Musculoskeletal Complications Of Sickle Cell Anaemia And Their Management Approaches In Makurdi, Nigeria

Abstract

Background:Musculoskeletal complications are responsible for up to 80% of indications for presentation to the hospital by sicklers during their life time.It is important to know when to expect the complications and the treatment options available.

Methods:A retrospective study was conducted involving all sickle cell anaemia patients treated between June 2012 and May 2017 at Benue State University Teaching Hospital (BSUTH), Makurdi, Nigeria. The data collected included age, sex, complications, anatomic site, stage of disease and treatment.Data obtained were analyzed using the software Statistical Package for Social Sciences for Windows version 15.0 (SPSS, Inc; Chicago, Illinois) and presented as frequencies (%) and mean values (SD) as appropriate, $P < 0.05$ was taken as statistically significant.

Results:Thirty one out of 85 sicklers presented with 53 musculoskeletal complications giving a prevalence rate of 36.4%.There were 18 males and 13 females with mean age of 14.2±1.03 years. Those ≤ 20 years had more complications than those 21years and above, P=0.0001 .The femur was involved in 20(37.7%) and avascular necrosis 17(20.1%) was the most common complication followed by septic arthritis13(15.3%) and chronic osteomyelitis8(9.4%).The mean Haemoglobin concentration 7.5±0.5mg/dl of the patients with AVN was higher than those without it, P=0.02. Conservative treatment was employed in treatment of 40(75.7%) of the complications while others had arthrotomies and arthroplasties.

Conclusion:Avascular necrosis,osteomyelitis and septic arthritis are the most common orthopaedic complication among sicklers in Makurdi.They occur predominantly in the younger age group and many are amenable to conservative treatment .

Keywords:Sickle cell anaemia,Musculoskeletal, Arthroplasty,Nigeria

1.INTRODUCTION

Sickle cell disease(SCD) is an autosomal recessive haematological genetic disorder in which there is an abnormality in the synthesis of the beta globin chain of haemoglobin at position 6.[1] Glutamic acid is replaced by valine at this position leading to the production of an abnormal haemoglobin (HbS) that assumes a sickle shape when exposed to adverse conditions like hypoxia,dehydration or infection.The sickle shaped cells occlude capillaries and other small caliber vessels in end organs leading to vasoocclusive crisis, ischaemia, infarction and osteonecrosis especially in the femoral head and humeral head. Sickle cell anaemia (SCA) is said to occur when

there is homozygote HbSS or composite heterozygote HbSC.[2]It is mainly seen inblack populationsin Africa or among Africans in the diaspora.[3]It was first recognized by Herrick[4]in 1910 when he described abnormal sickle-shaped cells in an anaemic patient of Negroid origin. Pauling et al[5] later on discovered the presence of abnormal haemoglobin in patients with sickle cell disease in 1949.[3]

Musculoskeletal complications are responsible for up to 80% of indications for presentation in the hospital by SCA patients during their life time.[6-10]Their main complaint is pain which arises either acutely following skeletal or soft tissue infarction or may present as chronic pain from avascular necrosis(AVN) of bone at various joints.[11]

Sickle cell anaemia patients present to the Orthopaedic surgeon with a spectrum of manifestations ranging from dactylitis in infancy to osteomyelitis, septic arthritis,avascular necrosis,vertebral collapse, protrusion acetabuli, malleolar ulcers[1] and pathological fractures. Some of thecomplications of SCA like dactylitis are treated conservatively with analgesics, antibiotics, rehydration and sometimes blood transfusion. However, septic arthritis usually requires arthrotomy and adequate drainage while acute osteomyelitis is treated by performing incision and drainage with or without bone drilling[12]

Avascular necrosis (AVN) of the femoral head is one of the most serious and incapacitating complications seen in young patients suffering from sickle cell anemia[13] In Nigeria, it is not common to find this bone complication in children but it affects almost 30% of sicklers who are over the age of 12 years.[14]The treatment of AVN of the femoral head depends on the Ficat and Arlet staging. This includes the use of analgesics and non-weight-bearing crutches or core decompression in the early stages(stage I and II) particularly when it is unilateral. Proximal femoral osteotomy with or without soft tissue release and hip arthroplasty is considered for late disease (Stage III and IV). Various types of hip arthroplasty have been recommended. They include hemiarthroplasty, bipolar arthroplasty, and total hip replacement.[6,15,16]

There are few studies in the West African sub-region documenting the various treatment options for the plethora of musculoskeletal complications in SCA.This study has been designed to identify the various musculoskeletal complications and to determine the available treatment options in our locality.

2. MATERIALS AND METHODS

2.1 Setting

The study was conducted at Benue State University Teaching Hospital (BSUTH) Makurdi, Benue State, Nigeria. The state is located in the north central region of Nigeria. It has a population of 4.2million. Benue State University Teaching Hospital (BSUTH) is a relatively young State-owned teaching hospital that came into full operation in April 2012.

2.2 Study Population

A retrospective study was conducted over a 5year period between June 2012 and May 2017 at BSUTH, Makurdi, Nigeria. It is one the two main referral tertiary health facilities in Makurdi, Benue State, Nigeria. Demographic and clinical data were extracted from hospital records .The data included age, sex, complications, anatomic site, stage of disease and treatment modality.Ethical clearance for the study was obtained from the Health Research and Ethics Committee(HREC) of the hospital

2.2.1 Musculoskeletal complications

Musculoskeletal complications were defined as any problem in a sickler affecting the bones and joints and/or their associated soft tissues that are traceable to their genotype.[3]

2.2.2 Avascular necrosis

Diagnosis of AVN was based on clinical evaluation and confirmation using radiographs.Classification of AVN was by Ficat and Arlet classification.

2.2.3 Osteomyelitis

Diagnosis of osteomyelitis was by clinical features (fever, bone pain and tenderness) and confirmed by radiological evidence in the affected bone(sequestrum,cloaca and involucrum).

2.2.4 Inclusion Criteria

All patients seen in the clinics or admitted in the hospital with HbSS genotype symptoms traceable to their genotype were included in the study.

2.2.5 Exclusion Criteria

Patients with incomplete data and those with congenital musculoskeletal anomalies or trauma from accidents were excluded.

2.3 Data Analysis

Data obtained was analyzed using the software Statistical Package for Social Sciences for Windows version 15.0 (SPSS, Inc; Chicago, Illinois). Data were presented as frequencies (%) and mean values (SD) as appropriate, and compared using either the chi square test (for proportions) or student's T test for mean values. $P < 0.05$ was taken as statistically significant.

3.RESULTS

A total of 85 patients with sickle cell anaemia (SCA) comprising of 47 males and 38 females and a median age of 13 years (range 5months to 51years) were seen during the period under review. Thirty one patients (31/85) presented with musculoskeletal complications giving a prevalence rate of 36.4%.

The were 18 males and 13 females among those with musculoskeletal complications .Their mean age was 14.2±1.03 years and the range was 18month to 34years(Table 1).The mean age of those without the complications was 14.01±10.5years.There was no significant difference between males and females presenting with musculoskeletal complications ,p=0.23. The mean Haemoglobin(Hb) concentration at presentation of those from rural areas was 5.06±1.3mg/dl while those from Urban areas had a mean Hb of7.2±1.4mg/dl, p=0.008.The mean Hb of the patients with AVN was 7.5±0.5mg/dl while those with other complications was 6.08±1.8mg/dl, p=0.02.Common musculoskeletal symptoms involving pains in the upper and lower limbs from vaso occlusive crisis was seen in 47 out of the 85 sicklers treated (55.1%).

There were a total of 53 musculoskeletal complications occurring in 31 patients with 17 of the patients presenting with more than one complication.The frequency of the various musculoskeletal complications is shown in Table 2 . The relationship between the musculoskeletal complications and patients' ages is shown in (Table3).Those ≤ 20 years had more complications than those 21years and above, p=0.0001 .The femur was involved in 20(37.7%)complications followed by tibia 8(15.1%), elbow joint7(13.2%), shoulder 4(7.5%), feet 3(5.6%) and ulna2(3.8%) respectively. The Hip joint,spine,calcaneum and ankle were involved in 1(1.9%) of the complications each. Conservative treatment was employed in treatment of 40(75.7%) of the complications (Table 4).Septic arthritis was the second most common musculoskeletal complication accounting for 13(15.3%). Patients with osteomyelitis 8(9.4%) and dactylitis 2(2.4%) were mostly within the first decade of life .Malleolar ulcers were the fourth common complication in our study and was found in 7(8.2%)of sicklers. Vertebral collapse was found to be uncommon 2(2.4%).

Seventeen patients 17(20%) had AVN of the femoral head Ficat and Arlet Stage II= 2 (2.4%),StageIII =10(11.8%) and Stage IV= 5(5.9%) respectively.The average age of the patients with AVN was 19.4 years.One patient had bilateral cementless total hip arthroplasty(THA) for bilateral AVN (Stage IV) of the hips .This was done sequentially four weeks apart.One other patient had bipolar hemiarthroplasty for AVN(Stage III) of his left hip. A second hemiarthroplasty was done with an Austin Moore endoprosthesis. Girdlestone excision arthroplasty was done for two patients who had septic arthritis with dislocation of the hip.

4.DISCUSSION

The study showed that the prevalence of musculoskeletal complications among patients with sickle cell anaemia in Makurdi is 36.4%.This is similar 32.1% reported in a study done in Nigeria [17] but higher than 16% reported in Belgium.[18]There may be environmental factors playing a role in the lower musculoskeletal complication rates in Europe because of the relatively better standard of living.[19]The mean haemoglobin concentration of our sicklers from rural areas was found at presentation to be significantly lower than those from urban areas .This also suggests that environmental and socioeconomic factors may contribute to the manifestation of the musculoskeletal complications in sickle cell anaemia.

The most common musculoskeletal complication among SCA patients in Makurdi was avascular necrosis of femoral head diagnosed in 20% of the patients .It is similar to 17.8% documented in a study in Nigeria and 20% reported in France where 457 sickle cell disease patients were followed up for ten years.[20,21]Younger age was a predictor of musculoskeletal complications as they were significantly more common in patients who were 20 years or less .This is in agreement with other studies.[20,22,23]There was a slight male preponderance to the complications in our study which was not statistically significant but there are many other studies that have also reported increased risk for musculoskeletal complications among male SCA patients.[1,20,24]

The Prevalence of AVN in our study was found to be highest in the second and third decades of life .The mean age for AVN was 19.4 years in our study and this agrees with 19.3years documented at National Orthopaedic Hospital Enugu and also 19years in a study conducted in Belgium.[1,18]This is because AVN results from the repeated episodes of vaso-occlusive crisis and bone infarction as the child grows into adolescence and adulthood.The mean haemoglobin concentration for patients with AVN was found to be significantly higher than patients with other musculoskeletal complications. A similar finding has been documented by other studies.[19, 20]However, a study by Akinyoola and his colleagues found no significant difference.[25]

Most of the patients were treated conservatively with analgesics and bed rest at home because of financial constraints. Among those with late AVN who could afford surgery, two had hemiarthroplasty(one bipolar and one Austin Moore endoprosthesis).One patient had bilateral cementless total hip arthroplasty(THA).The two patients who had hemiarthroplasties had no post-operative complications, however the patient who had THA had reactionary haemorrhage and superficial wound infection after operation in the first hip.He was resuscitated and the infection controlled before the second hip was operated. Complications during THA for sicklers are common so it is advocated that the surgeon should anticipate and arm himself against them. This could mean ensuring a preoperative Haemoglobin(Hb) level of 8–10 gm/dl and a preoperative HbS load decrease to <30%.[26]This can be achieved by giving aggressive preoperative transfusions or using plasmapheresis and exchange transfusion where the facilities exist.[26,27]This reduces the chances of development of postoperative acute sickle cell(SC) crisis especially in patients who have a history of acute SC crisis, acute chest syndrome, previous cerebrovascular accidents and Hb<5 gm/dl.

Intraoperative medullary canal sclerosis was cleared using intramedullary hand reamers but high speed burrs are preferable. The operating room temperature should be maintained at 220C and the patient kept hydrated and warm using a bair hugger blanket to prevent hypothermia.[26]The Patients are given warm intravenous fluids. Cementless implants are preferable to cemented implant because of ease of revision. Suction drains should be placed in all patients. Some of these ideals are difficult to achieve in developing economies like ours where there is dearth of infrastructure. However, we ensured the minimum standards were maintained to achieve good results.

One of patient had core decompression for AVN Ficat and Arlet Stage II disease.Septic arthritis was the second most common orthopaedic complication. It was found to be most frequent within the first decade of life.Six of the patients had arthrotomy after resuscitation but the others either resolved after administration of antibiotics or left because of financial constraints.

Patients with osteomyelitis and dactylitis were mostly within the first decade of life.This has been recorded in other studies as well.[20,23,28]The reason for the predilection among the younger patients is thought to be due to a combination of expanded marrow together with high oxygen demand and sluggish circulation resulting in infarction that acts as foci for infection.[26,29]All the patients were treated conservatively with antibiotics, analgesics, blood and intravenous fluid transfusion.

Malleolar ulcers were the fourth common complication in our study and was found in 8.2% of sicklers. This agrees with the study in France where 5.2% was recorded.[21]However in another study in Nigeria it was the most common complication accounting for 29.4%.[20]The ulcers were treated by wound debridement, antibiotics and skin grafting .

Vertebral collapse was found to be uncommon.It was treated with analgesics and spinal support in order to prevent neurological deficit.Primary prevention of musculoskeletal complications of SCA still depends on genetic counseling.Current treatment options in the treatment of SCA which may lead to the eventual reduction in these complications include the use of hydroxyurea,transfusion and exchange transfusion programmes and ultimately bone marrow transplantation. An increasing number of children within the age range of seven to ten years are receiving allogeneic bone marrow grafts from their HLA-matched relatives as curative treatment of their sickle cell disease.[30] Ablation of the recipient bone marrow is accomplished in this procedure with busulphan and cyclophosphamide without the need for total body irradiation.[30]

5.CONCLUSION

In conclusion,avascular necrosis,osteomyelitis and septic arthritis are the most common musculoskeletal complication among SCA patients in Makurdi.They occur predominantly in the younger age group and are amenable to conservative treatment in most of the cases.

ETHICAL APPROVAL

As per international standard or university standard, written approval of ethics committee has been collected preserved by the authors.

Consent Disclaimer:

As per international standard or university standard, patient's consent has been collected and preserved by the authors.

REFERENCES

1. Onyemaechi NO, Enweani UN, Maduka CO. Musculoskeletal complications of sickle cell disease in Enugu, Nigeria.Niger J Med. 2011;20(4):456-61.
2. Adedeji MO: The body defences against infection in SCA. Nig Med Pract. 1989; 17: 99-102.
3. Balogun RA, Obalum DC, Giwa SO, Adekoya-Cole TO, Ogo CN, Enweluzo GO. Spectrum of musculo-skeletal disorders in sickle cell disease in Lagos, Nigeria. J OrthopSurg Res. 2010;5:2
4. Herrick JB: Perculiar elongated and sickle-shaped red blood corpuscles in a case of severe anaemia. Trans Assoc Am Physicians. 1910; 25: 553-561.
5. Pauling L, Itano HA, Singer SJ: Sickle cell anaemia, a molecular disease. Science. 1949; 110: 543-10
6. Badhulkar SS, Pande K, Badhulkur S: The hand-foot syndrome in sickle cell haemoglobinopathy. J Bone and Joint Surg (Br). 1995; 77B: 310-312.
7. .Acurio MT, Friedman RJ: Hip Arthroplasty in patients with sickle cell Haemoglobinopathy. J Bone and Joint Surg (Br). 1992;71B: 367-371
8. Harkess JW: Fractures. Edited by: Rockwood CA, Green DP.1975, JB Lippincott. Philadelphia, 1-2. 1
9. Fagade OO, Salawu L, Owotade FJ, David-West B, Durosinmi MA: Osteomyelitis of the mandible in a Nigerian with sickle cell HBC Disease - a case report. The Nig Postgrad Med J. 1997;4: 25-26.
10. Omojola MC, Annobil S, Adzaku F, Addae SK, Mohammed S: Bone changes in SCA. East Afr Med J. 1993; 70: 154-158
11. Ebong WW: Pathological fracture complicating long bone osteomyelitis in patients with SCD. J PaedOrthop. 1986; 6: 177-81
12. Unkila-Kallis L, Kallis MJT, Peltola H. The usefulness of Creactiveprotein levels in the identification of concurrent septic arthritis in children who have acute haematogenous osteomyelitis. J Bone Joint Surg. 1994; 76: 848–53.
13. Bishop AR, Roberson JR, Eckman, JR, et al. Total hip arthroplasty in patients who have sickle cell hemoglobinopathy. JBoneJSurg. 1988;70(6):853-855
14. Cockshott WP. Hemoglobin SC disease. J Fac Radiol.1958;9: 211-216.
15. Bennett OM, Namnyak SS. Bone and joint manifestation of sickle cell anemia. JBone JSurg.1990;72:494-499.
16. Alonge,T.O,Shokunbi,W.A. The choice of arthroplasty for secondary osteoarthritis of the hip joint following avascular necrosis of the femoral head in sicklers. J Natl Med Assoc. 2004;96:678-681.
17. .Chinawa JM, Chukwu,BFIkefuna,AN,Emodi IJ. Musculoskeletal Complications Among Children with Sickle Cell Admitted in University of Nigeria Teaching Hospital Ituku - Ozalla Enugu: A 58 Month Review.Ann Med Health Sci Res. 2013; 3: 564–567.

18. De Gheldere, A, Docquier PL, Mousny M, RomboutsJJ.Orthopaedic complications associated with sickle-cell disease*ActaOrthop. Belg.*, 2006;72: 741-747
19. Clare A, FitzHenley M, Harris J, Hambleton I, Serjeant GR. Chronic leg ulceration inhomozygous sickle cell disease: the role of venous incompetence. British Journal ofHaematology. 2002;119:567–571.
20. MaduKA,UbesieAC,MaduAJ,Duru AN. Pattern and Risk Factors for Musculoskeletal Complications of Sickle Cell Anaemia in South-East Nigeria: A Retrospective Study. International Journal of TROPICAL DISEASE& Health 2013;3: 175-18
21. Halabi-Tawil M, Lionnet F, Girot R, Bachmeyer C, Lévy PP, Aractingi S. Sickle cell legulcers: a frequently disabling complication and a marker of severity. Br J Dermatol. 2008;158:339-4
22. Atkins BL, Price EH, Tillyer L, Novelli V, Evans J. Salmonella osteomyelitis in sicklecell disease children in the East End of London. J Infect. 1997;34:133-138.
23. Balogun RA, Obalum DC, Giwa SO, Adekoya-Cole TO, Ogo CN, Enweluzo GO.Spectrum of musculo-skeletal disorders in sickle cell disease in Lagos, Nigeria. JOrthopSurg Res. 2010; 5:2.
24. Minniti CP, Eckman J, Sebastiani P, Steinberg MH, Ballas SK**.** Leg ulcers in sickle celldisease. Am J Hematol. 2010;85(10):831-833.
25. Akinyoola AL, Adediran IA, Asaleye CM, Bolarinwa AR. Risk factors for osteonecrosisof the femoral head in patients with sickle cell disease. International Orthopaedics (SICOT). 2009;33:923–926
26. GulatiY,Sharma M ,Bharti B, BahlV,BohraI,Goswani A,Short term results of cementless total hip arthroplasty in sicklers.Indian J Orthop. 2015; 49: 447–451.
27. Harris WH. Traumatic arthritis of the hip after dislocation and acetabular fractures: Treatment by mold arthroplasty. An end-result study using a new method of result evaluation. J Bone Joint Surg Am. 1969;51:737–55
28. Ebong WW. Acute osteomyelitis in Nigerians with sickle cell disease. Ann Rheum Dis.1986;45:911-915.
29. Booth C, Inusa B, Obaro SK. Infection in sickle cell disease: a review. International Journal of Infectious Diseases. 2010;14:2-12.
30. Castro O.Management of sickle cell disease:Recent advances and controversies.British Journal Haematology.1999;107:2-11.

Table 1 Showing Age Distribution of Sicklers with musculoskeletal Complications in Makurdi.

Age	Frequency	Percentage
≤10	11	35.4

11-20	12	38.7
21-30	6	19.4
31- 40	2	6.5
	31	100

Table 2.Showing Distribution of Musculoskeletal Complications in Sickle Cell Anaemia Patients in Makurdi.

Complications	Number N=85	%
Avascular necrosis head of femur	17	20
Septic arthritis	13	15.3
Chronic osteomyelitis	8	9.4
Malleolar ulcer	7	8.2
Acute osteomyelitis	4	4.7
Vertebral collapse	2	2.4
Dactylitis	2	2.4

Table 3 Showing the Distribution of Musculoskeletal Complications among the various age groups..

	Age Range				
Complications	≤10	11-20	21-30	31- 40	Total
AVN Head of Femur	-	11	6	1	17
Septic Arthritis	11	2	-	-	13
Chronic Osteomyelitis	4	2	1	-	8
Malleolar Ulcer	-	4	3	-	7

Acute osteomyelitis	4	-	-	-	4
Vertebral Collapse	-	-	2	-	2
Dactylitis	2	-	-	-	2
Total	21	19	12	1	53
%	39.6%	35.8%	22.7%	1.9%	100%

AVN= Avascular necrosis head of femur

Table 4 ShowingTreatment Modalities for Orthopaedic Complications of Sickle Cell Anaemia in Makurdi.

Complication	**Frequency**	**Percentage**
Conservative	40	75.7
Arthrotomy	6	11.5
GirdlestoneArthroplasty	2	3.8
Hemiarthroplasty	2	3.8
Total Hip arthroplasty	2	3.8
Core Decompression	1	1.9
	53	100

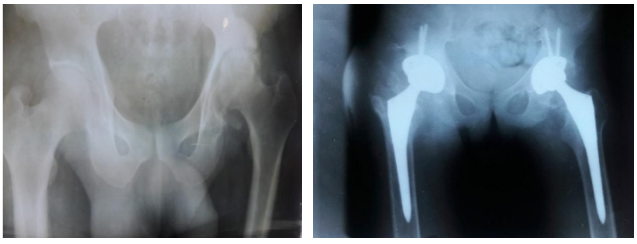

Figure A and B.Showing Pre-operative and post operative radiographs of a patient with bilateral Total hip arthroplasty following avascular n