Bacterial osteomyelitis in major sickling haemoglobinopathies: geographic difference in pathogen prevalence

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Abstract
Background: Controversy exists about the bacterial pathogen that is most often associated with osteomyelitis in major sickling haemoglobinopathies, that is, HbSS, HbSC, and HbSthalassemia.
Objective: To determine the existence of regional or continental differences in the prevalence of bacterial pathogens associated with osteomyelitis in sickling haemoglobinopathies
Method: A meta-analysis is done of 11 year hospital data set and published studies in African Journals Online (Ajol) and Pubmed electronic databases on the subject.
Results: Fifteen studies including two hundred and eighty one bacterial pathogens from SubSaharan Africa, United States, Europe and the Middle East were analysed. There were 129 (45.9%) salmonellae, 82 (29.2%) Staphylococcus aureus, 55 (19.6%) other Gram negative bacilli (GNB) and 15 (5.3%) other Gram positive cocci (GPC). There were 117 isolates in the studies from Africa out of which salmonellae accounted for 21.4%, S. aureus 38.5%, other GNB 34.2% and other GPC 6%. In contrast, out of 110 isolates in the studies from the USA, salmonellae were 70%, S. aureus 16.4%, other GNB 9.1% and other GPC 4.5%. Salmonellae and S. aureus accounted for 37.9% and 62.1%; 64% and 4.9% in isolates from the Middle East and Europe respectively.
Conclusions: Salmonellae are the most common bacterial pathogens of osteomyelitis in major sickling haemoglobinopathies in the USA and Europe whereas Staphylococcus aureus is the most common pathogen in SubSaharan Africa and the Middle East. The worldwide prevalence of salmonella may be reducing while that of S. aureus may be increasing. Possible reasons for this observation are suggested.
Key words: haemoglobinopathy, osteomyelitis, sickle cell disease, bacteria, salmonella, staphylococcus aureus.
African Health Sciences 2006; 6(4): 236-239

Introduction

It is generally accepted that *Staphylococcus aureus* (S. aureus) is the most common organism associated with osteomyelitis[1]. However, controversy has existed for decades about the most prevalent bacterial pathogens associated with osteomyelitis in patients with major sickling haemoglobinopathies[2,3,4].

Givner et al[5] attempted to resolve the controversy by studying a patient population derived from 8 published articles on the subject and concluded that salmonellae are the most common pathogens. All the patients in his series were from the USA. A similar review by Burnett et al[6] showed that salmonella is the most common pathogen in patients with sickle cell disease (SCD) in both developing and in developed countries. Recent series found S. aureus to be the most common pathogen in osteomyelitis in SCD. Apparently, the controversy persists.

This study is aimed at identifying regional or continental variations, if any, in the prevalence of bacterial pathogens in osteomyelitis in patients with major sickling haemoglobinopathies and also to identify any change in the worldwide prevalence.

Methods

The data on all patients with osteomyelitis in our hospital between January 1994 and December 2004 were reviewed and information information extracted from their case records. These informations include haemoglobin genotype, isolated bacterial pathogen, and source of specimen for microbiologic studies. This database was then searched for those with major sickling haemoglobinopathies that is, HbSthalassemia, HbSS, HbSC, and confirmed with electrophoresis.

Published articles on the subject were also identified and reviewed using Pubmed (online version of Medline) and Ajol (African Journals Online) as well as

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local library collection of journals. Pubmed and Ajol were searched in February 2005 using the key words haemoglobinopathy and osteomyelitis, sickle cell disease and osteomyelitis, haemoglobin genotype and osteomyelitis. Abstracted data include the study population size, age range, hemoglobin genotypes, isolated bacterial pathogen and the source of specimen for bacteriology. All included published articles were on osteomyelitis and included data on the bacteriology of the disease in major sickling haemoglobinopathies.

Inclusion criteria

All published articles on the subject were eligible for inclusion. However, articles with patient selection bias, for example, reports of Salmonella osteomyelitis without including the incidence of other organisms as well as isolated single case reports were excluded.

Results

Our hospital data revealed 17 patients with major sickling haemoglobinopathies over an 11 year period. All of them had HbSS. Out of ten positive cultures, S. aureus was isolated from three of them and Gram negative bacilli from seven others. The latter include three klebsiella species, two proteus and pseudomonas species each.

Fourteen other studies were eligible for study and were included in the analysis. They were all retrospective studies. As indicated in table 1, there are reports from Nigeria, USA, Europe and Saudi Arabia, involving a total of 304 patients and two hundred and eighty one isolates. There were 129 (45.9%) salmonellae and 82 (29.2%) S. aureus while other Gram negative bacilli (GNB) and other Gram positive cocci (GPC) accounted for 55 (19.6%) and 15 (5.3%) of the isolates respectively. Out of 117 isolates in the studies from Nigeria, salmonellae accounted for 25 (21.4%), S. aureus 45 (38.5%), other GNB and GPC were 40 (34.2%) and 7 (6%) respectively. In contrast, out of 110 isolates in the studies from the USA, there were 77 salmonellae (70%), 18 S. aureus (16.4%), 10 other GNB (9.1%) and 5 other GPC (4.5%). Reports from Saudi Arabia include11 (37.9%) salmonellae and 18 (62.1%) S. aureus isolates while those from Europe include 16 (64%) salmonellae and 1 (4.9%) S. aureus, table 2. The ratio of salmonellae to S. aureus is 1:1.8 in the Nigerian reports, 4.3:1 in the US reports, 1:1.6 in the Saudi and 16:1 in the European series.

Table 1. Geographic distribution of bacterial pathogens of osteomyelitis in patients with major sickling haemoglobinopathy

Study	country / continent	year of publication	Patients	Salmonellae	S. aureus	Other GNB	Other GPC	Negative culture
Ebong & Oyemade[10]	Nigeria	1978	6	4	0	2	0	
Givner et al[5]	USA	1981	66	50	7	5	4	
Okoroma et al[11]	Nigeria	1984	20	0	9	10	1	
Sadat Ali et al[12]	Saudi Arabia	1985	20	1	16	0	0	3
Ebong[13]	Nigeria	1986	32	15	6	0	0	11
Syrogiannopoulos[14]	Europe	1986	8	4	1	3	0	
Doppelt et al[15]	Europe	1990	17	12	0	2	3	
Eps et al[16]	USA	1991	14	6	8	0	0	
Piehl et al[17]	USA	1993	16	13	1	1	1	
Aken'Ova et al[18]	Nigeria	1995	25	1	7	11	6	
Burnett[6]	Nigeria	1998	5	5	0	0	0	
	Saudi Arabia	1998	12	10	2	0	0	
Nwadiaro et al[3]	Nigeria	2000	24	0	14	10	0	
Chambers et al[19]	USA	2000	10	8	2	0	0	
Onuminya[20]	Nigeria	2003	12	0	6	4	0	2
Present study	Nigeria		17	0	3	7	0	7
Total			304	129	82	55	15	23

Table 2. Geographic variation in the prevalence of bacterial isolates in osteomyelitis

Bacterial isolates	Nigeria n (%)	USA n (%)	Europe n (%)	Saudi Arabia n (%)	Total
Salmonellae	25 (21.4)	77 (70)	16 (64)	11 (37.9)	129
S. aureus	45 (38.5)	18 (16.4)	1(4.9)	18 (62.1)	82
Other GNB	40 (34.2)	10 (9.1)	5 (20)	0	55
Other GPC	7 (6)	5 (4.5)	3 (12)	0	15
Total	117 (100)	110 (100)	25 (100)	29 (100)	281

GNB: Gram negative bacilli
GPC: Gram positive cocci

Discussion

The results indicate that in Nigeria, S. aureus is the most common pathogen in osteomyelitis in patients with major sickling haemoglobinopathy. The prevalence of S. aureus in this country, 38.5%, is more than two times that in the reports from the USA (16.4%). However, the prevalence of salmonella in the USA reports, 70%, contrasts sharply (more than three times) with 21.4% in the Nigerian studies. Also, the prevalence of GNB is greater in the reports from USA than those from Nigeria and the other study regions. The prevalence pattern of salmonella and S. aureus is similar in Nigeria and Saudi Arabia, while the pattern in Europe is similar to that in USA but different from the other regions. The reasons for susceptibility to staphylococcal bone infection in general[1] and salmonella infection in haemoglobinopathy[7] have been previously discussed.

The overall ratio of salmonella to S. aureus osteomyelitis in SCD in this report is 1.6:1. Compared with a ratio of 2.2:1 in the review of Burnett[6] in 1998, there is a reduction in the relative prevalence of salmonella which was rather high in the 1981 review of Givner[5] of 7.1:1. The overall worldwide trend may be that of a declining relative prevalence of salmonella while that of S. aureus may be increasing in osteomyelitis in patients with SCD. This however requires confirmation with carefully designed studies.

It can be concluded that there are geographical differences in the prevalence of bacterial pathogens associated with osteomyelitis in patients with major sickling haemoglobinopathies. Salmonellae are the most common pathogens of osteomyelitis in major sickling haemoglobinopathies in the USA whereas S. aureus is the most common pathogen in Nigeria and the Middle East. These differences cannot be readily explained. However, salmonella infections in general are not uncommon in the USA and Europe, arising from consumption of raw food and use of animal waste in food production[8,9]. In Nigeria, boiling of food before eating is a common practice that may control the transmission of salmonella which may contaminate food. In addition, availability of antibiotics as over the counter drugs in many Nigerian cities may have resulted in abuse that could have controlled endemicity of salmonella infections thereby reducing its association with osteomyelitis in this region.

Acknowledgement

The contribution of Dr C.O. Alebiosu with data search and filtering, Resident doctors and Interns with case file extraction is gratefully acknowledged.

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