Untreated asthma, final height and sitting height/leg length ratio in Chile

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Summary

Objective: There is uncertainty as to whether asthma has an effect on final height. We investigated using subjective and objective assessments whether untreated asthma is associated with final height, leg length and sitting height to leg length ratio in an area of Chile in which almost no one received asthma treatment.

Methods: We collected data on 1232 males and females aged 22–28 years in a semi-rural area of Chile. Information on asthma was collected using the European Community Respiratory Health Survey (ECRHS) questionnaire. We assessed sensitisation to eight allergens and bronchial hyper-responsiveness (BHR) to methacholine as a dichotomous variable and as a log slope. Information on possible confounders in terms of smoking, birth weight, number of siblings and socio-economic factors such as household possessions, car ownership and education was available.

Results: Regardless of the asthma assessment used, there was no association between asthma symptoms, diagnosis of asthma, atopy, BHR as log slope, binary or categorical and height, leg length or the ratio of sitting height to leg length. The latter was used as a potentially more appropriate measure to assess a detriment of growth.

Conclusion: Asthma as assessed in community studies is unrelated to final height or body proportions.

Introduction

Early studies on the association between asthma and height demonstrated that asthma rarely, if at all, was the cause of severe height deterioration, \cite{1, 2} but asthma was associated with some loss of height
in children, especially during adolescence. This decrease of height was unrelated to steroidal treatment. However, Balfour-Lynn concluded that asthma had no direct influence on growth in height but was associated with delay in the onset of puberty.

The studies in the 1970s were carried out before standardised questionnaires for assessing asthma became available. As there is no gold standard for asthma, standardised tools to assess asthma are of great value in making comparisons between studies. In addition, since 1970 there has been a movement away from associating asthma with stigma and diagnostic practices have changed. As a result there is not a clear equivalence between subjects diagnosed as having asthma and those diagnosed in the 1970s. In more recent studies of height, there have been serious methodological problems in disentangling the effects of asthma from the effects of steroidal treatment. The current understanding is that asthma results in a delayed puberty and that would explain most of the short-lived height deficit. However, the conclusion was based on the early-published work. Most recent studies of height have tried to assess the possible effect of inhaled preventives of asthma such as budesonide and nedocromil. Inhaled steroids may have no lasting effect on height and their effect may be restricted to the early period of treatment. The current understanding is that if asthma and inhaled steroids have an effect on height, their effect is small.

We carried out a community study of young adults living in a semi-rural area of Chile. The population is highly interesting because asthma symptoms are prevalent in Chile, but outside the larger cities very few subjects have received appropriate management for their condition. It is a suitable population for assessing whether asthma on its own affects the final height of young adults, as a large percentage would have started their symptoms in childhood. We also assessed the sitting height/leg length ratio as it has been indicated that in nutritional stress leg length is more susceptible to growth interruption than the upper segment. We are unaware of any asthma studies that have assessed this ratio as an outcome variable of asthma.

Methods

Subjects

This was a non-concurrent longitudinal study centered on Limache, a semi-rural area of approximately 50,000 inhabitants about 120 km north-west of Santiago in Chile. Between 2001 and 2003, we collected information on 1232 subjects randomly selected using the birth register which included 3096 men and women born in the hospital of Limache between 1974 and 1978. We chose Limache for our study because of the high quality of the hospital birth registry and medical records in the first year of life, as these data were essential for other aims of the study. The low emigration rate in this population ensured that a large proportion of those born in Limache would remain in the area and could be found.

Respiratory symptoms, atopy and pulmonary function assessments

Participants completed the Spanish version of the European Community Respiratory Health Survey (ECRHS) questionnaire adapted to Chile. Skin test sensitisations to cat fur, dog hair, cockroach, Dermatophagoides Pteronyssinus, Alternaria Alternata, and blends of grass pollens, trees, and weeds and shrubs common in Chile were assessed (samples obtained from Allergy Therapeutics). A wheal size of 3 mm or over was considered positive. Following advice, this was unadjusted for histamine control. We assessed bronchial hyper-responsiveness (BHR) to methacholine using the tidal breathing methodology. Increasing concentrations of 0.5, 1.00, 4.00, 8.00 and 16 mg/ml were used with a Hudson nebuliser at a flow rate of 0.13 l/min over a period of 2 min. Forced expiratory volume at 1 s (FEV₁) was measured using a Vitalograph 2120 and software Spirotrac IV following the American Thoracic Society norms. An FEV₁ decrease of 20% in comparison to baseline FEV₁ at any concentration up to 16 mg/ml (PC₂₀) was considered to have positive BHR. We also subdivided BHR response into three groups: positive response at a methacholine concentration up to 8 mg/l, positive response to a concentration between 8.1 and 16 mg/l and negative BHR status. Participants were advised not to smoke, or take asthma relievers and preventives before the test for at least 1 and 6 h, respectively. Those with an expected FEV₁ below 70% of the predicted value, and those with a heart condition, epilepsy, current pregnancy or breast-feeding were excluded (2% of the sample). The tests and measurements were carried out in a health setting with ready access to medical facilities. Three university nurses trained for the study administered the questionnaire and carried out the tests. The Ethics Committee of the Faculty of
techniques are illustrated, and summarily ex-
scales to protect the baby. The measurement
adjust for the weight of any garment put on the
norms describe the equipment and advise staff to
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indicators of socio-economic level. We also
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months, waking with breathlessness in the last 12
months, the two asthma symptoms together,
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status, BHR response divided into three categories
and BHR log slope. In all our analyses we adjusted
for number of cigarettes smoked per day, gender,
birth weight, number of household belongings, car
ownership, participant’s level of education and
number of siblings in the family.

In the ECRHS, a dose–response slope was adopted
as a measure of BHR.21 This method has the
advantage of minimising censored information
in comparison with the BHR status as defined by a 20%
fall in FEV\textsubscript{1}. We estimated an equivalent BHR slope
by regressing percentage fall in FEV\textsubscript{1} on log\textsubscript{10}
concentration, referred to as BHR log slope. The
BHR log slope satisfied the statistical requirements
of normality and homoscedasticity. We excluded 55
participants from the analysis related to BHR log
slope because their values represented extreme
deviations to the left or right of the distribution.
The ratio of sitting height to leg length was used
as a measure of proportional contribution to total
height, as it might be more relevant in terms of
undernutrition. Leg length was calculated as the
difference between height and sitting height.

Results

Altogether, 10.5% of the selected sample did not
participate in the study because they refused to
participate, were serving a custodial sentence or
had a learning disability and were randomly
replaced using the original sampling frame. Two
per cent were excluded from the BHR test. Eight
deductors failed to perform the lung function
test satisfactorily. Data for all variables in the
analyses were almost 100% complete for each
participant, with the exception related to BHR log
slope explained in the analysis section.

Woken by breathlessness (P = 0.002), positive
BHR (P < 0.001), and diagnosed asthma (P = 0.018)
among the asthma variables were more common in
women than men (Table 1). Wheeze and waking
with breathlessness in the last 12 months, and
atopy were highly prevalent. Only two subjects
have ever received steroidal treatment for their
asthma in our study, and it was sporadic. The
proportion of participants reporting asthma was
very low (4.5%). Of those who had been diagnosed
with asthma, 79% of males and 71% of females were
diagnosed as such in childhood. These percentages
exclude three currently asthmatic women who did
not give information on asthma in childhood, two
males who gave information on childhood asthma
but not on current asthma and two males who
were in remission. Families tended to have a large
number of siblings and current smoking was highly
prevalent in comparison to the US and northern
Europe (Table 1). Adult height was well below
norms for developed countries.

Height was highly correlated with leg length and
sitting height (Table 2). Leg length and the sitting
height to leg length ratio were highly correlated
negatively. The other correlations were of inter-
mediate magnitude.

Height was unrelated to asthma symptoms,
diagnosed asthma, diagnosed asthma in childhood,
wheeze and atopic status, BHR status and BHR log
slope (Table 3). It was also unrelated to BHR status
divided into three categories (not shown). Unsur-
prisingly, given the high correlation between height
and leg length, there was also no association

Analysis

Medicine of the University of Chile approved the
study.

Height was measured as recommended by Ha-
bicht and sitting height was measured in all
respects as height, but the thighs were in a
horizontal plane, the feet firmly on the ground
and the two measurements were taken to the
nearest 1 mm below.\textsuperscript{21} We also collected information
on gender, age, current smoking, participant’s
education, number of household possessions, car
ownership and number of brothers and sisters. The
household possessions were a gas-fuelled water-
heating device known as a calefont, refrigerator,
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and leg length, there was also no association
Table 1  Prevalence of asthma variables, mean height, prevalence of smoking and family size by gender.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Males (N = 556)</th>
<th>Females (N = 676)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheeze in last 12 m (%)</td>
<td>147 (26.4)</td>
<td>189 (28.0)</td>
</tr>
<tr>
<td>Woken by breathlessness (%)</td>
<td>58 (10.4)</td>
<td>111 (16.4)</td>
</tr>
<tr>
<td>Positive BHR (%)</td>
<td>45 (8.1)</td>
<td>111 (16.4)</td>
</tr>
<tr>
<td>BHR (log slope and sd)</td>
<td>−0.318 (1.945)</td>
<td>0.488 (2.209)</td>
</tr>
<tr>
<td>Atopic to at least one allergen (%)</td>
<td>159 (28.6)</td>
<td>186 (27.5)</td>
</tr>
<tr>
<td>Diagnosed asthma (%)</td>
<td>14 (2.5)</td>
<td>35 (5.2)</td>
</tr>
<tr>
<td>Diagnosed asthma in childhood (%)</td>
<td>15 (2.7)</td>
<td>25 (3.7)</td>
</tr>
<tr>
<td>Adult height (cm and sd)</td>
<td>168.2 (6.0)</td>
<td>156.3 (5.5)</td>
</tr>
<tr>
<td>Leg length (cm and sd)</td>
<td>79.0 (4.1)</td>
<td>71.9 (3.7)</td>
</tr>
<tr>
<td>Current smokers (%)</td>
<td>379 (68.2)</td>
<td>344 (50.9)</td>
</tr>
</tbody>
</table>

Number of siblings

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 or 1 (%)</td>
<td>77 (13.9)</td>
<td>90 (13.4)</td>
</tr>
<tr>
<td>2 or 3 (%)</td>
<td>242 (43.6)</td>
<td>281 (41.8)</td>
</tr>
<tr>
<td>≥4 (%)</td>
<td>236 (42.5)</td>
<td>301 (44.8)</td>
</tr>
</tbody>
</table>

Table 2  Pearson’s correlations between the anthropometric measurements in the analysis.

<table>
<thead>
<tr>
<th></th>
<th>Height</th>
<th>Leg length</th>
<th>Sitting height</th>
<th>Sitting height to leg length ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leg length</td>
<td>0.91</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sitting height</td>
<td>0.83</td>
<td>0.52</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Sitting height to leg length ratio</td>
<td>−0.41</td>
<td>−0.75</td>
<td>0.16</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Table 3  Association between asthma in terms of subjective and objective assessments and height, leg length and sitting height to leg length ratio adjusted for gender, number of siblings, number of household belongings, birth weight, smoking, car ownership, and last year of fulltime education.

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No = 1190*</td>
<td>No = 899*</td>
<td>No = 899*</td>
</tr>
<tr>
<td></td>
<td>Coefficient¹(95%CI)</td>
<td>Coefficient¹(95%CI)</td>
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</tr>
<tr>
<td>Wheeze</td>
<td>0.35 (−0.12, 1.28)</td>
<td>0.39 (−0.18, 0.96)</td>
<td>−0.007 (−0.017, 0.003)</td>
</tr>
<tr>
<td>Waking with breathlessness</td>
<td>0.54 (−0.35, 1.44)</td>
<td>0.41 (−0.30, 1.13)</td>
<td>−0.002 (−0.004, 0.001)</td>
</tr>
<tr>
<td>Wheeze and waking with breathlessness</td>
<td>1.07 (−0.15, 2.28)</td>
<td>0.89 (−0.10, 1.88)</td>
<td>−0.011 (−0.028, 0.006)</td>
</tr>
<tr>
<td>Diagnosed asthma</td>
<td>0.44 (−1.13, 2.01)</td>
<td>0.04 (−1.18, 1.26)</td>
<td>0.003 (−0.018, 0.025)</td>
</tr>
<tr>
<td>Diagnosed asthma in childhood</td>
<td>−0.26 (−1.99, 1.47)</td>
<td>0.10 (−1.24, 1.44)</td>
<td>0.003 (−0.021, 0.026)</td>
</tr>
<tr>
<td>Atopic</td>
<td>−0.35 (−1.04, 0.33)</td>
<td>−0.55 (−1.10, 0.01)</td>
<td>0.007 (−0.003, 0.016)</td>
</tr>
<tr>
<td>Wheeze¹ and atopic</td>
<td>−0.20 (−1.23, 0.84)</td>
<td>−0.57 (−1.41, 0.27)</td>
<td>0.003 (−0.012, 0.017)</td>
</tr>
<tr>
<td>Positive BHR</td>
<td>−0.26 (−1.19, 0.68)</td>
<td>−0.43 (−1.20, 0.34)</td>
<td>0.004 (−0.009, 0.017)</td>
</tr>
<tr>
<td>BHR (log slope)</td>
<td>0.03 (−0.13, 0.18)</td>
<td>−0.06 (−0.17, 0.06)</td>
<td>0.002 (−0.0005, 0.004)</td>
</tr>
</tbody>
</table>

*Minimum number for some variables had two less subjects, except for BHR (log slope) in which 1122 subjects were included for height and 848 for the other two outcomes.

¹In the last 12 months.

²All coefficients were statistically insignificant.
between leg length and our asthma outcomes. The ratio of sitting height to leg length was also unrelated to the explanatory variables.

Discussion

In a population in which inhalers have been seldom used, we were able to confirm that asthma in the community, regardless of type of assessment, was unrelated to final height, leg length and the sitting height to leg length ratio.

The strengths of this study are that it was community based, asthma was assessed using standardised tools and the assessments were based on subjective and objective measurements, anthropometric measurements were taken using standardised protocols, final height should have been achieved in the total sample at the age of 22–28 years and a large suitable control group was available similar in all characteristics, except their asthma status. As participants were young adults, physical shrinkage, if any, was minimal. As this was a community study, we suspect that most of the asthmatic subjects had either mild or moderate asthma. It is possible that in a study including only patients with severe asthma an effect on height could have been found. However, such a study would have selected patients known to physicians, who might be more likely to receive steroidal treatment thus making it difficult to distinguish the asthma from the steroids effect on height or other anthropometric measurement.

The cross-sectional design of our study should not have affected our results because we were able to measure our outcomes accurately, recall bias would have been unlikely because the fieldworkers and the participants supplying the information on asthma were unaware of the hypothesis being tested and reverse causality, say height causing asthma, would be less likely after adjusting for gender, birth weight, smoking and socio-economic factors. The main weakness of this study was that asthma might have started in adulthood in a proportion of the subjects and this would have increased the risk of misclassification, as asthma onset in adulthood could not have influenced our anthropometric measurement outcomes. As most of the questions on asthma symptoms did not explore early onset, and atopy and BHR were assessed in adulthood, we were uncertain about the percentage of participants whose asthma symptoms, atopy and positive BHR started in childhood. Approximately three quarters of those with diagnosed asthma reported having their asthma since childhood. Unfortunately in semi-rural areas in developing countries, only a small proportion of individuals with asthma symptoms receive a recorded diagnosis of asthma from a doctor. This is the reason why the number of subjects with asthma symptoms in our study was disproportionately high in comparison to subjects with physician-diagnosed asthma. We believe that approximately between 65% and 80% of those with asthma symptoms started their symptoms in childhood. These percentage would broadly correspond to a longitudinal study carried out in a different setting in Australia. Wheeze on its own was probably a less useful variable in our study because many of those with current wheeze might have experienced it only recently in adulthood thus having little chance of influencing height. The suggestion that a large proportion of wheeze started in adulthood in our study is plausible because the prevalence of smoking in young adults in Chile is approximately 50%. Thus a large percentage of individuals with wheeze may be developing chronic bronchitis and some may in the future develop chronic obstructive pulmonary disease rather than asthma. It is difficult to distinguish between the three conditions in young adults.

Those with atopy and wheeze are more likely to have started their condition in childhood, but it is possible that some had atopy in childhood and wheeze later in adulthood. We speculate that the percentage who started their symptoms in childhood was higher in those who reported waking with breathlessness compared to those who said they had wheeze.

Undernutrition in infancy was common in Chile in the 1970s. Although at the time infant mortality was decreasing, the levels were 60–40 per 1000 in the period 1974–1978, when our subjects were born. The participants are a random sample of those who survived childhood and their average height in males is 6 cm less than the Spanish population in the 1990s, a population of partially similar genetic endowment to the Chilean population. We would have expected that if asthma has an effect on height it would be more noticeable in a population already nutritionally vulnerable. However, regardless of the outcome measure of asthma chosen or the measure of length included, there was not a single significant association. Gunnell et al. have contrasted results related to height and leg length trying to disentangle the association between anthropometric measurements and specific cause mortality based on their contention that leg length is more related to nutrition than height. However, we have demonstrated in this study that the correlation between height and leg length is so high that a distinction between these two measures.
Céspedes for training our fieldworkers in the measurements of lung function including methacholine challenge. The Wellcome Trust funded the study.

References

1. Lacey KA, Parkin JM, editors. Growth retardation in chronic asthma (letter to the editor). Lancet 1974;ii:42.

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