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Pattern of Infections among Patients with Sickle-cell Anaemia requiring Hospital Admission

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Summary

Maharajan R, Fleming AF and Egler LJ. Patterns of Infections among Patients With Sickle-cell Anaemia requiring Hospital Admission. *Nigerian Journal of Paediatrics* **1983; 1:13.** Twenty-nine females and 28 males with sickle-cell anaemia were studied to ascertain what infections precipitated crisis. Clinical diagnoses were bone pain crisis (26), osteomyelitis (13), pneumonia (8), abdominal crisis (4), meningitis (3), pharyngitis (2) and cystitis (1). Twenty-one (37%) had *Plasmodium falciparum*, associated predominantly with bone pain, although all were supposedly receiving prophylactic antimalarials. Pathogenic bacteria were isolated in 27 (47%). *Salmonellae* were isolated from pus of 8 with osteomyelitis (7 having bacteraemia) and from blood of 2 with bone pain. Other isolates from blood or pus of patients with osteomyelitis or bone pain were *Staphylococcus pyogenes* (5) and *Klebsiella* (2). *Streptococcus pneumoniae* was grown from the blood of all and from sputum of 7 of 8 with pneumonia. *Strept. haemolyticus* was isolated from the throats of both with pharyngitis and *Escherichia coli* from the urine of the patient with cystitis. No organisms were identified in 12 (21%) of the patients.

Introduction

SICKLE-CELL disease is a major problem in tropical Africa. For example, in the savana area of Nigeria, about two per cent of infants are born with homozygous sickle-cell anaemia.[1] Patients present frequently with a variety of anaemic and infarctive crisis, often precipitated by viral, bacterial or protozoal infections.[2]

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The commonest severe infections experienced by patients with sickle-cell disease are septicaemia, pneumonia, meningitis, osteomyelitis and pyelonephritis.[2-7] The organisms to which subjects with sickle-cell disease are particularly susceptible and which cause septicaemia, pneumonia and meningitis are *Streptococcus pneumoniae, Haemophilus infuenzae* and mycoplasma. Osteomyelitis is often due to *Salmonella*, but infections are commonly mixed, and other organisms include coliforms, *Staphylococcus pyogenes, Klebsiella* and *Pseudomonas*.[2 6] The organisms of bacteriuria include *Escherichia coli* other coliforms and *Klebsiella*.[2 14]

The frequency with which various infecting organisms are observed depends not only on the

susceptibility of the patients with sickle-cell disease, but also on the prevalence of the organism in the environment. It is valuable, therefore to identify in every geographical area, those organisms which commonly cause infections needing hospitalization. Such studies have been undertaken in the forest areas of Nigeria,[6] but not in the savana region. The present study was performed to identify the relative frequency of infection by various bacteria and by malaria in patients with sickle-cell anaemia requiring hospitalization in Zaria.

TABLE I

Age and Sex Distribution of Hospitalized Patients with Sickle-cell Anaemia

Age Group (years)	*Male*	*Female*	*Total*
0–4	4	7	11
5–9	5	4	9
10–14	8	11	19
15–25	12	6	18
Total	29	28	57

Subjects and Methods

Fifty seven patients (29 males, 28 females) with sickle-cell anaemia (Hb-SS) requiring hospitalization during a six-month period (June 1980 to November 1980) were studied. Thirty-nine patients were below 15 years, but 18 older patients have been included, because it seems illogical to impose an arbitrary cut-off point for a disease which is life-long, and secondly, chronic pyelonephritis and chronic osteomyelitis in adults are the late effects of damage incurred during childhood (Table I). All the patients were attenders at the Haematology Clinic, Ahmadu Bello University Hospital, Zaria, where they had been advised to take proguanil (dosage according to age) and folic acid, 5mg daily. The patients were grouped according to the clinical condition which caused them to be hospitalized (Table II). The diagnosis of bone pain crisis was made from complaints of pain, fever and tenderness over the bone without clinical or radiological evidence of osteomyelitis. Patients with severe abdominal pain, but no localizing signs, were diagnosed as having abdominal crisis. Osteomyelitis, pneumonia, meningitis, pharyngitis and cystitis were diagnosed by the clinical, radiological and laboratory criteria.

Microbiological investigations included blood culture in all the patients and cultures of pus, sputum, urine, stool and cerebrospinal fluid (CSF) as indicated. Haematological investigations included estimation of haemoglobin (Hb), packed cell volume (PCV), mean corpuscular haemoglobin concentration (MCHC), total and differential white cell-count, platelet count and reticulocyte index (RI) by standard techniques.[8,9] A thick blood film was examined for evidence of malarial parasites.

Clinical Features

Fifty-five out of the 57 patients were febrile on admission. Icterus was observed in 34 patients and cervical lymphadenopathy in 14 patients. The liver was palpably enlarged (average, 3 cm below the costal margin) in 40 patients. There was splenomegaly (average, 5 cm below the costal margin) in 18 patients who were all below the age of 10 years. The age distribution and the associated clinical conditions in the 57 patients are presented in Table II. Bone pain crisis occurred in 26 (45.6%) of the 57 patients. The next common condition was osteomyelitis which occurred in 13 (22.8%) patients.

Laboratory Findings

Pathogenic bacteria were identified in 27 (47.3%) of the 57 patients (Table III). The blood culture in the 26 patients with bone-pain crisis yielded organisms in only three of the patients (*S. paratyphi* (2), *Klebsiella* and *Staph.pyogenes* (1).

TABLE II

Age Distribution and Clinical Condition in 57 Patients with Sickle-cell Anaemia

Age group (years)	*Bone pain crisis*	*Osteomyelitis*	*Pneumonia*	*Abdominal crisis*	*Meningitis*	*Pharyngitis*	*Cystitis*	*Total*
0- 4	7	3	1	0	0	0	0	11
5- 9	2	2	3	0	0	2	0	9
10–14	7	4	4	2	2	0	0	19
15-25	10	4	0	2	1	0	1	18
Total	26	13	8	4	3	2	1	57

TABLE III

Associated Clinical Conditions and Organisms isolated in 57 Patients with Sickle-cell Anaemia

Condition	*No. of Patients*	*Bacteria isolated from*					*Malaria parasites in blood film*
		Blood Culture	*Pus*	*Sputum*	*Urine*	*Throat swab*	
Bone pain crisis	26	*S. paratyphi* (2) *Klebsiella* + *Staph. pyogenes* (1)	—	—	—	—	16
Osteomyelitis	13	*S. typhi* (5) *S. paratyphi* (2) *Staph. pyogenes* (2)	*S. typhi* (6) *S. paratyphi* (2) *Staph. pyogenes* (4) *Klebsiella* (1)	—	—	—	Nil
Pneumonia	8	*Strept. pneumoniae* (8)	—	*Strept. pneumoniae* (7)	—	—	2
Abdominal crisis	4	Nil	—	—	—	—	2
Meningitis	3	Nil	—	—	—	—	Nil
Pharyngitis	2	Nil	—	—	—	*Strept haemolyticus* (2)	Nil
Cystitis	1	Nil	—	—	*E. coli* (1)	—	1
Total	57	20	13	7	1	2	21

The culture in nine of the 13 patients with osteomyelitis yielded *S. typhi* (5), *S. paratyphi* (2) and *Staph. pyogenes* (2), while that in all the eight patients with pneumonia yielded *Strept. pneumoniae*. The culture in the remaining patients was sterile. In patients with osteomyelitis, the pus culture grew *S. typhi* (6), *S. paratyphi* (2), *Staph. pyogenes* (4), and *Klebsiella* (1). *Strept.pneumoniae* was cultured from the sputum of seven of the eight patients with pneumonia. Other positive cultures included *Strept. haemolyticus* from the two patients with pharyngitis and *E. coli* from the only patient who had cystitis.

Blood film examination revealed *Plasmodium falciparum* in 21 (36.8%) of the 57 patients including 16 (61.5%) of the 26 patients with bone-pain crisis, two each of the patients with pneumonia and abdominal crisis respectively, and the only patient with cystitis.

No infecting organism was identified in 12 (21.1%) of the patients (bone-pain crisis (7) abdominal crisis (2) and meningitis (3)).

The mean Hb (Table IV) was significantly lower in children, aged between birth and 14 years, than in those 15 years and above. Twenty-six patients had RI above 2.0, indicating erythroid hyperplasia, 31 had reticulocyte index in the normal range and none showed erythroid hypoplasia.

TABLE IV

Haemoglobin, Packed Cell Volume, Total White Cell-count, and Platelet-count in 57 Patients with Sickle-cell Anaemia

Age Group (years)	*No. of cases*	*Hb g/dl Mean ± SE*	*PCV % Mean ± SE*	*WBC x 10^9/l Mean ± SE*	*Platelets x 10^9/l Mean ± SE*
0–14	39	7.08 ± 0.53	21.63 ± 3.02	15.04 ± 1.19	163.2 ± 115
15–25	18	8.33 ± 0.31	25.0 ± 1.38	17.06 ± 1.10	180.3 ± 67.87

Discussion

In the present study, bacterial organisms were identified in 47% and malaria in 37% of the patients with sickle-cell anaemia who required hospitalization. No pathogen could be identified in 21% of the patients. The commonest organism in the series was *P. falciparum*, which occurred mostly in patients with bone-pain crisis. This finding has confirmed the importance of malaria infection as a trigger to infarctive crisis.[10] The parasitaemia in these patients who were supposed to be taking antimalarial prophylaxis seems unlikely to be due to resistance to proguanil, although this was not investigated, but was probably the result of the patients failing to take the drug.

The second most common group of organisms was *Salmonella*, which occurred in ten patients, eight of whom had osteomyelitis. This high frequency of salmonella is similar to that reported in the southern part of Nigeria and in Ghana.[2 6 10] *Strept. pneumoniae* was the third most common organism, being isolated from all eight patients with pneumonia. In north America, where there is no malaria and where good sewerage systems largely prevent the transmission of *Salmonella*, the *Pneumococcus* is the most common infecting organism afflicting patients with sickle-cell disease.[3] Other bacterial isolates in the present series included *Staph. aureus*, *Klebsiella*, *Strept. haemolyticus* and *E, coli*, the latter two being cultured from the throat and urine of patients with pharyngitis and cystitis respectively. Three

patients had clinical evidence of meningitis, but their CSF were sterile. However, the presence of lymphocytes in the CSF suggested that they probably had viral meningitis.

A bias towards the older children and adults was apparent in the present study probably because it was based in the department of Haematology, which assumes responsibility for patients over the age of five years. None of the 18 patients over 15 years of age in the present series had bacterial infections except four patients with osteomyelitis and one with cystitis, conditions which are associated with tissue-damage incurred during childhood.

Based on the experience in the management of the patients in the present series, a number of recommendations can be made. Specimens should be collected on admission for Hb estimation, total and differential white cell-count, thick blood film for malaria parasites and blood culture. Other specimens for microbiological studies will depend on clinical observations. All the patients should be treated with chloroquine followed by proguanil, without waiting for the results of the relevant laboratory investigations. Folic acid supplements should be continued. Hydration must be maintained, with intravenous fluids if necessary, which could include M/6 sodium lactate to counteract acidosis. Analgesics should be prescribed liberally to patients in pain.[11 12] Antibiotics are not usually indicated if there is no clinical evidence of infection and the temperature is less than 39°C.[7] If the temperature is above 39°C, treatment should commence with intravenous antibiotics, ampicillin or chloramphenicol if there is bone-pain, or penicillin in abdominal or other crises, while awaiting the results of blood cultures. Patients with pneumonia should be treated initially with intravenous penicillin and febrile patients with osteomyelitis with intravenous chloramphenicol or ampicillin.

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