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Outcome of adults with sickle cell disease admitted to critical care – Experience of a single institution in the UK

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4 **institution in the UK**
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Summary

Patients with sickle cell disease (SCD) are perceived to have a high mortality when admitted to critical care. We performed a retrospective analysis of all adult sickle admissions to Critical Care Unit (CCU) at a single centre over an eight year period between 1 January 2000 to 31 December 2007. Thirty eight patients (14 male) were admitted 46 times to CCU; the commonest reasons for admission were acute chest syndrome (14, 30%), multi-organ failure (8, 17%) and planned post-elective surgery (7, 15%). CCU mortality for patients with SCD was 19.6%, comparable to a CCU-wide mortality of 17.6% during the study period in the same institution. Re-admission to critical care **was high (16% over the eight year period) but** did not increase mortality risk.

Key words: intensive care, critical care, sickle cell disease

Introduction

Sickle cell disease (SCD) is one of the commonest reasons for admission to hospital in the UK and has the highest rate for multiple admissions for individual patients (London Health Observatory - Fellows, 2005 July ; London Health Observatory - Hofman, 2006 March). Acute pain is likely to account for the majority of these admissions (Perronne *et al*, 2002; Platt *et al*, 1994), and can precipitate acute organ failure requiring support in a critical care unit (CCU). Sickle patients are also vulnerable to CCU admission because they often have co-existing morbidities related to end organ damage (Powars *et al*, 2005) and increased susceptibility to infection (Booth *et al*, 2009).

The recent National Confidential Enquiry into Patient Outcome and Death (NCEPOD in 2008) (NCEPOD, 2008) recommended that the cause of death in sickle disease patients should be better evaluated. King's College Hospital (KCH), UK, has one of the largest cohorts of adult patients with SCD in the UK. We present our experience in the management and outcome of adults admitted to CCU at KCH over an eight year period.

Materials and Methods

This retrospective study included all adult patients (≥ 16 yrs) with SCD admitted to KCH adult medical and surgical critical care units between 1 January 2000 and 31 December 2007. Data were extracted from the KCH critical care database, KCH sickle database (total of 500 patients), KCH electronic patient record (EPR) system and patient case notes. Level 2 critical care is provided in the high dependency unit (HDU), and is typically where invasive ventilation is *not* required, contrasting with level 3 care in "ICU".

Data were extracted on organ failure and organ support as defined below:

- 1) Cardiovascular failure: bradycardia (HR<54/min), mean arterial BP < 49mmHg, Ventricular Fibrillation /Ventricular Tachycardia, or pH < 7.24 with PaCO₂<49mmHg.
- 2) Neurological failure: best GCS \leq 6/15.
- 3) Respiratory failure: RR<5, RR>49, PaCO₂>50mmHg, AaDO₂>350mmHg or ventilator dependence > 3 days.
- 4) Renal failure (*not for patients with underlying chronic renal failure prior to critical care admission*): urine < 479ml/24 hours, Ur>214mg/100ml, Cr>3.5mg/100ml.
- 5) Haematological failure: WBC<1000mm³,

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2 PLTS<20mm³, haematocrit < 30% (haematocrit of <30% is not applicable for patients in chronic renal failure or
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4 patients with SCD).
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9 Five methods of organ support were identified in critical care – inotropes, ventilation (both mechanical
10 ventilation and non-invasive positive pressure ventilation), haemofiltration, blood transfusions and antibiotics.
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12 For binary variables, mortality was assessed by odds ratios for mortality, **with 95% confidence intervals**. For
13
14 continuous / ordinal variables, Student's t-test was performed by splitting the data by outcome.
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17

18 19 **Results and Discussion**

20
21 Thirty eight patients with SCD accounted for 46 of the 10,465 admissions to KCH's adult CCU unit giving KCH
22
23 SCD patients an ~8% risk of at least one CCU admission in this 8 year period. The group comprised 24 females
24
25 and 14 males, of which 32 had HbSS, and 6, HbSC. Median age at admission to critical care was 31 years (range
26
27 17 to 59 years) for SCD patients compared to 58 years (range 10 to 101 years) for all CCU admissions.

28
29 Of the 46 sickle admissions, 16 were to the HDU which included all the six elective post-surgical cases.

30
31 Common co-morbidities included chronic renal failure (with end stage renal failure in four patients), diabetes
32
33 mellitus, hypertension, chronic pulmonary impairment, hepatic dysfunction and stroke. **None of the patients**
34
35 **were on hydroxycarbamide.**
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41 The reasons for admission to CCU were grouped under four categories: medical (directly related to SCD), acute
42
43 surgical, trauma and planned post-operative (Table 1). The most frequent 'medical' reason for admission to CCU
44
45 was acute chest syndrome (ACS) (n=14, 30%); in two cases ACS occurred as a complication following fractured
46
47 neck of femur, and splenic sequestration. The eight 'multi-organ failure' (MOF) cases were triggered variously
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49 by ACS, sepsis, acute renal failure, and cardiac arrest. The five neurological reasons for admissions included two
50
51 intra-cerebral haemorrhages, one case each of ischaemic stroke, seizures in a known epileptic, and a myasthenic
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53 crisis in a patient known to have myasthenia gravis. The one patient with a "renal" cause for admission, was a
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55 patient in end stage renal failure (secondary to sickle nephropathy) and with a transplanted kidney. The four
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2 other cases comprised a case each of bacterial endocarditis, gastro-intestinal bleed secondary to use of non-
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4 steroidal anti-inflammatory agents , acute left ventricular failure, and overwhelming sepsis.
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8 The five “acute surgical” reasons for CCU admission included one each of pyonephrosis, small bowel
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10 obstruction, Caesarean-section in a pregnancy complicated by acute sickle pain, vasculitis, and hip abscess. All
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12 patients survived the acute surgical CCU admission. All six planned post-elective surgical admissions (three
13
14 laparoscopic cholecystectomies, one hysterectomy, one total hip replacement and one adrenalectomy) stayed in
15
16 level 2 care overnight, and were discharged from hospital. Three patients (2 HbSC, 1 HbSS) were admitted to
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18 critical care following acute trauma which included a gunshot wound, a road traffic accident, and a violent head
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20 injury; the latter died **in the CCU**.
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26 Of the 46 admissions, nine died in critical care with a mortality of 19.6%, compared to an overall mortality of
27
28 17.6% for all adult admissions to KCH critical care during this period. The nine patients included seven HbSS
29
30 and two HbSC patients with an average age of 33 years (see Table 2). Apart from the one trauma admission
31
32 (acute head injury in HbSS patient), the eight non-survivors were all admitted for medical reasons. The overall
33
34 mortality for sickle patients rose to 21.7% at hospital discharge (one further death during the hospital admission),
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36 and 28.3% at 1-year follow up (3 further deaths). **No follow-up data are available for overall CCU admission.**
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41 Six patients had readmissions to critical care in the eight year study period; five had two admission, and one,
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43 four admissions, giving patients with previous CCU admission a relative risk of 2 for a subsequent admission to
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45 CCU in the eight year study period. The readmissions included, three MOF and one ACS for the patient who had
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47 four admissions.
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51 We calculated risk factors for mortality excluding those admissions due to trauma and the planned post surgical
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53 admissions (Table 3). Twenty-nine patients were admitted 37 times to critical care for medical or acute surgical
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55 reasons. Of the 29 patients, eight died while in critical care, one during his second admission. Risk factors for
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1
2 mortality were analysed for these 29 patients, and for those who had repeat admissions, it was based on the first
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4 admission.

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8 Odds ratios for mortality were calculated with 95% confidence intervals. In our study, no basic demographics
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10 presented statistically significant risk for mortality in critical care. HbSS genotype did not appear to confer
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12 increased mortality in critical care over HbSC. However, it should be noted that both the two HbSC admissions
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14 that did not survive critical care occurred post cardiac arrest and in the context of another significant disease
15
16 process – HIV and SLE, respectively.

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21 Length of stay on a general ward (medical or surgical) before admission to critical care ranged from 0 to 39
22
23 days. For survivors, average length of stay pre-admission to CCU was 4 days, and for non survivors, 8.1 days.
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25 This was not statistically significant in a t test ($p=0.25$). Length of stay in CCU ranged from 1 to 68 days. For
26
27 survivors, the average length of stay in CCU was 6 days, and for non-survivors, 16.6 days. This approached
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29 statistical significance in a t test ($p=0.078$).
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34 Data on organ failure and support were available for 19 of the 29 acute medical and surgical patients (Table 3).
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36 **Each of the five organ failures and five organ support methods recognised by CCU were analysed by odds**
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38 **ratio (with 95% confidence interval, CI) to see if organ failure or organ support is associated with higher**
39
40 **risk of death . There are statistical limitations with the small sample size, and consequent large 95% CIs.**
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42 **For organ failure, higher mortality was associated for those with cardiovascular (CVS) failure. For organ**
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44 **support, all seven patients who did not require ventilation (either mechanical ventilation or non-invasive**
45
46 **positive pressure ventilation) survived, while five of the 17 ventilated patients died (the odds ratio is**
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48 **undefined as none of the patients who did not require ventilation died). Blood transfusion use was**
49
50 **similarly predictive of mortality with an odds ratio 19.5 if transfusion is required; this is likely to be**
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52 **secondary to more severe underlying disease (although there was one transfusion-related**
53
54 **complication – malaria was transmitted to one patient via transfused blood).** Requirement for
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56 inotropes may also be predictive of mortality, **four of the eight needing support died, compared to one of 11**
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2 **who did not require inotropes, although it is not statistically significant. Use of haemofiltration or**
3
4 **antibiotic did not appear to influence mortality rate.** Haemofiltration support was used for both acute and
5
6 chronic renal failure, and so was not indicative of severe acute illness. Antibiotics were used in the large
7
8 majority of patients.
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12 In this first review of adult SCD patients in critical care, we found that risk factors for CCU admission include
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14 previous CCU admission and significant (often sickle-related) co-morbidities. Given the increasing life span of
15
16 SCD patients, irreversible organ damage is likely to represent an increasing problem and CCU admission may
17
18 become an escalating problem in future. Re-admission to critical care does not increase mortality risk; only one
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20 of the nine non-survivors has previously been admitted, while three patients who had two admissions and the
21
22 patient who had four admissions, were all alive at one year post-CCU discharge.
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28 Four of the nine deaths occurred on the day of admission to CCU and non-survivors had longer hospital length
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30 of stays before CCU admission, findings which suggest that we are not always admitting patients to critical care
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32 early enough, when there is the potential for response to acute critical management of impending organ
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34 failure(s). **Future multi-centre prospective studies may further refine which complications of sickle cell**
35
36 **disease are best managed in CCU, with favourable prognosis for recovery.**
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Legends

Table 1 Reason for admission to critical care

Table 2 Patient demographics and clinical data for non survivors

Table 3 Effect of organ failure and organ support required on mortality

For Peer Review

Table 1 Reason for admission to critical care

	N (46)	%
Medical	32	69.6
<i>Acute chest syndrome (ACS)</i>	14	30.4
<i>Multi organ failure (MOF)</i>	8	17.4
<i>Neurological</i>	5	10.9
<i>Renal</i>	1	2.2
<i>Other</i>	4	8.7
Acute surgical	5	10.9
Planned post-operatively	6	13.0
Trauma	3	6.5

Table 2 Patient demographics and clinical data for non survivors

Age/ sex	Genotype	Date	Level of care	Hospital stay pre- CCU (days)	CCU length of stay (days)	Reason for CCU admission	Organ support required	PMH
29 M	HbSS	Apr 02	3	13	1	Intracerebral bleed	V	<i>strokes, epilepsy, SVT thrombosis - warfarin</i>
19 M	HbSS	Aug 02	3	1	5	Trauma (frontal haematoma)	I,V,A	<i>G6PD deficiency, HBV</i>
37 F	HbSS	Dec 02	3	5	24	ACS	I,V,A	<i>ESRF (sickle), renal transplant, IDDM, HTN</i>
50 M	HbSS	Sep 03	3	8	18	ACS, then developed malaria	I,V,B,A	<i>SVT, CKD</i>
40 M	HbSS	Mar 04	3	1	1	Stroke	V,A	<i>Schizophrenia</i>
26 F	HbSC	Oct 05	3	2	1	Cardiac arrest, MOF	I,V,H, A,B	<i>SLE, proteinuria</i>
25 M	HbSS	Apr 06	3	1	3	Intracerebral bleed	V	<i>strokes, leg ulcers, epilepsy</i>
31 F	HbSC	June 06	3	39	68	Cardiac arrest, MOF	I,V,H, B,A	<i>bilateral proliferative retinopathy</i>
43 F	HbSS	July 07	2	2	1	ACS leading to MOF	No data	<i>Multiple strokes, PHT, duodenal stenosis,</i>

Footnotes:

Level of care: 2 (high dependency, not typically requiring mechanical ventilation) or 3 (intensive care).

Organ support required: I inotropes, V ventilation (mechanical or non invasive), H haemofiltration, A antibiotics, B blood transfusion

Reason for CCU admissions: ACS acute chest syndrome; MOF multi organ failure;

PMH (Past Medical History): PHT pulmonary hypertension, SVT supraventricular tachyarrhythmia, CKD

Chronic kidney disease, SLE Systemic lupus erythematosus, ESRF end stage renal failure, IDDM insulin dependent diabetes mellitus, HTN hypertension, HBV hepatitis B virus positive

Table 3 Effect of organ failure and organ support required on mortality

Organ failure(s)	Organ failed [total number (number who died)]	Did not fail [total number (number who died)]	OR (95% confidence interval)
CVS	7 (4)	12 (1)	14.677 (1.16 – 185.23)
Neuro	5 (3)	14 (2)	*
Resp	10 (4)	9 (1)	*
Renal	5 (3)	14 (2)	*
Haem	5 (2)	14 (3)	*
Organ support required	Support required [total number (number who died)]	Support not required [total number (number who died)]	OR (95% Confidence Interval)
Inotropes	8 (4)	11 (1)	*
Ventilation (NIPPV or MV)	12 (5)	7 (0)	undefined
Haemofiltration	3 (2)	16 (3)	*
Blood transfusion	4 (3)	15 (2)	19.5 (1.30 – 292.75)
Antibiotics	15 (4)	4 (1)	*

Footnote: *Odds ratio not provided as the large 95% confidence intervals consequent to the small sample invalidates any statistical significance