Sickle Cell Anaemia Complications as seen in Adults in a Tertiary Hospital in South-South Nigeria

Nwannadi lA, Alao 00,
Department of Haematology and Blood Transfusion, Benue State University, Makurdi, Nigeria.
Bazuaye GN, Isoa ME and Nwogoh B
Department of Haematology and Blood Transfusion, University of Benin, Benin-City, Nigeria.
Nwagu M and Borke M,
Department of Haematology and Blood Transfusion, Delta State University, Abraka, Nigeria.
Correspondence to: Nwannadi lA, E-mail:inwannadi@yahoo.co.uk
Nig Hosp Pract Vol. 9 No (5 - 6), 2012, 84 - 89

Summary

Sickle cell anaemia (SCA) complications namely stroke, osteomyelitis, retinopathy, pulmonary embolism, renal failure, chronic leg ulcers, cholelithiasis, acute chest syndrome, avascular necrosis (AVN) of the head of femur, and others, affect virtually all systems of the body. The prevalence and pattern of the complications of this disorder in south-south Nigeria had not been documented. The objective of the study was to detect and analyze frequency of occurrence of the different types of complications seen in adult SCA patients in south-south geopolitical region of Nigeria and to explore the determinants for the development of complications in adult SCA patients. A retrospective review of the medical records of one hundred and twenty-five (J25) SCA patients above the age of fifteen years who attended the Haematology clinic of a tertiary hospital in south-south Nigeria from January 2010 to December 2010 was carried out Information on biodata, complications and the stable haemoglobin levels were extracted and analyzed using the Statistical Package for Social Science (SPSS) version 15. *Out of 1080 SCApatients seen over the period of study,* 125 (11.6%) *had complications. Complications were found to be more common in females* 71.2% *(n=89) compared to* 28.8% *(n=36) in males. The mean age of the study population was 30.9* ± 8.8 *years and the age range was* 16 *to 60 years. The commonest complication noted in these patients was chronic osteomyelitis (36.0%). This was followed by chronic renal failure* (17.6%). *The frequencies of the other complications were as follows, chronic leg ulcers (11.2%), cholelithiasis* (11.2%), *acute chest syndrome and avascular necrosis (AVN) of the head of femur occurred equally (4.0%),pulmonary embolism* (2.4%), *stroke* (2.4%), *the least common complication was seizure* (1.6%). *The most common complication of SCA patients* in *south-south Nigeria was chronic osteomyelitis. The pattern of complications was generally lower than what was reported in other parts of the world. Some complications were not recorded; examples were pulmonary hypertension and ocular complications. This may probably be as a result of low index of suspicion and lack of adequate facilities to make correct diagnosis.*

Key words: *Sickle Cell Anaemia, Complications, South-south, Nigeria.*

Introduction

seA complications are diseases or disorders arising in a patient with SeA as a consequence of his haemoglobin SS phenotype. SeA is a chronic haemolytic anaemia that results from the homozygous inheritance ofhaemoglobin S.' Even though sickle cell disease (SeD) is caused by a single-nucleotide mutation (GAG-GTG in the sixth codon of axon 1 of the Bglobin gene), its clinical presentation involves a multitude of complications involving.all organs ofthe body.'

Majority of seA complications result from vaso-occlusion, ischaemia and necrosis in the major o-rgans of the body. These complications include stroke, seizure, acute chest syndrome, pulmonary hypertension, pulmonary embolism, cholesthiasis,: priapism, avascular necrosis of the head of femur, chronic leg ulcers, osteomyelitis, and others. Some complications lend themselves to simple management, whereas others, including aseptic necrosis of the hip, priapism and leg ulcers, require prompt referral for specialized treatment"

It is important to study the pattern of SeA complications because in some instances, seA may present first with the complications rather than the primary manifestation of the disease. In these conditions, high index of suspicion plays a key role in elucidating the primary disease. There have been instances where SeA presented initially with chronic leg ulcer that resembled tuberculosis ulcer.

There is also paucity of data on pattern of these complications among patients with sickle anaemia the study centre. This work will provide background data in future prospective studies in our environment. .

Materials and Methods

This study was carried out at the University of Benin Teaching Hospital, Edo state, Nigeria-a tertiary health institution that renders specialist services to its host community, and serves as a referral centre to neighbouring states in the south-south geopolitical region of Nigeria. The target population was 1080 (which was the total number of seA patients attending the haematology clinic over the study period). The study population consisted of HbSS patients with complications attending the Haematology clinic of the above hospital from January 2010 to December 2010 (cluster sampling). The diagnoses ofHbSS were previously established by haemoglobin electrophoresis. Those patients with other sickle cell disorders other than HbSS were excluded from the study. Also excluded were HbSS patients without complications and patients below the age of 15 years. One hundred and twenty-five patients (125) satisfied the inclusion criteria and were studied. The 125 sample size also satisfied the minimum sample size requirement for this study which was 24 as calculated from the formula n= {exp(1-p)}/m2 where; n = required sample size, t = confidence level at 95% (standard value of 1.96), p = estimated prevalence of sickle cell anaemia in the project area (2%), m = margin of error at 5% (standard value of 0.05).

Demographic features of the patients, type of seA complications, and stable haemoglobin levels were retrieved from their case files and the data were analyzed using Statistical Package for Social Science (SPSS) version 15.

Results

Out of 1080 cases of SeA seen during the study period, 125 (11.6%) had complications.

Table 1: Socio-demographic characteristics of the study population

Characteristics	Frequency n=125	Percentage (%)
Age groups		
16-30	65	52.0
31-45	54	43.2
46-60	6	4.8
Mean age=30.9± 8.8 years		
Sex		
Female	89	71.2
Male	36	28.8
Marital status		
Married	23	18.4
Single	102	8l.6
Educational background		
Educated	83	66.4
Non -educated	42	33.6
Employment		
Employed	21	17.1
Unemployed	104	82.9
Religion		
Christians	123	98.0
Moslems	2	2.0
Tribe		
Bini	71	56.8
Esan	8	6.4
Others	46	36.8

Table 2: Distribution of SCA complications and average haemoglobin concentrations among the study population

Complications	Male	Female	Total	Percentage (%,)	Mean Hb conc (g/dl)
Stroke	0	3	3	2.4	5.7
Seizure	0	2	2	1.6	5.7
Acute chest syndrome	1	4	5	4.0	7.8
Pulmonary Embolism	1	2	3	2.4	7.4
Cholelithiasis	5	9	14	11.2	4.5
Avascular Necrosis of femoral head.	1	4	5	4.0	7.4
Chronic leg ulcers	3	11	14	11.2	5.1
Chronic renal failure	5	17	22	17.6	4.3
Chronic osteomyelitis	8	37	45	36.0	5.3
Priapism	12	0	12	9.6	7.1
Total	36	89	125	100.0	

Key- Hb= Haemoglobin

The mean age of the study population was 30.9 ± 8.8 years and the age range was 16 to 60 years. Complications were statistically significantly more in females 71.2% (n= 89), more among the singles 81.6% (n=102), the educated 66.4% (n=83), the unemployed 82.9% (n= 104), the Christians 98% (n=123) and the Bini tribe

Table 2 revealed that the most common complication of SCA in the study group was chronic osteomyelitis (36.0%), this was followed by chronic renal failure (17.6%), cholelithiasis and chronic leg ulcers (11.2% each), priapism (9.6%), acute chest syndrome and avascular necrosis of the head of femur occurred equally (4.0% each), pulmonary embolism and stroke (2.4% each), the least common complication was seizure (1.6%).

The table also showed that average haemoglobin concentrations were high (more than 7.0gldl) in those that had acute chest syndrome, pulmonary embolism and priapism and very low (less than 5.0g/dl) in those that had cholelithiasis, chronic renal failure and stroke.

Discussion

Majority (52%) of the patients with SCA complications were aged 16-30 years. This is as a result of low life expectancy of these patients in the developing countries. Life expectancy in SCA patients in our environment is still low although many now survive beyond the 4th decade with optimal management. [6] Reports from Boston revealed that among children and adults with sickle cell anemia, the median age at death was 42 years for males and 48 years for females. [7] They also reported that SCA patients with acute chest syndrome, renal failure, seizures, a base-line white-cell count above 15,000 cells per cubic millimeter, and a low level of fetal hemoglobin were associated with an increased risk of early death.

Females were more affected than males. The reason for this was not clear but we proposed that it is likely that females tend to seek medical attention more than males in our study area. It may actually be that there were more female SCA patients than males in the study area, but no studies have been carried out to support that. George et a1[8] in Port Harcourt south-soutllNigeria reported a male prepond- ay

erance of SCA patients with male: female ratio of 1.3:1, though that was among children. Female preponderance in this study may also suggest that females are genetically more prone to develop complications than males but this is yet to be proved. Lastly, females tend to have lower stable haematocrit levels than males because of blood loss during monthly menstrual cycle and this tend to make them more vulnerable to complications than the males. In Saudi Arabia, Udezue et a1[9] reported a similar female preponderance 51% to 49%.

In this study we noted that there were more singles than married. It couid be that SCA patients are stagnated in terms of marriage as they may be stigmatized as a result of their status. Marriage may modulate SCA presentation because of the extra care that comes from the spouses but it can also worsen the condition if the marriage comes with added stress.

As regards the distribution of the complications, the most common complication was chronic osteomyelitis. SCA patients have increased susceptibility to infections as a result of abnormalities in the defense mechanisms, resulting from functional hyposplenism," an abnormality in the alternative pathway of complement activities, [11] and defective neutrophil function. [12] Salmonella, Staphylococci, Pneumococci, Haemophilus and E. coli have been postulated as the incriminating factors towards increased frequency of infections.

Chronic renal failure was the second most common complication in the study centre. The renal medulla is susceptible to damage in SCA because of its unique environment characterized by anoxia, hyperosmolarity and low pH which predisposes it to sickling. [13] Renal damage results from chronic vaso occlusion of the glomerular apparatus and subsequent ischaemia and necrosis of the renal tissue. Chronic renal failure due to sickle cell nephropathy-manifests itself with hypertension (high blood pressure), proteinuria (protein loss in the urine), haematuria (loss of red blood cells in urine) and worsened anaemia. If it progresses to end-stage renal failure, it carries a poor prognosis. [14]

Chronic leg ulcers (CLU) and cholelithiasis followed. In our earlier study, we noted that CLU is the commonest cutaneous manifestation of SCA [15]. The prevalence of CLU in this study (11.2%) is less than the report from Jamaica (75%).16 We also noted that a lower stable haemoglobin, ignorance and poverty played important role in worsening chronic leg ulcers in sickle cell disease. Cholelithiasis results from the increased haemolysis and formation of pigment stone in this group of patients. In the UK, Bond et al" reported that 58% of SCA patients had gall stones. This is higher than the 11.2% that we noted in our study. Ware et al [18] advocated Laparoscopic cholecystectomy if patient has severe recurrent right upper quadrant pain or an episode of cholecystitis, common duct obstruction or pancreatitis.

Avascular necrosis and acute chest syndrome were next in frequency. Akinyoola et al [19] in Ile-ife, Nigeria reported that Sixty-six (15.9%) patients 35 males (53%) and 31 females (47%) had clinical and radiologic features of avascular necrosis (AVN) of the femoral head. This was higher than the 4.0% that we noted in our study. They recommended regular screening of patients with sickle cell disorder for AVN and regular community educational programmes for early diagnosis. In Kuwait, Marouf et al [20] reported the prevalence rate of (48.6%) of varying degrees of avascular necrosis of the femoral head (AVNFH). The high prevalence was as a result of better diagnostic tools including MRI which was able to detect mild cases.

Acute chest syndrome was present in 6% of 102 adolescents and adults in a monocentric study conducted in Lagos, Nigeria". However, studies done elsewhere have shown that it is a common complication that occurs in about 50% of patients with SCA and is recurrent in about 80% of them. [22,23]

These values both within and outside Nigeria were higher than the 4.0% that we noted in this study.

Stroke and pulmonary embolism followed in frequency (2.4%) in our study. Wang" in Memphis reported that overt stroke occurs in 1 in 10 (10%) children with haemoglobin SS. This was higher than we reported in our study, although our study was conducted among adult SCA patients not children. The observed frequency of stroke in SCA patients varies from 6% to as high as 34% in different reports."

Central nervous system involvement in sickle cell diseases is common with obstruction of small or medium-sized arteries causing ischemia and infarction. Patients presenting with acute neurologic events should always be admitted. The use of trans cranial Doppler ultra-sonography screening allows the identification of patients at high risk for clinical stroke as well as stroke prevention by chronic transfusion. [24]

This study revealed that the average haemoglobin concentrations were high (more than 7.0gldl) in those that had acute chest syndrome, pulmonary embolism and AVN and low (less than 5.0gldl) in those that had cholelithiasis, chronic renal failure and stroke. These findings were in keeping with what has been reported widely in literature. [1]

Some complications were not noted in this study; notable among them were pulmonary hypertension and ocular complications. This was likely due to low index of suspicion among the physicians and also lack of facilities for accurate diagnosis.

Conclusion

The most common complication ofSCA patients in the study area was chronic osteomyelitis. The pattern of complications was generally lower than what was reported in other parts of the world. Some complications were not recorded e.g. pulmonary hypertension and ocular complications, probably as a result oflow index of suspicion and lack of adequate facilities to make correct diagnosis.

References

1. Ashutosh Lal and Elliott P Vichinsky. Sickle Cell Disease. In Postgraduate Haematology. Blackwell Publishing Ltd. ISBN 1-4051-0821-5. 2005: 104-118
2. Ballas SK. Neurocognitive complications in Sickle Cell Anaemia in Adult, JAMA2010; 303: 186-90
3. Smith JA. Bone disorders in sickle cell disease. Hematol Oncol Clin NorthAm, 1996; 10: 1351-4.
4. Eckman JR. Leg ulcers in sickle cell disease. Hematol Oncol Clin North Am, 1996; 10: 1333.-44.
5. Powars DR, Johnson CS. Priapism. Hematol Oncol Clin North Am, 1996; 10: 1363-72.
6. Chijioke A ,Kolo PM. The Longevity anti 'Clinical Pattern of Adult Sickle Cell Anaemia in Ilorin. Eur J ofSc Res.2009: 32: 528-532.
7. Platt OS, Brambilla DJ, Rosse WF, Milner PF, Castro O, Steinberg MH, Klug PP. Mortality in sickle cell disease. Life expectancy and risk factors for early death. N Engl J Med. 1994;330: 1639-44.
8. George 10, Frank-Briggs AI, and Ihezie CO. Childhood Osteomyelitis: A five-year analysis of patients with sickle cell anaemia in Port Harcourt, Nigeria. Pak J Med Sci 2011;27: 107-109
9. Udezue E, Abdel MG. Differences between males and females in adult sickle cell pain crisis in eastern Saudi Arabia. Ann Saudi Med 24: 179-182
10. Bahebeck J, Atangana R, Techa A, Monny-Lobe M, Sosso M, Hoffmeyer P. Relative rates and features of musculoskeletal complications in adult sicklers. Acta Orthop Belg, 2004;70: 107-111.
11. Almeida A, Roberts I. Bone involvement in sickle cell disease. Br J Haematol, 2005;129:482-490.
12. Piehl FC, Davis RJ, Prugh SI. Osteomyelitis in sickle cell disease. J Pediatr Orthop, 1993;13:225-227.
13. Saborio P, Schiemann n. Sickle Cell Nephropathy. Jam Soc Nephrol, 1999 ;10: 187,
14. Powars DR, Elliott-Mills DD, Chan L, et al. Chronic renal failure in sickle cell disease: risk factors, clinical course, and mortality. Ann. Intern. Med, 1991; 115 : 614-20.
15. Bazuaye GN, Nwannadi AI, Olayemi EE. Leg Ulcers In Adult Sickle Cell Disease Patients In Benin City Nigeria. Gomal J ofMed Sci, 2010; 8.
16. Serjeant GR. Leg ulceration in homozygous sickle cell disease in Jamaica. International aspects of sickle cell disease. Proceeding of the international conference on sickle cell disease. A World Health problem. Washington DC, 1976. p. 103.
17. Bond LR, Hatty SR, Horn MEC, et al.

Gallstones in sickle cell disease in the United Kingdom. Br Med J, 1987;295 :234-236.

18. Ware RE, Kinney TR, Casey JR~Pappas TN, Myers WC. Laparoscopic cholecystectomy in young patients with sickle hemoglobinopathies. J Pediatr, 1992 ;120 :58-61.
19. Akinyoola AL, Adediran lA, Asaleye CM. Avascular necrosis of the femoral head in sickle cell disease in Nigeria: a retrospective study. Niger Postgrad Med J,2007;14:217-20.
20. Marouf R, Gupta R, Haider MZ, Al-Wazzan H, Adekile AD. 'Avascular necrosis of the femoral head in adult Kuwaiti sickle cell disease patients. Acta Haematol, 2003;110: 11-5.
21. Ibidapo, MO, Akinyanju, OO. Acute sickle cell syndromes in Nigerian adults. Clin. Lab. Haem,2000; 22,151-154.
22. Golden C, Styles L, Vichinsky E. Acute chest syndrome and sickle cell disease. CurroOpin. Haematol, 1998; 5, 89-92.
23. Leong CS, Stark P. Thoracic manifestations of sickle cell disease. J. Thorac. Imaging, 1998; 13, 128-134.
24. Wang WC. Central nervous system complications of sickle cell disease in children: an overview. Child Neuropsychol,2007;13:103-19.
25. Samaik, Sharada AM, Lusher BS, Jeanne MM. Neurological complications of sickle cell anemia.J of Ped HematiOnco, 1982- 4