Nocturnal haemoglobin oxygen desaturation in urban and rural East African paediatric cohorts with and without sickle cell anaemia: a cross-sectional study

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ABSTRACT
Low haemoglobin oxygen saturation (SpO2) predicts complications in children with sickle cell anaemia (SCA) in the North but there are few data from Africa, where the majority of the patients reside. We measured daytime and overnight SpO2 in children with SCA in routine follow-up clinic, and controls without symptoms of SCA, comparing rural (Kilifi, Kenya) and urban (Dar-es-Salaam, Tanzania) cohorts. Daytime SpO2 was lower in 65 Tanzanian children with SCA (TS; median 97 (IQR 94–100)%); p<0.0001) than in 113 Kenyan children with SCA (KS; 99 (98–100)%). Controls (TC; median 98 (97–100)% in Tanzania and 100 (98–100)% in Kenya) had higher daytime and mean and minimum overnight SpO2 compared with rural Kenyan children with SCA and 19 TC who returned for overnight oximetry, mean (KS 99.0 (96.7–99.8)%; TS 97.9 (95.4–99.3)%; TC 98.4 (97.5–99.1)%; p=0.01) and minimum nocturnal SpO2 (92 (86–95)%; 87 (78.5–91%); 90 (83.5–93)% p=0.0001) were lower. The difference between children with SCA persisted after adjustment for haemoglobin (p=0.004). Urban children with SCA and without SCA, experience greater exposure to low daytime and night-time SpO2 compared with rural Kenyan children with SCA. Possible explanations include differences in the prevalence of obstructive sleep apnoea or asthma, alterations in the oxyhaemoglobin desaturation curve or cardiovascular compromise, for example, to shunting at atrial or pulmonary level secondary to increased pulmonary artery pressure. The fact that non-SCA siblings in the urban area are also affected suggests that environmental exposures, for example, air pollution, nutrition or physical exercise, may play a role. Further studies should determine aetiology and clinical relevance for the SCA phenotype in children resident in Africa.

INTRODUCTION
Homozygous sickle cell anaemia (SCA) is one of the most common monogenetic conditions in the world, with more than 70% of sufferers living in sub-Saharan Africa. Approximately 98% of oxygen carried in the blood is transported by haemoglobin with the remainder dissolved in plasma. The dysfunctional haemoglobin and right-shifted oxyhaemoglobin dissociation curve in SCA affect haemoglobin oxygen saturation, which can be measured by pulse oximetry (SpO2). Children spend half their lives asleep; sleep is associated with a natural fall in SpO2 as minute ventilation falls. Daytime and night-time (episodic and continuous) desaturation is common in Western populations with SCA and predicts complications.

In a Jamaican study, rural SCA populations achieved higher physical and mental health scores, with fewer limitations in daily living activities and better quality of life. In non-SCA adults enrolled in the Sleep Heart health study, sleep-disordered breathing and nocturnal hypoxaemia correlated with short-term changes in particle traffic pollutant level. Even though the major burden of SCA remains in sub-Saharan Africa, where air quality in cities is often poor (http://www.unep.org/transport/...
of sleep-disordered breathing. Non-parametric statistics (median and IQR as descriptives; Kruskal–Wallis test for comparison between groups) are reported for non-normally distributed variables. A two-tailed p value of p<0.05 was considered to be significant. Scheffe’s test was used for post hoc testing to compare means of the Kenyan and Tanzanian children with SCA and the controls.

**METHODS**  

The study was approved by the Kenya National Ethical committee (SCC 688) and the Muhimbili University College of Health Sciences research committee (MU/RP/AECNoI.XII/77). Children were recruited from confirmed HbSS, but otherwise unselected, cohorts of patients attending outpatient clinics in rural Kenya (Kilifi) in 2004 and urban Tanzania (Dar-es-Salaam) in 2009. In Tanzania, household controls without symptoms of SCA were also recruited. Blood samples and pulse oximetry were obtained >12 weeks post-transfusion, and >12 weeks following acute illness. Resting daytime and overnight oximetry were obtained >12 weeks post-transfusion, and >12 weeks following acute illness. Raising daytime and overnight recordings of SpO2 were recorded by pulse oximetry (Masimo Irvine, California, USA) using a 2 s averaging time continuously during sleep. The data were analysed using Download 2001 software (Stowood Scientific, UK). Any residual movement artefact was excluded manually. We examined the overnight data for mean SpO2, and percentage of time spent with SpO2<90%.

**Data entry and analysis**  

Analyses were performed using the statistical software package SPSS V21.0. χ2 was used to compare prevalence of symptoms with SCA and urban children with and without SCA.

<p>| Table 1 Differences between rural children with SCA and urban children with and without SCA |
|----------------------------------|------------------|------------------|------------------|------------------|------------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>Urban Tanzanian Non-SCA Controls (n=19 [20]) Median (IQR)</th>
<th>Urban Tanzanian SCA Controls (n=54 [65]) Median (IQR)</th>
<th>Rural Kenyan SCA Controls (n=95 [113]) Median (IQR)</th>
<th>P* for comparison between groups</th>
<th>Pt for comparison with Tanzanian patients</th>
<th>Pt for comparison with Kenyan patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>8.0 (4.0–10.4)</td>
<td>7.3 (5.1–10.6)</td>
<td>6.4 (3.7–10.1)</td>
<td>0.216</td>
<td>0.4</td>
<td>0.059</td>
</tr>
<tr>
<td><strong>BMI z-scores</strong></td>
<td>−0.11 (−0.97 to 0.66)</td>
<td>−0.98 (−1.89 to 0.052)</td>
<td>−1.3 (−2.1 to −0.6)</td>
<td>0.005</td>
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<tr>
<td><strong>Haemoglobin (g/dL)</strong></td>
<td>7.1 (6.6–7.8)</td>
<td>7.1 (6.6–7.8)</td>
<td>7.5 (6.8–8.2)</td>
<td>0.076</td>
<td></td>
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</tr>
<tr>
<td><strong>Median daytime haemoglobin</strong></td>
<td>100 (98–100)</td>
<td>97 (94.8–99.1)</td>
<td>99 (98.0–100)</td>
<td>0.001</td>
<td>0.018</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Oxygen saturation (%)</strong></td>
<td>98.6 (97.5–99.1)</td>
<td>97.7 (95.1–99.3)</td>
<td>99.0 (96.7–99.8)</td>
<td></td>
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<tr>
<td><strong>Median overnight haemoglobin</strong></td>
<td>90 (83.5–93)</td>
<td>87 (78.5–91)</td>
<td>92 (86–95)</td>
<td>0.001</td>
<td>0.2</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>Oxygen saturation (%)</strong></td>
<td>88.0 (81.9–97.5)</td>
<td>93.3 (85.2–102.9)</td>
<td>90.2 (79.1–102.1)</td>
<td>0.3</td>
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<td></td>
</tr>
</tbody>
</table>

Values in square brackets for whole cohort recruited.

*Kruskal–Wallis test.

†Post hoc comparison using Scheffe’s test.

BMI, body mass index; SCA, sickle cell anaemia.
attended for overnight pulse oximetry compared with those
who did not in either the Kenyan or the Tanzanian SCA cohort ($\chi^2$, $p=0.6$ and $0.7$, respectively). Overnight mean SpO$_2$ was sig-
ificantly lower in urban Tanzanian children with SCA com-
pared with rural Kenyan children with SCA (table 1), including
after adjustment for haemoglobin ($p=0.004$), and was similar to
Tanzanian controls. Similarly, minimum SpO$_2$ was lower in
urban Tanzanian children with SCA than in rural Kenyan chil-
dren with SCA (table 1).

**DISCUSSION**

Urban children with SCA in Tanzania experience greater expo-
sure to intermittent and continuous nocturnal haemoglobin
oxygen desaturation in comparison with rural Kenyan children
with SCA despite similar haemoglobin levels and both living at
sea level. This may indicate that these two otherwise similar
East African coastal populations may follow a different clinical
course of disease, perhaps related to genetic or environmental
factors such as nutrition or pollution.

The aetiology of the differences in haemoglobin oxygen satu-
rations is not clear. The $\alpha$-thalassaemia 3.7 deletion is asso-
ciated with daytime and nocturnal SpO$_2$ in the Tanzanian SCA
population, but this is unlikely to explain the difference as the
prevalence is very similar in the two SCA populations
(Williams-TN, personal communication). Obstructive sleep
apnoea is a possible explanation. The lack of difference in
symptom prevalence and absence of overweight children in the
samples provide no positive evidence and central apnoeas are
also relatively common in SCA; investigation of their relative
importance with polysomnography in this setting would require
considerable funding. Asthma and previous acute chest syn-
drome might play a role, but are rare in African settings and
were not diagnosed in our patients. A vascular effect of air pol-
lution, for example, increased pulmonary artery pressures with
returning did not have more clinical evidence for sleep-
disordered breathing than those who did not.

In summary, urban Tanzanian children, with and without
SCA, experience greater exposure to low daytime and night-
time SpO$_2$ compared with rural Kenyan children with SCA. The
aetiology of the desaturation is uncertain but differences in air
quality might be a factor. The clinical relevance in an African
setting requires further investigation.

**Contributors** FJK, SEC, CRN and JM designed the study with VSL and TE. VSL
undertook data collection in Dar-es-Salaam, Tanzania together with DS, SEC and
JM. TE (nee Ajala-Agbo) undertook data collection in Kilifi, Kenya together with AK.
VSL, TE, SEC, FJK and CMH analysed the data. VSL and TE wrote the first draft of
the paper which was edited by DS, AK, CRN, SEC, JM, FJK and CMH. All authors
read and approved the final version for submission.

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**Competing interests** None declared.

**Ethics approval** Muhimbili University College of Health Sciences research
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**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data sharing statement** We are willing to share our unpublished data on request
after appropriate consultation with the principal investigators and the Wellcome
Trust.

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