these studies—that birth weight is negatively related to symptoms—are not supported by Barker et al or by our study. This may be due to confounding by a cohort effect21; adults now aged 50–70 years are likely to have had different environmental influences as children than present day young adults. The conflicting results might also be due to different wheezing phenotypes at different ages or to a lack of power in our study and that of Barker et al compared with the British cohort study of Shaheen et al20 and the European Community Respiratory Health Survey reported by Svanes et al23 who had much bigger samples to analyse binary outcomes.

Alternatively, the relationship between childhood wheezing symptoms and adult lung function may be complex and influenced by the nature of childhood wheeze. We have previously reported that, in this cohort, childhood asthma was associated with reduced lung function at age 35–40 years whereas the children with wheezy bronchitis achieved normal lung function at that age.24 Interestingly, the group with childhood wheezy bronchitis is now showing a more rapid rate of decline in lung function than the normal controls.25

Table 2 Characteristics of subjects’ mothers at time of birth (n = 323)

| Age (years)* | 27.2 (5.5) |
| Height (cm) | 158.2 (5.5) |
| Gestation (weeks) | 40.3 (1.7) |
| Place of subjects’ birth | Aberdeen Maternity Hospital 286 (89%); Home birth 37 (11%) |
| Parity | 0 124 (38%); 1 99 (31%); 2 65 (20%); 3 21 (7%); 4 10 (3%); 5 or more 4 (1%) |
| Smoked during subjects’ childhood | 200 (62%) |

*pValues shown as mean (SD).

Table 3 FEV1 and FVC values adjusted for age, height, weight, current smoking status, deprivation category (Depcat), and childhood group according to quintiles of unadjusted birth weight

<p>| Men (n = 163) | Women (n = 160) |</p>
<table>
<thead>
<tr>
<th>FEV1</th>
<th>FVC</th>
<th>Difference</th>
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<th>FEV1</th>
<th>FVC</th>
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<tr>
<td>Unadjusted birth weight score (quintiles)</td>
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<tr>
<td>Lowest 20%</td>
<td>26</td>
<td>3.10</td>
<td>4.28</td>
<td>40</td>
<td>2.29</td>
<td>3.07</td>
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<tr>
<td>21–40%</td>
<td>31</td>
<td>3.31</td>
<td>0.21 (0.03 to 0.40)</td>
<td>4.54</td>
<td>26</td>
<td>0.26 (0.03 to 0.49)</td>
<td>3.45</td>
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<td>41–60%</td>
<td>32</td>
<td>3.27</td>
<td>0.17 (0.01 to 0.35)</td>
<td>4.58</td>
<td>30</td>
<td>0.30 (0.07 to 0.52)</td>
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<td>61–80%</td>
<td>27</td>
<td>3.30</td>
<td>0.20 (0.03 to 0.37)</td>
<td>4.59</td>
<td>31</td>
<td>0.31 (0.10 to 0.52)</td>
<td>3.56</td>
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<tr>
<td>Highest 20%</td>
<td>27</td>
<td>3.37</td>
<td>0.27 (0.08 to 0.46)</td>
<td>4.70</td>
<td>42</td>
<td>0.42 (0.18 to 0.65)</td>
<td>3.73</td>
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<td>β coefficient</td>
<td>0.18</td>
<td>0.25</td>
<td>0.17</td>
<td>0.23</td>
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<td>Adjusted for maternal smoking</td>
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Forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) values are shown as mean.
Barker et al. did not find an association between FVC and birth weight, in contrast to our findings and those of Stein et al. The significance of FVC in such studies is more difficult to interpret than FEV₁. It is well recognised that FVC may be reduced in obstructive lung disease where it reflects early airway closure and gas trapping. Both subject technique and equipment used to measure FVC may influence the results obtained, and none of the studies reported in date can definitively address whether the FVC measurements obtained reflect obstructive or restrictive aspects of function.

The birth data collected for our subjects in the 1950s by AMND were more limited than would now be available. In particular, the measurement of baby length, which allows calculation of ponderal index, was not done. Ponderal index is the ratio of birth weight to length and is an indicator of fatness or thinness of the neonate. However, the AMND did provide more maternal information than other studies of cohorts of similar age. The use of Campbell’s birth weight standards removed any inherent factors that might affect birth weight independent of poor fetal growth. Controlling for birth weight, in contrast to our findings and those of Stein et al., Maternal smoking and diet have been cited as possible factors, but what may cause this adverse environment. Maternal smoking and diet have been cited as possible factors, but what may cause this adverse environment. Maternal smoking and diet have been cited as possible factors, but what may cause this adverse environment. Maternal smoking and diet have been cited as possible factors, but what may cause this adverse environment. Maternal smoking and diet have been cited as possible factors, but what may cause this adverse environment. Maternal smoking and diet have been cited as possible factors, but what may cause this adverse environment. Maternal smoking and diet have been cited as possible factors, but what may cause this adverse environment. Maternal smoking and diet have been cited as possible factors, but what may cause this adverse environment. Maternal smoking and diet have been cited as possible factors, but what may cause this adverse environment. Maternal smoking and diet have been cited as possible factors, but what may cause this adverse environment.

However, this study contributes little to our knowledge of what may cause this adverse environment. Maternal smoking21–24 and diet25–28 have been cited as possible factors, but in the 1950s these were not recorded routinely. Our only indicator of maternal smoking is the report by subjects in the studies of 1989 and 1994 (aged between 30 and 40 years at this time) of whether their mother smoked during their early childhood. This study found a relationship between reported maternal smoking in the first year of life and birth weight among female subjects but not for males, and no relationship between reported maternal smoking and midlife lung function. However, these results can only be exploratory in nature because of the imprecise data used. In essence, all that we are controlling for is whether the mother had “ever smoked” in the subject’s childhood; we cannot believe that they smoked at the time of pregnancy.

The results of this study support the “fetal origins hypothesis” that an adverse environment in utero can affect fetal growth and influenced lung function in adult life, and that birth weight is a marker for adult lung function. By controlling for maternal and adult factors, the case has been strengthened. However, birth weight was not a marker for wheeze in middle age.

ACKNOWLEDGEMENTS

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