The importance of using ethnically appropriate reference ranges for growth assessment in sickle cell disease

R A Patey, K P Sylvester, G F Rafferty, M Dick, A Greenough

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Height and weight were measured and body mass index (BMI) calculated in 56 sickle cell disease (SCD), 57 Caucasian (CC), and 63 African/Caribbean (AC) 3–9 year old children. The SCD children were taller, but had similar weight and BMI to the CC controls. The SCD group had lower weight and BMI than the AC controls. The AC controls were of greater height, weight, and BMI than CC controls. These data highlight the importance of using ethnically appropriate reference ranges.

Sickle cell disease (SCD) has been reported to impair prepubertal growth.1 Children with SCD studied in Jamaica and the USA were lighter and smaller than unaffected children. Comparison, however, was made with either ethnically mixed or Caucasian controls. African/Caribbean children have different body proportions1 and body fat mass2 from Caucasian children, and so the latter may be an inappropriate comparator group for children with SCD. Our aim was to determine whether UK born children with SCD had growth impairment and whether abnormalities were highlighted by comparison with children of similar ethnic origin.

SUBJECTS AND METHODS
Children aged 3–9 years with homozygous SCD were recruited from two specialist clinics. Controls were either HbAA siblings, or children of African/Caribbean (AC control) or Caucasian (CC control) origin from local schools. All children had been born in the UK. Standing and sitting height were measured using a wall mounted stadiometer (Holtain Ltd, Crymych, UK). Weight was measured using Avery scales (Avery Berkel, UK). Body mass index (BMI) was calculated as weight (kg) divided by the standing height (m)², and body proportion ratio as the sitting height divided by the standing height. Subischial leg length was derived by subtracting the sitting height from the standing height. The research ethics committees of both hospitals approved the study and parents gave informed written consent for their children to take part.

Statistical analysis
The data were normally distributed (Shapiro Wilk test); differences between groups were assessed for statistical significance using Student’s t test (Statview software, SAS Institute Inc, Cary, NC). Standard deviation scores (z scores) were calculated using the Child Growth Foundation software (Child Growth Foundation, London, UK).

RESULTS
A total of 176 children (56 SCD, 63 AC, 57 CC) were recruited. The mean (SD) ages (SCD: 6.3 (1.7) years; AC: 6.4 (1.5) years; CC: 6.6 (1.4) years) and proportions of males (50% SCD, 59% AC, 51% CC) were similar in the three groups. The children with SCD had greater height (p = 0.02) (fig 1) and lower body proportion ratios (p < 0.0001), but similar subischial leg length, weight, and BMI to the CC controls (table 1). The SCD children had similar height, subischial leg length, and body proportion ratios, but lower weight (p = 0.002) and BMI (p = 0.002) than the AC controls. The AC controls had greater height (p < 0.0001), subischial leg length (p = 0.007), weight (p < 0.0001), and BMI (p = 0.01), but lower body proportion ratios (p = 0.003) than the CC controls.

DISCUSSION
Monitoring of height, weight, and BMI is important in children with SCD as they are vulnerable to poor growth by their increased metabolic demands.3 Our data highlight that SCD children may apparently have “good” growth if compared to Caucasian children. The children with SCD had similar weight to the CC controls, but were significantly lighter than the AC controls. The AC and CC controls differed significantly with respect to both height and weight. In addition, the SCD children had similar BMI to the CC controls, but this was significantly lower than that of the AC controls. BMI is used as a measure of nutritional status1 and may be particularly useful...

Abbreviations: AC, African/Caribbean; BMI, body mass index; CC, Caucasian; SCD, sickle cell disease

Table 1 Height, weight, BMI, body proportion ratio, and subischial leg length according to sickle cell status and ethnic origin

<table>
<thead>
<tr>
<th></th>
<th>SCD</th>
<th>CC</th>
<th>AC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height z score</td>
<td>0.28 (1.16)</td>
<td>-0.18 (0.91)</td>
<td>0.59 (1.05)</td>
</tr>
<tr>
<td>Weight z score</td>
<td>0.32 (1.06)</td>
<td>0.11 (1.05)</td>
<td>0.93 (1.01)</td>
</tr>
<tr>
<td>BMI z score</td>
<td>0.23 (1.00)</td>
<td>0.30 (1.15)</td>
<td>0.82 (1.04)</td>
</tr>
<tr>
<td>Body proportion ratio</td>
<td>0.52 (0.02)</td>
<td>0.54 (0.02)</td>
<td>0.53 (0.03)</td>
</tr>
<tr>
<td>Subischial leg length (cm)</td>
<td>57.2 (6.9)</td>
<td>54.9 (5.3)</td>
<td>57.9 (6.3)</td>
</tr>
</tbody>
</table>

Results reported as mean (SD).
in children with chronic disease. Interpretation of BMI, however, is age dependent. In addition, children with a high BMI enter puberty at a younger age and children with SCD enter puberty later than controls. Thus, to minimise bias related to age, we analysed data only from children aged less than 10 years and highlight significant differences. We conclude, therefore, that if the true impact of SCD on growth is to be assessed, it is essential to make comparison with children of similar ethnic origin.

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**Figure 1** The relation of standing height and age in CC controls (closed circles) and AC controls (open circles). Individual data are shown. The solid line represents the regression line for CC controls (height = 6.41 age + 75.8, $r^2 = 0.81$, $p < 0.0001$). The dashed line represents the regression line for AC controls (height = 6.05 age + 81.9, $r^2 = 0.78$, $p < 0.0001$). (Not shown: regression line for SCD children: height = 5.73 age + 82.1, $r^2 = 0.76$, $p < 0.0001$).