Respiratory impairment in children with sickle cell anemia (SCA): differences between the UK and Nigeria

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Respiratory complications in sickle cell disease

- Acute chest syndrome
- Thromboembolisms
- Nocturnal oxyhaemoglobin desaturation
- Bronchial hyperreactivity and Asthma
- Pulmonary hypertension
- Sickle Cell Chronic Lung Disease (SCCLD)

Miller AC Am J Respir Crit Care Med. 2012
Greenough A. InTech 2016 DOI: 10.5772/64365
Longitudinal changes in lung function in subjects with SCA

FEV1 and TLC: 2-3% predicted/year decline at 8-18 years
(MacLean JE, AJRCCM 2008)

Restrictive abnormalities increase with age

Restrictive lung disease: Over 70% of HbSS adults (pre-Hydroxyurea)
(Klings ES, AJRCCM 2006)

Differences in liters between measured and predicted values across age for FEV1 (left) and TLC (right) in subjects with SCA aged 8-18 years. MacLean JE. Am J Respir Crit Care Med. 2008 Nov 15;178(10)
Respiratory impairment in children with SCA: differences between the UK and Nigeria

Rationale
Earlier onset of restrictive lung disease in subjects with SCA living in Africa?

Objectives:
To compare spirometry lung function in pediatric subjects with SCA from Nigeria and UK

To investigate risk factors for restrictive spirometry pattern
Subjects with Sickle Cell Anemia (SCA) (SS, Sβ⁰) of black African origin, aged 6-18, years at steady state

101 subjects
(126 before exclusions)
Evelina London Children’s Hospital, UK

154 subjects
(186 before exclusions)
Barau Dikko Teaching Hospital Kaduna, Nigeria

341 healthy controls in Nigeria

MEDICAL HISTORY
Current asthma
Atopy
Fatigability
Age at diagnosis
Hydroxyurea yes/no
N. Pain crises in the last year
Previous ACS
Previous stroke

ANTHROPOMETRY

SPIROMETRY
Easy on-PC
(low quality tests excluded)

CLINICAL EVALUATION
SpO2
Tonsillar Hypertrophy
Splenomegaly (in cm)

FULL BLOOD CELL COUNT
(not if Hydroxyurea)

Spirometry patterns classification

Spirometry z-scores: GLI2012-black equation
(Quanjer PH, ERJ 2012)

Lower Limit of Normal (LLN) = -1.64 z-score

The PI performed 92% of spirometry tests
Frequency of clinical variables potentially related to lung function in children with SCA from UK and Nigeria

<table>
<thead>
<tr>
<th>Variable</th>
<th>SCA UK (N. 101)</th>
<th>SCA NIGERIA (N. 154)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current hydroxyurea treatment</td>
<td>47.5%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Current asthma</td>
<td>21.7%</td>
<td>6.7%</td>
</tr>
<tr>
<td>X-ray confirmed acute chest syndrome</td>
<td>34%</td>
<td>16.3%</td>
</tr>
<tr>
<td>At least 3 pain crises in the past year</td>
<td>24.7%</td>
<td>49.3%</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>2.9%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Chronic transfusion regime</td>
<td>3.9%</td>
<td>1.2%</td>
</tr>
<tr>
<td>SpO2 at baseline &lt;96%</td>
<td>13.4%</td>
<td>39%</td>
</tr>
<tr>
<td>White blood cell count &gt; 15.000/mmic</td>
<td>15.9% (7/44)</td>
<td>21.5% (34/125)</td>
</tr>
<tr>
<td>Hemoglobin level &lt; 7.5 g/dL</td>
<td>18.1% (8/44)</td>
<td>31.2% (39/125)</td>
</tr>
<tr>
<td>Platelets count &gt; 450.000/mmic</td>
<td>18.1% (8/44)</td>
<td>28.8% (36/125)</td>
</tr>
</tbody>
</table>

**Current asthma:** either doctor-diagnosis or asthma medication in the past 12 months, with or without current symptoms/wheeze (Lum S. et al Eur Respir J. 2015; 46(6): 1662–1671)

**Acute chest syndrome:** medical record indicating new pulmonary infiltrate on chest x-ray + fever, chest pain, and/or respiratory symptoms.
RESULTS

Anthropometry and spirometry z-scores in subjects with sickle cell anemia (SCA) from the UK and Nigeria

<table>
<thead>
<tr>
<th></th>
<th>SCA UK</th>
<th>SCA NIGERIA</th>
<th>Mean diff. UK-NIG (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%male)</td>
<td>101 (51%)</td>
<td>154 (54%)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>11.8 (2.7)</td>
<td>11.4 (3.2)</td>
<td>0.4 (-0.37; 1.1)</td>
</tr>
<tr>
<td>Height z-score</td>
<td>0.30 (1.24)</td>
<td>-1.77 (1.21)</td>
<td>2.00 (1.76; 2.3)</td>
</tr>
<tr>
<td>BMI z-score</td>
<td>0.19 (1.25)</td>
<td>-1.38 (1.34)</td>
<td>1.57 (1.24; 1.91)</td>
</tr>
<tr>
<td>FEV$_1$ z-score</td>
<td>-1.00 (1.04)</td>
<td>-1.38 (0.96)</td>
<td>0.38 (0.13; 0.63)</td>
</tr>
<tr>
<td>FVC z-score</td>
<td>-0.71 (1.04)</td>
<td>-1.21 (0.96)</td>
<td>0.51 (0.25; 0.75)</td>
</tr>
<tr>
<td>FEV1/FVC z-score</td>
<td>-0.68 (0.98)</td>
<td>-0.47 (0.98)</td>
<td>-0.20 (-0.43; 0.02)</td>
</tr>
</tbody>
</table>

Results expressed as mean (SD), unless otherwise specified. Spirometry z-scores based on GLI-2012 black- equations (Quanjer PH, ERJ2012). Anthropometry z-scores based on WHO2007 standards.

The GLI-black equation fitted well 341 Nigerian controls [mean(SD) z-score -0.34(1) for FEV$_1$ and -0.28(0.97) for FVC]
Spirometry patterns in subjects with SCA from Nigeria and the UK

The dashed lines represent -1.64 z-scores (5° PC)
Trends of spirometry z-scores with age in pediatric subjects with SCA from Nigeria (A, B, C) and the UK (D, E, F)

The trend lines are obtained by simple linear regression

Logistic regression: unit increase of age (year) associated with restrictive/mixed spirometry pattern [OR 1.2 (1.08-1.33); p<0.001]
**Strengths**

Consistent methodology

**Limitations**

Prospective data are missing

Incomplete lung function assessment (no TLC)

Reliability of medical history information in Nigerian patients?
Conclusions

Children and adolescents with SCA from Nigeria: lower dynamic lung volumes and higher prevalence of restrictive spirometry pattern

The deterioration of lung function seems to be faster in subjects with SCA living in Africa

Inequalities in health care provisions might account for some of differences