East African Medical Journal Vol. 95 No. 4 April 2018
OUTCOME OF INTENSIVE CARE MANAGEMENT OF ACUTE CHEST SYNDROME IN A NIGERIAN TEACHING HOSPITAL: A PRELIMINARY REPORT
Zakari Aliyu Suleiman, Department of Anaesthesia, University of Ilorin, Nigeria and University of Ilorin Teaching Hospital, Ilorin, Nigeria MBBS, FWACS; Israel Kayode Kolawole, Department of Anaesthesia, University of Ilorin, Nigeria and University of Ilorin Teaching Hospital, Ilorin, Nigeria MBBS, FWACS MBBS, FWACS; Isoken Enaworu, MBBS, University of Ilorin Teaching Hospital, Ilorin, Nigeria; Aminudeen Abdulrahman, MBBS, University of Ilorin Teaching Hospital, Ilorin, Nigeria; Benjamin Olusomi Bolaji, MBBS, FMCA, FWACS, Department of Anaesthesia, University of Ilorin, Nigeria University of Ilorin Teaching Hospital, Ilorin, Nigeria.

Corresponding author: Dr Z. A. Suleiman, Department of Anesthesia, University of Ilorin. Email: suzack71@yahoo.com or suleiman.za@unilorin.edu.ng

OUTCOME OF INTENSIVE CARE MANAGEMENT OF ACUTE CHEST SYNDROME IN A NIGERIAN TEACHING HOSPITAL: A PRELIMINARY REPORT

Z.A. Suleiman, I.K. Kolawole, I. Enaworu, A. Abdulrahman and B. O. Bolaji

ABSTRACT

Objectives: **Acute chest syndrome (ACS) is a common complication of vaso-occlusive crisis in sickle cell disease patients. It causes respiratory failure which may require mechanical ventilation in the intensive care unit, but outcome of such intervention has been sparingly reported in our environment. This study highlights the intensive care management and outcomes of acute chest syndrome in our centre.**

Design: **This was a retrospective descriptive study**

Setting: **This study was carried out at the intensive care unit of a tertiary hospital in Nigeria**

Subjects or participants: **These were 27 sickle cell disease patients with acute chest syndrome managed in our intensive care unit from January 2013 to December 2017.**

Methods: **We reviewed the medical records of all the 27 sickle cell disease patients managed in our intensive care unit on account of acute chest syndrome in the last 5 years. Relevant information on supplemental oxygen administration, modes of ventilation, transfusion, length of stay in the ICU and mortality rate was also extracted.**

Main outcome measure: **The main outcome measure was the number of patients who survived and discharged from the intensive care unit.**

Results: **Nine (50%) out of the 18 patients with acute chest syndrome, complicated by severe respiratory insufficiency, ventilated mechanically survived. The median length of ICU stay was 6 (12) days.**

Conclusion: **Mechanical ventilation of patients and adequate pain control can help reduce the mortality and enhance the quality of life of sickle cell disease patients with acute chest syndrome.**

INTRODUCTION

Acute chest syndrome (ACS) is one of the manifestations of vaso-occlusive complication in patients with sickle cell disease (SCD). This life-threatening condition, diagnosed by a new infiltrate on chest x-ray with one or more of fever, cough, sputum production, dyspnoea, or hypoxia, can be precipitated by infection, atelectasis, fat embolism and true thrombo-embolism with eventual compromised ventilation and increased sickling.[1] Combination of poor chest expansion caused by painful rib and vertebral infarction and suppressed respiratory drive due to opiates usually leads to atelectasis.[1] Prevention or reversal of atelectasis, the commonest lung finding during an acute painful crisis affecting the chest wall, requires respiratory support and may necessitate admission of patients with ACS into intensive care unit. Acute chest syndrome is the second most common cause of admission after painful vaso-occlusive crises; and can progress to adult respiratory distress syndrome (ARDS) with consequent significant morbidity and mortality.[2,3] Reports have shown that about half of the patients with sickle cell disease will experience at least an episode of acute chest syndrome before they die, with adults being at a fourfold increased risk of dying from acute chest syndrome than children.[4,5] Prompt and aggressive control of pain of vaso-occlusive crisis in adult and early administration of effective antibiotics to address any potential infection in children are likely to prevent development of acute chest syndrome in patients with SCD.[3,5] Besides non-invasive oxygen supplementation and nebulization of airway with bronchodilators, respiratory supports in patients with severe acute chest syndrome also involves mechanical ventilation. The risks of intubation in hospitalized adolescent and young adults (16-25years) with SCD and acute chest syndrome are higher among patients managed by the general practitioners compared to specialized units.[6] This observation underscores the importance of early referral of patients with acute chest syndrome to a facility that can provide optimal respiratory care. A recent study from the United States showed that mechanical ventilation was utilized to augment oxygenation and ventilation in 13% of patients with ACS.[3] The average ICU length of stay was found to be 10.5 days with mortality rate of 3%, mostly affecting adult patients.[3]

However, there is a dearth of literature on the outcomes of patients with acute chest syndrome admitted and managed in intensive care unit (ICU) in our environment. Thus, there is lack of adequate information to facilitate effective communication with patients and relatives on challenges and outcomes of management which may further worsen their fear and anxiety over admission to ICU.

The objectives of this 5-year review were to present the intensive care management provided to patients with acute chest syndrome and determine their chance of survival when managed in a resource-challenged intensive care unit like ours.

MATERIALS AND METHOD

In this retrospective study, medical records of all the 32 patients with sickle cell disease patients admitted to our ICU between 1st January 2013 and 31st December 2017 were reviewed. Information on age, sex, indications for admission, number of days on the ward before admission to ICU, peripheral arterial oxygen saturation on admission, respiratory

rate, and packed cell volume (PCV) were obtained and recorded. The review of the chest x-ray revealed presence of bilateral basal infiltrates. Other data extracted from the records included presence of bone or chest pain, history of intubation, mechanical ventilation and modes, duration of ventilation, history of transfusion, presence of co-morbid medical conditions, length of stay in the ICU and number of deaths.

The data were analyzed with SPSS 20.0 version. Descriptive statistics were used to indicate clinical outcomes for this patient cohort. The impact of mechanical ventilation, age group, length of stay on the ward before ICU admission and transfusion on the outcome were analyzed with Fisher's exact test Continuous variables were expressed as mean ± standard deviation, whereas categorical data were expressed as proportions. A p-value of 0.05 was deemed to be statistically significant.

RESULTS

A total of 32 (4.1%) out of 782 patients managed in our ICU between 2013 and 2017 had sickle cell disease; 27 (3.5%) were managed for acute chest syndrome and the remaining 5 (0.6%) patients were managed for severe vaso-occlusive crisis. The mean age of the patients with acute chest syndrome was 18.8 ± 7.1 years and male to female ratio was 1.25:1, Table 1.

Table 1

Socio-demographic characteristics and clinical data

Variables		**N (%)**
Age (years)		
Mean ± SD	18.8±7.1	
<15years		17 (63)
>15years		10 (37)
Sex		
Male		15 (55.6)
Female		12 (44.4)
Pre-admission:		
PCV (%)	21.0±4.1	
SPO_2 (%)	68.3±15.6	
Duration of stay on the ward before ICU admission: Median hours (IQR)	48(141)	
Duration of ventilation: Median hours (IQR)	2(10)	
Modes of oxygenation		
Mechanical		18 (63)
Oxygen supplementation		9 (37)
Transfusion		
Yes		18 (66.7)
No		9 (33.3)

Types of blood transfusion		
No		11 (40.7)
Simple		16 (59.3)
Exchange		2 (7.4)
End organ damage		
Myocardial ischaemia		1 (3.7)
Acute kidney injury		1 (3.7)
Outcomes		
Discharge		17 (63)
Overall mortality		10 (37)
<15years		4 (14.8)
>15years		6 (22.2)

PCV= Packed cell volume; SPO_2= Peripheral arterial oxygen saturation.

Ten children (<15 years) compared with the 17 adults (≥15 years) were admitted to ICU on account of acute chest syndrome with mortality rate of 4 (14.8%) in children in comparison with (6) 22.2% among the adult patients. The mean pre-admission packed cell volume and arterial oxygen saturation were 21 ± 4.5% and 68.3 ±15.6% respectively. The median hours spent on the ward before ICU admission was 48 (141). Eighteen patients were transfused; 16 (59.3%) patients had simple transfusion and exchange blood transfusion was done in 2 (7.4%), Table 1.

Maintenance of peripheral arterial oxygen saturation was achieved with oxygen supplementation, using nasal catheter and face mask, in 9 (33.3%) patients 1 child and 8 adults with mild respiratory insufficiency, and all survived. Invasive mechanical ventilation via endo-tracheal intubation (ETT) was employed in 18 (66.7%) of the patients with severe respiratory insufficiency; SIMV mode in 16 patients, CPAP/SIMV and CPAP only modes in one patient each respectively. However, 9 (50%) out of the 18 mechanically ventilated patients survived and the remaining 9 (50%) patients died, Table 2.

Table 2

Interventions employed to improve oxygenation

Methods of oxygenation		**N (%)**
SIMV		16 (59.3)
SIMV/CPAP		1 (3.7)
CPAP		1 (3.7)
Nasal catheter		9 (33.3)

SIMV= Synchronous Intermittent Mandatory Ventilation; CPAP= Continuous Positive Airway Pressure.

Chest pain, rated as severe, was part of the presenting symptoms in 25 (92.6%) of the patients despite prior history of analgesic use. While on admission, the pain severity steadily improved following parenteral morphine and paracetamol administrations in all but one

patient. The control of persistent pain in a patient was achieved when ketamine infusion, 0.15mg/kg/hr, was added to the analgesic regime. The median length of ICU stay was 6 (12) days and the mortality rate was higher in the adults (22.2%) compared with the younger patients (14.8%) but the overall mortality rate was 37%, Table 1.

Mortality was recorded in 6 (46.2%) out of the 13 adults and 2 (40%) out of the 5 children that were ventilated; and in 7 (41.2%) out of the 17 patients that spent <72 hours and 3 (30%) out of the 10 patients that spent >72 hours on ward before ICU admission. Similarly, 3 (42.9%) out of the 7 patients that received packed cells and 6 (30%) out of the 20 patients who were not transfused died while being managed in the ICU in our study. (NB: Severity of the disease may be responsible). Furthermore, mortality of 6 (35.3%) out of the 17 adults and 4 (40%) out of the 10 children were observed. However, the impacts of variables (mechanical ventilation, length of stay on the ward prior to ICU admission, packed cell transfusion, and age group) on the outcome were not statistically significant (p=1.000, 0.6919, 0.6527, and 1.000 respectively), Table 3.

Table 3:

Relationship between some variables and outcome in patients with acute chest syndrome managed in the ICU

Variables	Number of patients discharged	Number of patients died	Total	P values
Mechanical ventilation				
Ventilated	7	6	13	1.000
Not ventilated	3	2	5	
Length of stay on the ward				
<72hrs	10	7	17	0.6919
>72hrs	7	3	10	
Packed cell transfusion	4	3	7	0.6527
Transfused	14	6	20	
Not transfused				
Age group				
Adults (>17yrs)	11	6	17	1.000
Children (<17yrs)	6	4	10	

P<0.05 is statistically significant

P value was calculated using Fisher's exact test

DISCUSSION

This retrospective study revealed that acute chest syndrome is an important indication for ICU admission in patients with sickle cell disease with higher mortality in adult than paediatric patients. Moreover, our findings showed the mortality-reduction benefit of mechanical ventilation in the management of some patients with acute chest syndrome especially in the face of persistent moderate-to-severe hypoxaemia despite optimal administration of supplemental oxygen.

In concordance with previous studies[2,5,7] this retrospective study showed that more adult than children developed acute chest syndrome with concomitant higher mortality. The cited studies reported four-fold mortality in adult compared with children. This is comparatively higher than the one and half times mortality in the adults compared with children recorded in the present. However, the higher mortality would have been expected in children given their poor respiratory reserve due to low functional residual capacity, increased oxygen consumption and relative rapidity of development of respiratory failure and progression to cardiac arrest.

Similarly, our study identified mechanical ventilation as a life-saving intervention in the care of acute chest syndrome and this agrees with the results of studies carried out by Castro and colleagues,[4] Gladwin and associates,[8] and Allareddy et al.[9] Despite the fact that about two-third (66.7%) of patients in our study were mechanically ventilated, the mortality was high (37%). and this is consistent with the findings from the experience of a single centre intensive care unit that similarly reported a very high mortality in invasively mechanically ventilated acute chest syndrome patients.[10] However, the two studies differed in terms of age characterization of the enrolled participants. While we grouped the subjects into children and adult (<15 years and >15 years respectively), Tawfic and colleagues' study reported on subjects age ranged 12-52 years.

The high mortality rates observed in the Tawfic and colleagues' study[10] and this present study contrasts with figures of 0.6%, 4.6% and 13% reported respectively by Jan and coworkers[6], Allareddy et al[9] and Castro and colleagues.[4] The relatively high mortality figure observed in the present audit could be due to delayed presentation of patients to our ICU and inadequate facility required for provision of standard management strategies for respiratory failure. In addition, unlike in the Gladwin's study[8] where the recorded low mortality was ascribed to advances in medical care and management strategies, valuable clinical information from analyses of arterial blood gases was lacking in the care of acute chest syndrome in our ICU. Furthermore, our patients spent median hours of 70 (46) on the ward and this might just be long enough to cause severe disruption of ventilation-perfusion milieu in the setting of on-going respiratory failure.

About two-third of our patients was transfused with packed cells to prevent hypoxic injury to the vital organs such as kidneys, heart, and brain; and this is consistent with the findings from other studies that demonstrated that transfusion of sickle cell disease patients with acute chest syndrome reduces the occurrence of end organ damage.[4,9,11,12,13] However, the proportion of patients (7.4%) who had exchange blood transfusion in our study is slightly above the 6% reported Allareddy et al,[9] and sharply contrast with the 3% reported by Jan and coworkers.[6] This again may be a

reflection of the severity of the disease in our patients.

We also observed, in the present audit, that the two adult patients who had exchange blood transfusion died. Researchers have suggested that the timing and impact of exchange blood transfusion on outcomes in sickle cell disease adult patients with acute chest syndrome needs to be investigated.[9] Possibly, the death that occurred despite exchange blood transfusion, could have been prevented if it had been done within the yet-to-be-determined golden hours.

Studies have linked the outcome of care in sickle cell disease patients, among others, to the status and facilities available in the hospital.[14] Our healthcare facility is a teaching hospital, where mechanical ventilators are available, regularly manages patients with sickle cell disease by specialists. Thus, it is regarded as a facility with considerable experience in the care of critically ill patients compared to a primary or secondary healthcare centres. The unavailability of facility for regular assessments of arterial blood gases in most patients with acute chest syndrome in our hospital might be partly responsible for the high mortality.

In our study, adequate pain control was prioritized in both the ventilated and non-ventilated patients. Appropriate adjustments were made to the traditional intramuscular pentazocine and paracetamol analgesics regimen prior to ICU admission. Parenteral morphine and paracetamol were commenced on admission to the ICU to downgrade the pain severity to mild or no pain category. However, a patient continued to experience severe pain despite the escalations of morphine dose. Consequently, presence of neuropathic pain as a component of global pain experience by the patient was then considered and ketamine infusion commenced which resulted in good pain control. Neuropathic pain is rarely considered in these patients in our environment and the quality of life of the patients remains poor due to the persisting pain that is conventionally dubbed as "difficult-to-treat pain." Receptors such as N-methyl-D-aspartate (NMDA), α-amino-3-hydroxyl-5-methyl-3-isoxazaoleproprionic acid (AMPA), and M-glutamate (M-glu) receptors have recently been implicated to be playing large role in central sensitizations or pain wind up.[15,16] The binding of glutamate and aspartate, released in response to persistent noxious stimuli, to the NMDA receptors in the dorsal horn of the spinal cord is believed to be one of the important processes in the development of central sensitizations.[17,18] The NMDA antagonistic-property of ketamine has been exploited to address neuropathic pain syndrome.[15,19,20] Thus, ketamine infusion at the rate of 0.15mg/kg/hr was included on the analgesic regime and the pain control was achieved in the patient.

The small sample size, despite 5 years study duration, in this retrospective study is a serious limitation of the study. It could be responsible for the lack of statistical significance in the analyzed variables (mechanical ventilation, age group, length of stay on the wards before ICU admission, and packed cell transfusion) to predict the outcome of ICU care of acute chest syndrome in this study. It is possible that outcome could be predicted from these variables if the sample size was large. In this regard, a multi-centre study is highly recommended in order to increase the sample size and hence the power of the study.

Given the fact that this is the first study that appraised the ICU outcome of acute chest syndrome in any Nigerian hospital, it is our considered opinions that findings of this

descriptive study can be used to predict the ICU outcome of patients with acute chest syndrome in our environment.

CONCLUSION

Mechanical ventilation reduced the mortality in sickle cell disease patients with severe life-threatening respiratory insufficiency. Ventilatory support enhances oxygenation and allows excellent pain control with strong opioid analgesics without fear of respiratory depression.

REFERENCES

1. Mak V, Davies SC. The pulmonary physician in critical care c Illustrative case 6: Acute chest syndrome of sickle cell anaemia. Thorax 2003; 58:726–728
2. Platt OS, Brambilla DJ, Rosse WF, Milner PF, Castro O, Steinberg MH et al. Mortality in sickle cell disease: Life expectancy and risk factors for early death. N Engl J Med. 1994;330(23):1639
3. Vichinsky EP, Neumayr LD, Earles AN, Williams R, Lennette ET, Dean D et al. Causes and outcomes of the acute chest syndrome in sickle cell disease. N Engl J Med. 2000; 342:1855–1865
4. Castro O, Brambilla DJ, Thorington B, Reindorf CA, Scott RB, Gillette B et al. The acute chest syndrome in sickle cell disease: incidence and risk factors: The Cooperative Study of Sickle Cell Disease. Blood. 1994; 84(2):643.
5. Vichinsky EP, Styles LA, Colangelo LH, Wright EC, Castro O, Nickerson B et al. Acute chest syndrome in sickle cell disease: clinical presentation and course. Cooperative Study of Sickle Cell Disease. Blood. 1997;89(5):1787-1792.
6. Jan S, Slap G, Smith-Whitley K, Dai D, Keren R, Rubin MD et al. Association of hospital and provider types on sickle cell disease outcomes. Pediatrics. 2013;132(5):854–861.
7. Powars D, Weidman JA, Odom-Maryon T, Niland JC, Johnson C. Sickle cell chronic lung disease: prior morbidity and the risk of pulmonary failure. Medicine. 1988; 67:66–76.
8. Gladwin MT, Vichinsky E. Pulmonary Complications of Sickle Cell Disease. N Engl J Med. 2008;359:2254–2265.
9. Allareddy V, Roy A, Lee MK, Nalliah RP, Rampa S, Allardy V, et al. Outcomes of Acute Chest Syndrome in Adult Patients with Sickle Cell Disease: Predictors of Mortality. PLoS ONE. 2014; 9(4): e94387.
10. Tawfic QA, Kausalya R, Al-Sajee D, Burad J, Mohammed AK, Narayanan A, et al. Adult sickle cell disease: A Five year experience of Intensive care management in a University hospital in Oman. Squ Med J. 2012; 12(2): 177–183.
11. Mallouh AA, Asha M. Beneficial effect of blood transfusion in children with sickle cell chest syndrome. Am J Dis Child. 1988; 142:178–182.
12. Emre U, Miller ST, Gutierez M, Steiner P, Rao SP, Rao M. Effect of transfusion in acute chest syndrome of sickle cell disease. J Pediatr. 1995; 127:901–904.
13. Vichinsky EP, Haberkern CM, Neumayr L, Earles AN, Black D, Koshy M, et al. A comparison of conservative and aggressive transfusion regimens in the perioperative management of sickle cell disease: the Preoperative Transfusion in Sickle Cell Disease Study Group. N Engl J Med. 1995; 333:206–213.
14. McCavit TL, Lin H, Zhang S, Ahn C, Quinn CT, Glenn F. Hospital volume, hospital teaching status, patient socioeconomic status and outcomes in patients hospitalized with sickle cell disease. Am J Hematol. 2011 86(4): 377–380.
15. Stubhaug A, Breivik H. Longterm treatment of chronic neuropathic pain with NMDA receptor antagonist ketamine. Acta Anaesth Scand. 1997;41:422–426.
16. Fundytus ME, Coderie TJ. MgluRs and opioid dependence: further examination of the mechanisms.Pain Forum 1999;8:59–63
17. Mao J, Price DD, Mayer DJ. Mechanisms of hyperalgesia and morphine tolerance: a current view of their possible interactions. Pain 1995;62:259–274.
18. Persson J, Axelsson G, Hallin RG, Gustafsson LL. Beneficial effects of ketamine in a chronic pain state with allodynia, possibly due to central sensitization. Pain 1995;60:217–222.

19. Rabben T, Skjelbred P, Oye I. Prolonged analgesic effect of ketamine, an N -methyl-D-aspartate receptor inhibitor, in patients with chronic pain. J Pharm Exp Therap. 1999; 289:1060–1066.

20. Crowley KL, Flores JA, Hughes CN, Iacono RP. Clinical application of ketamine ointment in the treatment of significant allodynia and hyperalgesia associated with chronic neuropathic pain. J Pharm Comp. 1998; 2:123–127.