HEMOGLOBINOPATHY AND PATTERN OF MUSCULOSKELETAL INFECTION IN CHILDREN

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Background: The bacterial pathogens associated with osteomyelitis in patients with hemoglobinopathy (HbSS) are controversial. There is insufficient data on the common musculoskeletal (MSS) infections in patients with hemoglobinopathies and the associated bacterial pathogens in Nigeria.

Objectives: To identify the common MSS infections in children and the associated bacterial pathogens, especially in those with abnormal hemoglobin genotypes.

Methods: A retrospective case review was done of pediatric and adolescent patients admitted with bone and soft tissue infections over a seven-year period in a Nigerian teaching hospital.

Results: One-hundred-nineteen patients were studied, with mean age 7.9±5.6 years and male–female ratio of 1.3:1. Out of 78 patients with known genotype, 62.8% had HbAA, 20.5% HbSS, 9% HbAS, and 7.7% HbAC. The most common MSS infections were osteomyelitis (64.7%), pyomyositis (17.6%), and septic arthritis (10.1%). Others were cellulitis (5.9%), tuberculous arthritis (0.8%), and necrotizing fasciitis (0.8%).

Staphylococcus aureus (S. aureus) was isolated from 62% of chronic osteomyelitis (COM) and 58% of pyomyositis, while Gram-negative bacilli accounted for 34% and 42%, respectively. S. aureus was isolated from 63% of patients with HbAA, 40% with HbSS, 58% with HbAS, and 58% with HbAC, while Gram-negative bacilli accounted for 33%, 60%, 33%, and 33%, respectively.

Osteomyelitis and pyomyositis appear to be similarly common in patients with and without HbSS (RR 1.29; 95% CI 0.47–3.50). Osteomyelitis and soft tissue infections in general also appear to be equally common in them (RR 1.16; 95% CI 0.39–4.11). However, osteomyelitis appears to be more common among patients with HbSS than those with HbAA (RR 2.29; 95% CI 0.58–8.99) and those with other hemoglobinopathies (RR 2.23; 95% CI 0.66–7.49)

Conclusions: Osteomyelitis, pyomyositis and septic arthritis are common MSS infections in hospitalized pediatric and adolescent patients, while tuberculous arthritis is uncommon. The most common bacterial pathogen in these infections is S. aureus—even in patients with HbSS and other hemoglobinopathies. Gram-negative bacilli are important causes of MSS infections in hospitalized children with HbSS. HbSS may be an independent risk factor for osteomyelitis in these patients. (*J Natl Med Assoc.* 2004;96:224–228.)

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INTRODUCTION

Bacterial MSS infections—including osteomyelitis, pyomyositis, and pyogenic arthritis, among others—are important causes of morbidity in children. Morbidity in these conditions may be

Table 1. Clinical and Demographic Features of the 119 Patients

Number (%)	Age
<13 years	57
13–18 years	62
Sex	
Male	68 (57.1)
Female	51 (42.9)
Genotype	
HbAA	49 (62.8)
HbSS	16 (20.5)
HbAS	7 (9)
HbAC	6 (7.7)
Signs and Symptoms	
Pain	83 (69.7)
Swelling	79 (66.4)
Tenderness	69 (58)
Sinus	31 (26.1)
Ulcer	13 (10.9)
Limp	4 (3.4)
Temperature	
Mean	38.6°C±0.7°C
Range	37.4°C–40.5°C

increased by hemoglobinopathies.

Sickle cell disease (SCD) is a genetic disorder that is known to be associated with an increased susceptibility to bacterial infections. Many reasons have been adduced for this. These include a weakness in phagocytic and chemotactic activities of polymorphonuclear leucocytes, functional hyposplenism, defective opsonization, and recurrent ischemia[1-3]. The MSS system is a major site of involvement with vasoocclusive episodes in sickle cell hemoglobinopathies[4]. This propensity for decreased perfusion may increase the risk of bacterial invasion of these tissues in children suffering from SCD.

The most common bacterial pathogen in osteomyelitis in patients with SCD is controversial. Salmonella sp is usually considered the most prevalent organism associated with osteomyelitis in SCD[5-7]. However, other reports have shown that Salmonella osteomyelitis may no longer be common[8,9] in this condition. On the other hand, clinical experience has also shown that Gram-negative bacilli in orthopedic infections are increasing (unpublished data). This is supported by the report of Aken'Ova et al.[9] in which 48% of the isolated organisms in osteomyelitis were Gram-negative bacilli.

The aim of the present study is to analyze the pattern of bacterial MSS infections in hospitalized children with and without abnormal genotype, as seen in our hospital. Also, it is to identify the types of infections and the associated bacterial pathogens and differences, if any, in the pattern of these infections in children with and without hemoglobinopathies, in a tertiary hospital setting.

Table 2. Prevalence of Musculoskeletal Infections and Bacterial Pathogens

Diagnosis	Number	%
Chronic osteomyelitis	64	53.8
Acute osteomyelitis	13	10.9
Pyomyositis	21	17.6
Cellulitis	7	5.9
Septic arthritis	12	10.1
Tuberculous arthritis	1	0.8
Necrotizing fasciitis	1	0.8
Bacterial Isolate		
Staphylococcus aureus	38	47.5
Klebsiella sp	11	13.8
Pseudomonas sp	9	11.3
Proteus sp	5	6.3
Non hemolytic streptococcus	2	2.5
E. coli	1	1.3
No growth	14	17.5
Total	**80**	**100**

Patients and Methods

This study was carried out at the Olabisi Onabanjo University Teaching Hospital, Sagamu, Nigeria. All pediatric and adolescent patients admitted between January 1996 and December 2002 were identified from the admission records of the orthopedic and pediatric services. These were compared with the central medical records to ensure completeness of identification. All patients with bone and soft tissue infections were then selected. Sociodemographic data as well as data of clinical presentation, genotype, bacterial isolates, and hematological profile were studied. Specimens for bacteriological studies were swabs/aspirates of pus from wounds, sinus, or ulcer. Anaerobic cultures were not done during the study period.

No patient had HIV infection. Blood cultures were excluded from the analysis since blood stream infection (BSI) was not a subject of the present study. Diagnosis and differentiation between acute and chronic osteomyelitis (COM) were both clinical and radiological.

Table 3. Distribution of Bacterial Pathogens by Genotype

	Bacterial Pathogens						
Genotype	*S. aureus*	*Pseudomonas*	*Klebsiella*	*E. coli*	*Proteus*	*Nonhem. Str.*	*No growth*
HbAA	17	4	5	0	0	1	9
HbSS	4	3	1	1	1	0	2
HbAS	4	2	0	0	0	0	0
HbAC	3	0	1	0	1	1	1
Total	**28**	**9**	**7**	**1**	**2**	**2**	**12**

S. aureus: Staphylococcus aureus
E. coli: Escherichia coli
Nonhem str: Nonhemolytic streptococcus

Statistical analysis was done with Epi Info version 6 (Centers for Disease Control). Observed differences among patients groups were compared using Fisher's exact test. A p value less than 0.05 was taken to be significant.

Results

A total of 119 patients were studied. Their mean age was 7.9±5.6 years. Sixty-eight (57.1%) of them were males and 51 (42.9%) were females, giving a male–female ratio of 1.3:1 As shown in Table 1, among 78 patients whose genotype were determined, 49 (62.8%) had hemoglobin genotype AA (HbAA) and 16 (20.5%) had HbSS, while seven (9%) and six (7.7%) had HbAS and HbAC, respectively.

The most common MSS infection was COM—53.8%. The least common were tuberculous arthritis and necrotizing fasciitis—one patient each—Table 2. Others include pyomyositis (17.6%), septic arthritis (10.1%), and cellulitis (5.9%). Septic arthritis affected the knee in 55.6% of patients, while the hip, elbow, and shoulder joints were affected in 22.2%, 11.1%, and 11.1%, respectively.

Sixty-six bacterial pathogens were isolated from 59 patients. Fifty-two were isolated in single cultures and 14 in mixed cultures. Staphylococcus aureus (S. aureus) was the most common pathogen—57.6% (38/66). Others were Klebsiella sp—16.7% (11/66), Pseudomonas sp—13.6% (9/66) and Escherichia coli (E. coli)—1.5% (1/66). S. aureus accounted for 62% (29/47) of the pathogens isolated in COM and 58% (7/12) in pyomyositis. On the other hand, Gram-negative bacilli accounted for 34% (16/47) and 42% (5/12) of these infections respectively. S. aureus was the most common single pathogen isolated from patients with HbAA—63% (17/27), HbSS—40% (4/10), and from those with HbAC and HbAS—58% (7/12). The prevalence of Gram-negative bacilli in these groups of patients was 33%, 60%, and 33%, respectively (Table 3).

Pain and swelling were the most frequent presenting complaint, occurring in 83 (69.7%) and 79 (66.4%) patients, respectively. Fever was present on admission in 42 patients. The mean temperature on admission was 38.6ºC±0.7ºC (range 37.4ºC–40.5ºC). Thirty-one (26%) patients presented with a discharging sinus, while 13 (10.9%) had an ulcer (Table 1). Radiographic evidence of COM was documented in 33 (51.6%) of the 64 patients with this condition. Total leucocyte count ranged between 2,700 and 26,390 per cumm (mean 8,796±5,056 per cumm). Erythrocyte sedimentation rate (ESR) on admission ranged from 2- to 80 mm/hour (mean 53±14 mm/hour).

Table 4 shows that COM was the most common MSS infection in all patients irrespective of genotype. It accounted for 63% (31/49) of the infections in those with HbAA, 50% (8/16) in those with HbSS, 57% (4/7) in those with HbAS, and 67% (4/6) in those with HbAC. Patients with hemoglobinopathies in general seem to be equally as likely as those with normal genotype to have osteomyelitis rather than pyomyositis—22/25 versus 35/42 (RR=1.29; 95% CI 0.47–3.50), P=0.4. Also they appear to be equally likely to have osteomyelitis compared with soft tissue infections generally, 22/29 versus 35/49 (RR=1.16; 95% CI 0.39–4.11), P=0.9. The likelihood of having osteomyelitis among hospitalized patients with HbSS is twice that of those with HbAA, 14/16 versus 35/49 (RR2.29; 95% CI 0.58–8.99) p=0.3. Also

Table 4. Distribution of MSS Infections by Genotype

	Genotype (%)				
Diagnosis	*HbAA*	*HbSS*	*HbAS*	*HbAC*	*Total*
Chronic osteomyelitis	31 (63.3)	8 (50)	4 (57)	4 (67)	47
Acute osteomyelitis	4 (8.2)	6 (38)	0	0	10
Pyomyositis	7 (14.3)	1 (6)	2 (29)	0	10
Cellulitis	3(6.1)	1 (6)	0	0	4
Septic arthritis	3 (6.1)	0	1 (14)	2 (33)	6
Necrotizing fasciitis	1(2.0)	0	0	0	1
Total	**49**	**16**	**7**	**6**	**78**

patients with HbSS are twice as likely, as those with the other hemoglobinopathies, to have osteomyelitis 14/16 versus 8/13 (RR=2.23; 95% CI 0.66–7.49) p=0.2. These differences are not statistically significant.

DISCUSSION

Bacterial infections of bone and its soft tissue envelope are serious disease conditions especially in communities where abnormal hemoglobin genotype is common. The prevalence of HbSS and HbAS in Nigeria is 1.6–2% and 25–30%, respectively[10,11]. Morbidity resulting from disabilities from some of these conditions may be life long. Mortality is also not infrequent. A review of death in the accident and emergency dept by Adesunkanmi et al.[12] showed that pyomyositis accounted for 14% of deaths in surgical nontrauma conditions.

Our results indicate that COM is the most common MSS infection for which these patients are hospitalized. This suggests that there exists a large burden of chronic MSS disease of infectious origin in children and may complicate the socioeconomic situation by contributing significantly to the rate of dropout from school with adverse social consequences. Continuous public education is required on the symptomatology of acute osteomyelitis and the need for prompt and adequate treatment to prevent chronicity.

The prevalence of pyogenic arthritis—12% in this report—suggests that it is not uncommon. It may actually predispose to osteoarthritis later in life. Involvement of the knee in 56% of affected patients may result in similar prevalence of knee involvement in adult osteoarthritis. This report also suggest that pyomyositis is not a common complication of SCD[13]. However, this is not true of sickle cell trait. Clinical experience in Nigeria has shown a worrisome level of antibiotic abuse. This may have contributed to the greater number of children with osteomyelitis and septic arthritis, compared with cellulites.

Our results support previous observation that S. aureus is the most common pathogen in osteomyelitis and pyomyositis[14-16]. Furthermore, S. aureus is the most prevalent individual pathogen in those infections with hemoglobinopathies in this African population. This is also consistent with the report of Nwadiaro et al.[8] on COM in SCD. Reports of Salmonella osteomyelitis are predominantly from outside the African continent[17,18]. It is possible that Salmonella osteomyelitis is common in environments where Salmonella infections are generally common. Gram-negative bacilli are important causes of MSS infections in children with HbSS, as indicated by the rate of 60% in this report. This supports the observation of a change in the trend of causative organisms[9].

This report indicates that hospitalized children with and without hemoglobinopathies have a similar risk of developing MSS infections. It is possible that environmental factors determine to a large extent who actually develops a MSS infection. HbSS, however, is likely to be an independent risk factor for bone and soft tissue infections in these patients.

From the foregoing, it can be concluded that tuberculous arthritis is uncommon in children, unlike osteomyelitis and pyomyositis. S. aureus is the most common bacterial pathogen in MSS infections in hospitalized children—even in those with abnormal genotypes. However, Gram-negative bacilli are important pathogens in patients with HbSS in particular and in those with other hemoglobinopathies in general. Hemoglobin SS is probably an independent risk factor for bone and soft tissue infections.

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