Prediction of lung function in the inadequately nourished

T J Ong, A Mehta, S Ogston, S Mukhopadhyay

Abstract
Background—In animal models, nutritional deficiency leads to profound qualitative changes in the lung beyond an effect on organ size. Although lung growth is non-isotropic, predictive values for spirometric lung function in children are corrected for height alone. Prediction of lung function should consider isotropic growth and nutritional status concurrently.

Aim—to establish whether nutritional status influences lung function following the exclusion of the effect of isotropic growth.

Methods—Nutritional status (weight, body mass index, mid-upper arm circumference, and subcapular and triceps skinfold thicknesses) was assessed, and lung function (forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and peak expiratory flow rate (PEFR)) was measured in 391 healthy school age children with normal respiratory history and examination in a rural setting in West Bengal, India.

Results—Lung function normalised for sitting height and stature correlated significantly with indices of nutrition in both sexes. Adding weight as an independent variable to sitting height, new reference prediction equations for FEV1, FVC, and PEFR were calculated.

Conclusions—Nutritional differences influence qualitative aspects of lung development in childhood beyond simple isotropic lung growth. Prediction of lung function must take account of these differences if change as a result of disease is to be accurately measured. The identification and correction of relevant dietary deficiencies might help to improve lung function in children.

Keywords: lung development; lung function; nutrition; reference prediction equation

Lung function measured by spirometry (SLF) is an important surrogate measure in the assessment of childhood respiratory status in health and disease.1 In order to correct for differences in lung function resulting from growth, SLF in boys or girls is normalised for height.2 3 However, the postnatal lung demonstrates non-isotropic growth (whereby the size increment in alveolar dimensions is significantly greater in relation to airway dimensions) and human lung volume correlates directly with body weight.4 8 Recent animal models show that relatively severe prenatal and postnatal nutritional deficiency profoundly disturbs lung development, resulting in a major qualitative change beyond an effect on lung size.9 10 We hypothesised that similar effects in man lead to diminished lung function in the undernourished child, beyond a simple effect on isotropic growth. Such effects are less likely to manifest in healthy children in the developed world, most of whom are above the international baseline for nutritional status. Hence, we chose a remote rural setting in a developing country for our study.

Methods
The study took place in Kiarana (in the district of Medinipur, about 100 km southwest of Calcutta, West Bengal, India) in a completely isolated rural setting with no electricity or piped water, telecommunication, or tarred road/rail links. The inaccessibility of this village results in the total unavailability of standard formula milk, and the study population was breast fed during infancy (lactation failure is usually managed by wet-nursing). Maternal smoking is very rare, and is unlikely to be a confounder, because families spend almost all their waking hours (and frequently sleep) outdoors, except during the short winter period (late November to January). In summary, the questionnaire identified a study population consisting of children with no history of significant cough or sputum production, wheeze, dyspnoea disproportionate to exertion, or acute chest illness (in the six weeks before our study). Of the 810 questionnaires distributed, 623 were returned. One hundred and fifty one of the children were excluded after reviewing the returned questionnaires because of a history of respiratory illness, and the remaining 472 school children attended

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Number</th>
<th>%</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–5</td>
<td>8</td>
<td>3.3</td>
<td>3</td>
<td>2.1</td>
</tr>
<tr>
<td>6–8</td>
<td>13</td>
<td>5.2</td>
<td>8</td>
<td>5.5</td>
</tr>
<tr>
<td>9–11</td>
<td>61</td>
<td>24.6</td>
<td>51</td>
<td>35.5</td>
</tr>
<tr>
<td>12–14</td>
<td>123</td>
<td>49.6</td>
<td>61</td>
<td>42.1</td>
</tr>
<tr>
<td>15–17</td>
<td>43</td>
<td>17.3</td>
<td>22</td>
<td>15.2</td>
</tr>
</tbody>
</table>

Table 1 Age distribution of boys and girls in the study population
Table 2  Characteristics of the study population

<table>
<thead>
<tr>
<th></th>
<th>Boys (n = 246)</th>
<th>Girls (n = 145)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Centile</td>
</tr>
<tr>
<td>Age (years)</td>
<td>12.3 (2.5)</td>
<td>11.9 (2.5)</td>
</tr>
<tr>
<td>Stature (cm)</td>
<td>146.2 (14.7)</td>
<td>25 (2)</td>
</tr>
<tr>
<td>Sitting height (cm)</td>
<td>74.5 (7.4)</td>
<td>10 (1)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>32.4 (9.0)</td>
<td>20 (5)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>14.8 (1.6)</td>
<td>10 (1)</td>
</tr>
<tr>
<td>MUAC (cm)</td>
<td>19.5 (2.79)</td>
<td>&lt;= 50</td>
</tr>
<tr>
<td>SSCF (cm)</td>
<td>5.6 (1.7)</td>
<td>30 (6)</td>
</tr>
<tr>
<td>TSF (cm)</td>
<td>5.00 (1.31)</td>
<td>10 (3)</td>
</tr>
</tbody>
</table>

Centiles are compared against a normal, healthy British population. The reference MUAC data did not contain a centile distribution. BMI, body mass index; MUAC, mid-upper arm circumference; SSCF, subscapular skinfold thickness; TSF, triceps skinfold thickness.

Finally, 391 children (246 boys and 145 girls; see table 1 for age group distribution) were selected for the study, and their respective age, height (sitting and standing), indices of nutritional status (weight, mid-upper arm circumference, and subcapular and triceps skinfold thicknesses), and indices of lung function (forced vital capacity (FVC), forced expiratory volume in one second (FEV₁), using a portable spirometer, and peak expiratory flow rate (PEFR)) were measured for the study population by TJO, in accordance with recommended standards. Ethical approval and support was provided by Dr B G Panda, senior medical practitioner for the village and president of the school governing board.

The suitability of the lung function data (FEV₁, FVC, and PEFR) for log, transformation to stabilise variance was verified as described previously. The association between lung function and nutritional indicators independent of linear growth was analysed after adjustment for sitting height; these isotropic growth corrected variables are denoted with the subscript “c”, such as in ln(FEV₁c) and ln(weightc). This was achieved by calculating partial correlation coefficients of ln(lung function) and ln(nutrition) with sitting height as the controlled variable. Finally, prediction equations were derived from the multiple regression of each index of lung function on ln(sitting height) and ln(weight). Statistical analyses were performed on Statistical Package for Social Sciences (SPSS).

Results

Table 2 shows the nutritional status of the study population in relation to healthy British children. Reference data for nutritional status of the local population was not available for comparison. Table 3 shows the partial correlation coefficients of linear regression analyses between indices of lung function and nutrition, after correction for sitting height (similar results were obtained for stature normalisation, except the R values were lower). The scattergram in fig 1 (ln(FEV₁) vs ln(weight)) is an illustration of how the data summarised in table 3 was derived, and the subscript “c” denotes correction for sitting height. Weight is the only variable that shows significant correlation with all lung function parameters in both boys and girls, independent of isotropic growth. The multiple regression of ln(FEV₁) against ln(weight) and ln(sitting height) results in significant reduction (p < 0.001) in variability, when compared with ln(FEV₁) against ln(sitting height) or ln(stature) alone. Similar outcomes were obtained for ln(FVC) and ln(PEFR) in both boys and girls. However, the inclusion of additional variables did not lead to significant improvement in variability (p > 0.05). Thus, the derivation of prediction equations for SLF incorporated transformed data of weight and sitting height (table 3). Both residuals and antilog of the residuals exhibited consistent normal distributions without skewing; table 4 shows the means and standard deviations of the antilogged residuals, which are the ratios of actual to predicted lung function. The results were lower). The scattergram in fig 1 (ln(FEV₁) vs ln(weight)) is an illustration of how the data summarised in table 3 was derived, and the subscript “c” denotes correction for sitting height. Weight is the only variable that shows significant correlation with all lung function parameters in both boys and girls, independent of isotropic growth. The multiple regression of ln(FEV₁) against ln(weight) and ln(sitting height) results in significant reduction (p < 0.001) in variability, when compared with ln(FEV₁) against ln(sitting height) or ln(stature) alone. Similar outcomes were obtained for ln(FVC) and ln(PEFR) in both boys and girls. However, the inclusion of additional variables did not lead to significant improvement in variability (p > 0.05). Thus, the derivation of prediction equations for SLF incorporated transformed data of weight and sitting height (table 3). Both residuals and antilog of the residuals exhibited consistent normal distributions without skewing; table 4 shows the means and standard deviations of the antilogged residuals, which are the ratios of actual to predicted lung function. The results were lower). The scattergram in fig 1 (ln(FEV₁) vs ln(weight)) is an illustration of how the data summarised in table 3 was derived, and the subscript “c” denotes correction for sitting height. Weight is the only variable that shows significant correlation with all lung function parameters in both boys and girls, independent of isotropic growth. The multiple regression of ln(FEV₁) against ln(weight) and ln(sitting height) results in significant reduction (p < 0.001) in variability, when compared with ln(FEV₁) against ln(sitting height) or ln(stature) alone. Similar outcomes were obtained for ln(FVC) and ln(PEFR) in both boys and girls. However, the inclusion of additional variables did not lead to significant improvement in variability (p > 0.05). Thus, the derivation of prediction equations for SLF incorporated transformed data of weight and sitting height (table 3). Both residuals and antilog of the residuals exhibited consistent normal distributions without skewing; table 4 shows the means and standard deviations of the antilogged residuals, which are the ratios of actual to predicted lung function.

Table 3  Partial correlation coefficients of linear regression analyses between indices of lung function and nutrition after correction for sitting height (denoted by subscript “c”)

<table>
<thead>
<tr>
<th></th>
<th>Boys (n = 246)</th>
<th>Girls (n = 145)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ln(FEV₁c)</td>
<td>0.45*</td>
<td>0.45*</td>
</tr>
<tr>
<td>ln(BMIc)</td>
<td>0.25*</td>
<td>0.25*</td>
</tr>
<tr>
<td>ln(MUACc)</td>
<td>0.18*</td>
<td>0.21*</td>
</tr>
<tr>
<td>ln(SSCFc)</td>
<td>0.05†</td>
<td>0.15†</td>
</tr>
<tr>
<td>ln(TSFc)</td>
<td>0.05†</td>
<td>0.15†</td>
</tr>
</tbody>
</table>

*p < 0.05; †p > 0.05.

BMI, body mass index; MUAC, mid-upper arm circumference; SSCF, subscapular skinfold thickness; TSF, triceps skinfold thickness.
function values. This information can be used to calculate SLF standard deviation scores or centile positions for individual children.\textsuperscript{14}

Discussion

By demonstrating that lung function normalised for isotropic growth correlates strongly with indices of nutrition in both sexes, we present supportive data from human subjects consistent with the hypothesis, recently generated from animal models, that nutritional deficiency profoundly affects qualitative aspects of lung development in early life.\textsuperscript{7–10} Beyond simple changes in organ size. It follows that a reduced per capita GDP is associated with indices of malnutrition, with reduced daily calorie intake and with diminished lung function. Based on these observations, we think that it is important to

Table 4  Proposed multiple regression equations of ln(lung function) on ln(sitting height) and ln(weight) in undernourished children in a rural population of West Bengal, India

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Regression coefficients</th>
<th>Distribution of exp(residual)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ln (sitting height)</td>
<td>ln (weight)</td>
</tr>
<tr>
<td>Boys (n = 246)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ln (FEV\textsubscript{1})</td>
<td>1.080</td>
<td>0.657</td>
</tr>
<tr>
<td>ln (PCV)</td>
<td>1.000</td>
<td>0.669</td>
</tr>
<tr>
<td>ln (PEFR)</td>
<td>0.781</td>
<td>0.614</td>
</tr>
<tr>
<td>Girls (n = 145)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ln (FEV\textsubscript{1})</td>
<td>1.268</td>
<td>0.518</td>
</tr>
<tr>
<td>ln (PCV)</td>
<td>1.233</td>
<td>0.527</td>
</tr>
<tr>
<td>ln (PEFR)</td>
<td>1.545</td>
<td>0.338</td>
</tr>
</tbody>
</table>

*Actual lung function \( = \) predicted lung function.

Our findings demonstrate that in the undernourished population, nutritional status definitely influences lung function independent of isometric growth, and weight represents an important and convenient surrogate marker of nutritional state. Therefore, prediction of lung function in an undernourished child must take into account weight and sitting height, if change as a result of pulmonary disease is to be assessed accurately. The equations presented in this paper achieve this purpose.

SLF performance varies between apparently “healthy, well nourished” ethnic groups and, so far, the reported differences have been attributed to anthropological factors; consequently, reference predicted values and equations have been proposed for each group.\textsuperscript{21–22} To explore the hypothesis that other underlying factors could explain this variation, we have merged data from three studies and of our own to enable us to draw fig 2. It is interesting to note that SLF from Singaporean Chinese children are very similar to the data from white children in Britain, but at least 10% higher than their Malaysian Chinese counterparts at every point on the plot; in addition, lung function data from our study population of Indian children is considerably lower. Because Singaporean Chinese and Malaysian Chinese children are ethnically similar, the observed differences in SLF between races cannot be explained on the basis of ethnic anthropometric attributes alone. The per capita Gross Domestic Product (GDP) for Singapore, Great Britain, Malaysia, and India are: US$21\,493, US$18\,138, US$8763, and US$1280, respectively, and the corresponding average daily calorie intake for each person is 3198, 3149, 2774, and 2243. Thus, a lower per capita GDP is associated with reduced daily calorie intake and with diminished lung function. Based on these observations, we think that it is important to
examine the following hypotheses: (1) nutritional differences account for variations in SLF between different ethnic groups in the world, and (2) a predictive equation for lung function that accounts for nutritional status beyond isometric growth is universally valid (that is, for all ethnic groups). We hope that our work will facilitate future international collaboration aiming to address these important issues.

We thank Dr B Panda (Mobar, Calcutta), physician, philanthropist, and president of the governing board of Moyna Shikhyatan (the school) for the organisation of this project, and the participating children, parents, teachers, and administrators of Kiaranavillage for their cooperation. This work was sponsored by the Commonwealth Foundation, Chest, Heart and Stroke Foundation, British Medical and Dental Students’ Trust, and Pharmacia; TJO was a Rogers Fund scholar with the Medical Research Council (UK).

Appendix

The calculation of “percentage of predicted FEV1,” of a 12 year old boy with a stature of 146 cm, sitting height of 74.5 cm, weight of 27 kg, and FEV1 of 1.65 litres is as follows:

Predicted FEV1, from white clinical reference data (using stature alone) = \( \exp(2.83 \times \ln(146) - 13.43) = 2.25 \) litres

Percentage of predicted = \( \frac{1.65}{2.25} \times 100 = 73.3\% \)

Predicted FEV1, using the our study’s equation for stature = \( \exp(2.83 \times \ln(146) - 13.43) \times 1.93 \) litres

Percentage of predicted = \( \frac{1.65}{1.93} \times 100 = 85.5\% \)

Predicted FEV1 from our study’s proposed equation (for sitting height and weight) = \( \exp(1.08 \times \ln(74.5) + 0.657 \times \ln(27) - 6.261) \) = 1.75 litres

Percentage of predicted = \( \frac{1.65}{1.75} \times 100 = 94.3\% \)

Reference data from the British population was chosen for comparison because it is still widely used by clinicians in the UK and in India when assessing lung function in children. A previously published prediction equation of lung function in West Bengal children was derived from non-representative sedentary, middle class, urban children.24


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Arch Dis Child 1998 79: 18-21
doi: 10.1136/adc.79.1.18

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