Intensive Care Management of Sickle Cell Disease

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Abstract- Sickle cell disease (SCD) is one of the most common hereditary disorders in the world, and it is most prevalent in the Middle East, the Mediterranean region, Southeast Asia, and sub-Saharan Africa, particularly in Nigeria. Sickle cell disease (SCD) is an autosomal recessive blood illness that is marked by clinical variability that may be influenced by environmental variables, racial and ethnic identity, socioeconomic status, and genetic and epigenetic factors. A variety of genotypes resulted in SCD characterized by the presence of one βs gene and one of the following genes: another βs (homozygous disease known as sickle cell anemia), a hemoglobin C gene, a gene for β+ or β°-thalassemia or a hemoglobin D or hemoglobin E gene. Sickle cell anemia (SCA) is the most common genetic variant of SCD, accounting for 70% of cases worldwide.

I. INTRODUCTION

Sickle cell disease (SCD) is one of the most common hereditary disorders in the world, and it is most prevalent in the Middle East, the Mediterranean region, Southeast Asia, and sub-Saharan Africa, particularly in Nigeria.[1,2] Sickle cell disease (SCD) is an autosomal recessive blood illness that is marked by clinical variability that may be influenced by environmental variables, racial and ethnic identity, socioeconomic status, and genetic and epigenetic factors.[3] A variety of genotypes resulted in SCD characterized by the presence of one βs gene and one of the following genes: another βs (homozygous disease known as sickle cell anemia), a hemoglobin C gene, a gene for β+ or β°-thalassemia or a hemoglobin D or hemoglobin E gene. Sickle cell anemia (SCA) is the most common genetic variant of SCD, accounting for 70% of cases worldwide.[4]

International organizations like the United Nations and the World Health Organization consider sickle cell disease as a global health issue. Sub-Saharan Africa and tropical areas of Asia and America are the most severely impacted regions.[5] The HbS gene became prevalent in different parts of the world due to selective pressure because the heterozygote (HbAS) is protected from some of the deleterious effects of malaria. Hence, SCD is found at its highest frequencies in parts of the world where malaria is or was endemic. In addition, because of slave trade and recent migrations, it is now found even more widely in other countries including in Europe and the USA.[6] However, the prevalence is highest in tropical Africa, and Nigeria is the nation with the largest burden, where the traits occur in 25–30% of people and sickle cell anemia affects about 2% of all births.[7]

SCD remains a life-threatening disease that shortens patients life expectancy of by about 25 years compared to the general population[8]. The leading causes of death are ACS, infection, stroke, and end-stage organ failure.[9–11]

Few studies of patients with SCD admitted to the ICU are available. The most common cause for admission of SCD patients to the intensive unit is ACS as reported in some studies[12] However, VOC, which has an unpredictable cause has also been recounted to be a primary cause for hospital admissions In the event of severe VOC, people with SCD may need to be admitted to the intensive care unit (ICU)[13]. Cases of VOC that are not carefully managed can advance easily to morbidities that justify for intensive care unit (ICU) admission.[5,14] ICU mortality has ranged from 7 to 19.6%[15,16]. Risk factors for mortality were older ages, frequent prior hospitalizations, longer ICU

length of stay (LOS), use of mechanical ventilation and/or vasoactive drugs, a high haemoglobin level, a fast respiratory rate, and acute kidney injury (AKI) at ICU admission[8,9]. Blood transfusion in the ICU was also a risk factor for death in one study.

Recently, with rising awareness of the disease and better systems of healthcare, there has been some improvement in the survival of SCD patients even into adulthood[18,19] While this decreases the mortality rate of SCD, these patients however have the challenge of debilitating SCD co-morbidities. They frequent experience vaso-occlusive crises (VOCs), causing frequent bone pain crises, end-organ damage to the liver, lung, spleen, kidneys, and brain, among others. These lead to frequent emergency room visits, and lengthy hospital stays in those with comorbodities. Patients with SCD carry this burden all through their lives leadinf to a poor quality of life.

The disease outcome has considerably improved over the years, The key factor responsible for this improvement is the accessibility of comprehensive healthcare, disease-modifying agents, newborn screening for early diagnosis and blood transfusion programs [20]penicillin prophylaxis,[21] pneumococcal vaccination[22,23]and the use of transcranial Doppler (TCD) ultrasound to predict patients at risk of stroke who are then treated on chronic transfusion programmes.[24,25] Use of hydroxyurea, which is effective in reducing the frequency of painful crisis, acute chest syndrome and anaemia, has improved the outlook of the disease both in adults and children.[26] Nevertheless, there is still a gap in the management of SCD in Nigeria due to the high burden of the disease. SCD forms a minor part of the clinical practice of most general duty doctors, as there is gross absence of sickle cell centre. Thus, it may be hard to keep abreast of current knowledge and practices in the treatment of SCD Our objectives in this study is to highlight the features of patients with SCD admitted to the PICU, and to demonstrate the reason, different interventions done at the PICU, to check whether there are any associations between mortality and some clinical parameters, and finally, to show the outcomes of SCD patients in the PICU.

II. MATERIALS AND METHOD

This was a descriptive cross-sectional study was carried out in University College hospital, Ibadan. After the hospital ethical committee approval, a written, informed, signed consent of the patients was duly obtained. The questionnaire was self-administered and contained different sections. Section A contained questions on socio-demography, types of heamoglobin, PCV level, EWS and GCS. Section B contained questions on indications for admission; surgical and non-surgical indications. Section C contained questions on outcome and factors associated with outcomes. subarachnoid block, epidural anaesthesia, brachial plexus block, auxiliary block, femoral block, etc. The data collected were coded and analysed with the use of Statistical Package for Scientific Solutions (SPSS version 22). The variables in each section were presented using a frequency and percentage table with bar graphs, and analysis was done using Chi square test. Significant p-value was set at <0.05.

III. RESULTS

In a total of 86 respondents, there were 30 (65.2%) females and 16 (34.8%) males. High records of patients were found in young adults 80.4%, adolescents (10.9), child (4.3), middle aged (4.3). Thirty-two (69.4) of respondents are HbSS while fourteen (30.4) are HbSC. Twenty-two (47.8) patients had a PCV level of >25 while nineteen (41.3) had a PCV level of 19-25 and 5(10.9) had a PCV level of <19. Twenty four (52.2) of the patients had an EWS of ≥5 compared to twenty two (47,8) patients who had an EWS of <5. Thirty-three (71.7) patients had a GCS range of 13-15, while 8(17.4) had a GCS range of 9-12 and 5(10.9) had a GCS range of 3-8.

Demographic and clinical characteristics of patients

Variable	Frequency	Percent
Age		
Child (≤9)	2	4.3
Adolescent (10-19)	5	10.9

Young adult (20-44)	37		80.4
Middle aged (45-64)	2		4.3
Mean age ± SD			28.96±10.34 (years)
Gender			
Male	16		34.8
Female	30		65.2
Type of haemoglobin			
HbSS		32	69.6
HbSC		14	30.4
PCV level (%)			
Mean ± SD 24.59±4.21			
<19		5	10.9
19-25		19	41.3
>25		22	47.8
EWS			
<5		22	47.8
≥5		24	52.2
GCS			
3-8		5	10.9
9-12		8	17.4
13-15		33	71.7

Table 2: Indications for admission

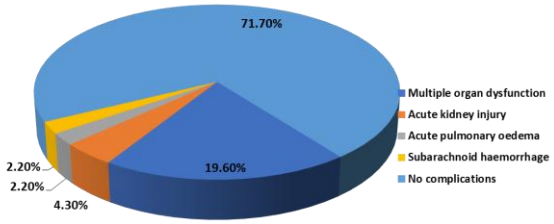
Twenty-seven (58.7) of patients had surgical indications for admission while for the patients that had non-surgical admissions, VOC was found in higher records of patients (19.6%), multiple-organ failure was found in 5(10.9) patients and sepsis was found in 3(6.5) patients

Variables	Frequency	Percent
Surgical (post-operative admission)	27	58.7
Non-surgical		
Acute Chest Syndrome	1	2.2
Vaso-occlusive crises	9	19.6
Multi-organ failure	5	10.9
Sepsis	3	6.5
Anaemic heart failure	1	2.2
Postpartum eclampsia	1	2.2
ASD	1	2.2
PDA	1	2.2

Atrial Septal Defect (ASD), Patent Ductus Arteriosus (PDA)

There was no complication in 71.70% of the patients, majority of the patients 19.60% had multiple organ dysfunction, while 4.30% had acute kidney injury, followed by 2.20% of the patients having acute pulmonary oedema and subarachnoid hemorrhage respectively.

Figure 1: Distribution of complications and non-complications developed



Outcome

A total of 37 admissions for those who survived were with those with no co-morbidities (80.4%) in comparison to 9 admissions among those who died (44 %).

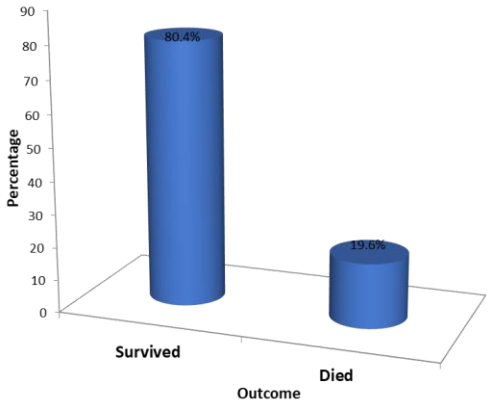


Table 3: Factors associated with outcome

PCV was positively correlated with mortality level, 20.78±4.47, $P = 0.002$.

Variables	Survived	Died	P value
	Mean ± S.D	Mean ± S.D	
Age	29.65±9.46	26.11±13.75	0.364
PCV	25.52±3.63	20.78±4.47	0.002*
	Median (IQR)	Median (IQR)	
Length of ICU stay (days)	2.0 (7)	2.0 (21)	0.525#

* *Significant association* PCV- Pack Cell Volume
# Mann Whitney U value reported

Table 4: Relationship between clinical variables and ICU outcome of patients

EWS, GCS, Ventilation, Ionotropic support, complications have a positive correlation with survival outcome. Twenty-four (52.2) respondents with a EWS of ≥5 have cases of mortality compared with twenty two (47.8) respondents with an EWS of <5 where no death was recorded. Out of 33(71.7) patients with a GCS range of 13-15, there are 32 numbers of survivors compared to1 survivor out of 5(10.9) in patients who had a GCS range of 3-8. No mortality was recorded all patients 35(76.1) who had non-invasive ventilation while 9 cases of death was found in 9 out of 11(23.9) patients who had invasive ventilation. There are 35 survivors out of 36(78.3) patients who had no inotropic support compared to 2 survivors out of 10(21.7) patients who had inotropic support. Out of 36(78.3) patients who had no complications, there are 35 survivors, compared to 2 survivors out of 10(21.7) patients who had complications.

Variables	Frequency n (%)	Survived	Died	P value
Gender				
Male	16 (34.8)	12	4	0.698
Female	30(65.2)	25	5	
Type of haemoglobin				
HbSS	32(69.6)	25	7	0.701
HbSC	14(30.4)	12	2	
EWS				
<5	22(47.8)	22	-	0.002*
≥5	24 (52.2)	15	9	
Indications for admission				
Surgical	27(58.7)	25	2	0.022*
Non-surgical	19(41.3)	12	7	
GCS				
3-8	5(10.9)	1	4	0.001*
9-12	8(17.4)	4	4	
13-15	33(71.7)	32	1	
Tracheostomy				
Yes	1(2.2)	-	1	0.196
No	45(97.8)	37	8	
Ventilation				

Invasive	11(23.9)	2	9	0.001*
Non-invasive	35(76.1)	35	0	
Ionotropic support				
Yes	10(21.7)	2	8	0.001*
No	36(78.3)	35	1	
Blood transfusion				
Yes	17(37)	11	6	0.067
No	29(63.0)	26	3	
Complications				
Had complication	10(21.7)	2	8	0.001*
No complication	36(78.3)	35	1	

** Significant values, p <0.05*

IV. DISCUSSION

The aim of our study was to assess the indications for admission into the ICU and Predictors of outcome of patients in the ICU with SCD admitted to the ICU and to identify factors associated with adverse outcomes defined as death in the ICU and/or use of life supporting treatments. The main reason for admission was VOC, which was consistent with past descriptions27 About nine out of forty six patients experienced adverse outcomes and died. Factors independently associated with adverse outcomes were PCV, EWS and GCS prior to ICU admission, Ventilation, Ionotropic support, complications at ICU admission.

In concordance with previous studies11,28,29 this retrospective study showed that more adult than children developed acute chest syndrome with concomitant higher mortality. 2 out of 7 patients who died were not homozygous for SCD, and genotype did not independently predict adverse outcomes as defined for our study , consistent with this findings is a study by Agbakou et al, 12 where it was discovered that only a third of the study population who were hb died.

Less than quarter of the patients had complications, some complications developed by patients in our study were; multiple organ dysfunction, acute kidney injury, acute pulmonary oedema and subarachnoid hemorrhage.

CONCLUSION

SCD confers a high burden and results in morbidity and mortality worldwide. The priorities for the future management of infectious complications in SCD differ by geographic and socioeconomic circumstances. In the resource-rich nations where perinatal screening, antibiotic prophylaxis, and robust vaccination programs exist, mortality from infection is greatly reduced. In these areas of the world, prevention of chronic organ injury and improvement of quality and duration of life have become the principal goals of therapy.

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