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DOI:

[10.1111/j.1365-2141.2010.08272.x](https://doi.org/10.1111/j.1365-2141.2010.08272.x)

Document Version

Publisher's PDF, also known as Version of record

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Citation for published version (APA):

Bartram, J. L., Thein, S. L., Gardner, K., Egberongbe, Y., D'Silva, P., Height, S., Dick, M., O'Driscoll, S., & Rees, D. C. (2010). Outcome of children with sickle cell disease admitted to intensive care: a single institution experience. *British Journal of Haematology*, 150(5), 614-617. <https://doi.org/10.1111/j.1365-2141.2010.08272.x>

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Outcome of children with sickle cell disease admitted to intensive care – a single institution experience

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Received 5 March 2010; accepted for publication 28 April 2010

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Sickle cell disease (SCD) is one of the commonest severe genetic disorders in England, affecting over 1 in 2000 live births (Streetly *et al*, 2009). Children with SCD can become critically ill requiring referral to intensive care units. The most common causes of death in children with SCD are acute, and include infection, acute chest syndrome (ACS) and stroke (Leikin *et al*, 1989; Mancini *et al*, 2003). To our knowledge, there are no published data on the outcome of children with SCD admitted to paediatric intensive care (PICU).

Population based data on the epidemiology of all children admitted to PICU in the UK are reported to the Paediatric Intensive Care Audit Network (PICANet) (Universities of Leeds and Leicester 2008), established in 2002. However, there is little published experience about children with SCD admitted to PICU. There have been several studies reporting outcomes for children with other conditions admitted to PICU, with mortality rates of 44% and 38% for children with bone marrow transplants (Jacobe *et al*, 2003) and HIV

Summary

We retrospectively audited children with sickle cell disease (SCD) admitted to paediatric intensive care (PICU) at King's College Hospital between January 2000 and December 2008. Forty-six children with SCD were admitted, on 49 separate occasions. Ages ranged from 4 months to 15 years (median 7.6 years). Three children died in PICU, however two presented to hospital in cardiorespiratory arrest; overall mortality was 6%. The most common reason for admission was acute chest syndrome (43%). 88% of admissions required blood transfusion, of which 74% had exchange blood transfusions. The mortality among children with SCD admitted to PICU is low.

Keywords: Sickle cell disease, children, paediatric intensive care unit.

(Cooper *et al*, 2004), respectively. We audited the admission of children with SCD admitted to PICU at King's College Hospital (KCH) over 9 years, to define the reasons for admission and outcome for this group, and to make comparisons with all children admitted to PICU.

Methods

We retrospectively audited all children with SCD admitted to our PICU between 1st January 2000 and 31st December 2008. KCH looks after about 400 children with SCD. We included all patients admitted to PICU with SCD from birth to 16 years. Information collected included presentation, treatment and outcome; outcome data included reason for and length of admission, the need for respiratory and inotropic support, use of blood transfusion and antibiotics, time to hospital discharge and mortality. Data were collected from PICU admission books, patient case notes and electronic records.

Table I. Demographics of patients admitted to the intensive care unit ($n = 46$).

Genotype	HbSS: 43, HbSC: 3
Median age, years (range)	7.6 (0.4–15.7)
Hydroxycarbamide	2 (4%)
History of previous ACS	10 (22%)
Prescribed penicillin prophylaxis	46 (100%)
History of previous CVA	5 (11%)
Receiving regular blood transfusions	1 (2%)
Previous admission to PICU	5 (11%)
Transferred from outside hospital	13 (28%)

ACS, acute chest syndrome; CVA, cerebrovascular accident; PICU, paediatric intensive care unit.

Results

Patient demographics

Forty-six children with SCD (3 HbSC, 46 HbSS) were admitted to PICU 49 times, accounting for 2% PICU admissions over this 9-year period (Table I). Approximately 1000 children with SCD live in the area served by KCH PICU, giving an admission rate of approximately 0.5/100 patient years.

Reasons for admission

The most frequent reasons for admission to PICU were ACS (43%, $n = 21$) and stroke (24%, $n = 12$), including three subarachnoid haemorrhages (SAH) (Table II). Four (8%) elective postoperative admission were planned due to a history of complications. Acute surgical admissions comprised two patients with acute hydrocephalus (one immediately post-stent and coil embolization for cerebral aneurysm; one with a brain tumour) and one patient with slipped upper femoral epiphysis for central venous access and urgent exchange transfusion pre-operatively. One patient was admitted with upper airway obstruction due to massively enlarged tonsils. The patients with other neurological problems include two with isolated seizures, one with pneumococcal meningitis, and one with cerebrovascular disease for urgent exchange transfusion. Two patients with acute sepsis presented to hospital in cardiac arrest and rapidly developed multi-organ failure.

Length of admission pre admission to PICU

Twenty-eight percent of patients ($n = 13$) were admitted directly from the Emergency department to PICU. The majority of patients were admitted to normal hospital wards for at least 24 h (with 22% being admitted for more than 4 d) before requiring admission to PICU. The majority of patients with cerebrovascular accident (CVA) presented with acute neurological symptoms and were transferred directly to PICU on day 0, whereas typically patients with ACS were in hospital for at least 24 h before being transferred to PICU.

Table II. Reason for admission to paediatric intensive care, need for ventilatory support, and outcome.

Reason for admission	No. (%) of total admissions ($n = 49$)	Ventilatory support (% of Admission Group)	Survived to PICU discharge (% of Admission Group)
ACS	21 (43)	6 (29)	21 (100)
CVA	12 (24)	2 (17)	11 (92)
Overwhelming sepsis	2 (4)	2 (100)	0 (0)
Other neurological	4 (8)	2 (50)	3 (75)
Elective post operative	4 (8)	1 (25)	4 (100)
Acute surgical	3 (6)	2 (67)	2 (100)
Upper airways obstruction	1 (2)	1 (100)	1 (100)
Pain control	1 (2)	0 (0)	1 (100)
Aplasia unknown cause	1 (2)	1 (100)	1 (100)
Total	49 (100)	17 (35)	46 (94)

PICU, paediatric intensive care unit; ACS, acute chest syndrome; CVA, cerebrovascular accident.

Respiratory support

Thirty-five percent of patients ($n = 17$) required respiratory support, one following CVA, two with multiorgan failure and 14 with ACS. The median length of respiratory support (including non-invasive ventilation) was 2 d (range 1–18 d). High frequency oscillatory ventilation (HFOV) was used in seven admissions (14%). Five of these admissions were for ACS and two had multi-organ failure secondary to sepsis. Five (10%) were treated with inhaled nitric oxide (iNO); all had ACS and survived to at least 6 months follow-up (Table II).

Inotropic support

Sixteen percent of patients ($n = 8$) required inotropic support: three ACS, two multiorgan failure, one cerebral aneurysm, one pneumococcal meningitis, one transient aplasia. Three of these died (both multiorgan failure patients and the child with the cerebral aneurysm). The five remaining patients survived to at least 6 months follow-up.

Blood transfusion

Eighty-eight percent of patients ($n = 43$) required blood transfusion on PICU, of which 74% ($n = 32$) had exchange transfusions. Exchange blood transfusion was most commonly performed for ACS (35%, $n = 17$), which accounted for 80% of transfusions in those patients with ACS; the remaining patients with ACS all had simple transfusion. Ten out of the 12 patients with CVA had exchange transfusion, and the other two were already on a transfusion programme, with satisfactory parameters at the time of admission.

Antibiotics and lines

Eighty-two percent of patients ($n = 40$) were prescribed antibiotics; all had an intravenous cephalosporins. 61%, ($n = 30$) also had a macrolide. All admissions had peripheral venous access. 30% ($n = 15$) had central venous catheters and 71% ($n = 35$) had arterial lines inserted.

Length of stay, treatment related morbidity and discharge outcome

The median length of stay was 1 d (range 1–18 d). There was one central line-associated thromboembolism, one delayed transfusion reaction and one death was due to complications post neurosurgical procedure. Three patients (6%) died on PICU, although two of these had been transferred straight from the Accident and Emergency department, having presented in cardiorespiratory arrest. Median time to discharge from hospital after discharge from PICU was 4 d (range 0–95 d). There were no further deaths before discharge from hospital; one death occurred 4 months post-discharge due to complication of a brain tumour, unrelated to SCD.

Comparison with PICANet data

Comparison of our data with that from all PICU admissions in the UK (2005–2007) showed that children with SCD were more significantly less likely to require ventilatory or inotropic support, and had a similar mortality rate (Table III).

Discussion

This is the first study to characterize the use of PICU by children with SCD. ACS and CVA were the commonest reasons for admission. Three patients died during their admission to PICU. One death was post-stent and coil embolization for cerebral aneurysm causing a SAH, a proce-

dures that has a recognised mortality rate (Kurre & Berkefeld, 2008). The other two deaths were a result of multi-organ failure secondary to presumed sepsis. Both of these children were less than 2.5 years old, presented directly to the emergency unit in cardiorespiratory arrest, and died within 24 h of admission. An earlier study, looking at out-of-hospital paediatric cardiac arrest found that survival to hospital discharge in children requiring cardiopulmonary resuscitation in the emergency department was low, at 15% (Schindler *et al*, 1996).

ACS was the most common reason for admission. There were no deaths in this group. The outcome for ventilated patients with ACS was very good, even those requiring maximal support with HFOV and iNO. Our study confirms previous reports that ACS is the leading cause of admission to PICU in SCD (Platt *et al*, 1994). CVA was the second commonest reason for admission to PICU. All CVA patients received blood transfusion, with 83% having exchange transfusions (Vichinsky *et al*, 2000); those not exchanged were already on a transfusion programme with low HbS levels. In young children, exchange transfusion is particularly difficult and is often facilitated by the use of an arterial line for blood removal, which necessitates admission to PICU. PICUs are also useful in the care of children with acute neurological symptoms in that close observation and neuroprotection are easier than on a general ward.

One child presented with severe hypovolaemic shock secondary to acute anaemia, with a haemoglobin of 17 g/l; the reticulocyte count was low initially but repeated Parvovirus B19 serology and nucleic acid testing were negative. The patient required full PICU support but made a good recovery. Only three children were admitted with septicaemia, and in only one case was pneumococcus isolated. Other studies in the United Kingdom have also observed lower than expected rates of pneumococcal sepsis in patients with SCD (Telfer *et al*, 2007), suggesting the benefit of prophylactic antibiotics and vaccination.

Fifteen (33%) of the patients admitted to PICU had a history of either ACS or CVA. Thirty-eight percent of patients admitted to PICU with ACS had a previous history of ACS and 63% of those previously required admission to PICU. Three patients with CVA had previously had CVA; two of these patients were not on a regular transfusion programme as secondary stroke prevention; following prolonged discussions and counselling, one family had decided to stop regular transfusions and the other had started hydroxycarbamide. This gives further support to the use of transfusion to prevent recurrent stroke and demonstrates that discontinuing transfusion increases the risk of further strokes (Pegelow *et al*, 1995; Ohene-Frempong *et al*, 1998).

Mortality in the SCD patients was similar to that for all patients admitted to PICU (Table III), although children with SCD were significantly less likely to need ventilatory or inotropic support. The most common reasons for admission in the PICANet data were: ventricular septal defect 8%, respiratory failure 6.5%, status epilepticus 5.5%, sepsis 4.8%,

Table III. Comparison of our experience and with PICANet data. *P*-values calculated using Chi-squared test with Yates' correction.

	PICANet 2005–2007 $n = 43841$	SCD cohort	
		KCH 2000–2008 $n = 49$	<i>P</i>
% needing non-invasive ventilation	13%	2%	0.039
% needing invasive ventilation	66%	33%	<0.0001
% needing inotropes	31%	16%	0.039
Mortality	5%	6%	0.97
Length of stay (d)	32% stayed 1–3 d	Median 1; mean 2	

PICANet, paediatric intensive care audit network; SCD, sickle cell disease; KCH, King's College Hospital NHS Foundation trust.

pneumonia 4.1%, asthma 2% and intracranial tumour 2%. Although the reasons for admission were different, length of stay was similar. Limited inferences can be made from our audit because it is a single-centre, retrospective study involving relatively small numbers, although outcome appears to be equivalent to unselected PICU admissions.

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