BACTERIAL INFECTIONS IN CHILDREN IN SICKLE CELL CRISIS

AT

THE KENYATTA NATIONAL HOSPITAL

A dissertation submitted in part-fulfilment for the degree

of

MASTER OF MEDICINE (PAEDIATRICS AND CHILD HEALTH)
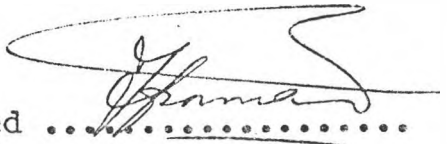
of the

UNIVERSITY OF NAIROBI, KENYA

by

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DECLARATION

This dissertation is my original work and has not been presented for a degree in any other University.

signed ....

(DR. F. ESAMAI)

This dissertation has been submitted for examination with my approval as University Supervisor.

signed ....

(DR. J. S. MEME)

C O N T E N T S.

LIST OF TABLES.

S U M M A R Y.

This is a prospective study of forty children in sickle
cell crisis with suspected bacterial infections seen at the
Kenyatta National Hospital, Nairobi.

Eighteen of these children were found bacteriologically
positive on various cultures of blood, urine, stool and
throat swabs.

The bacteriological data, age distribution and haemato-
logical data are presented and discussed.

From this study its apparent that bacterial infections
are a common cause of hospitalisation of children with sickle
cell disease especially in those under six (6) years of age
and that respiratory tract infections is the commonest reason
for hospitalisation of these children.

DISSERTATION FOR MASTER OF MEDICINE (PAEDIATRICS AND CHILD HEALTH)

TOPIC:

BACTERIAL INFECTIONS IN CHILDREN IN SICKLE CELL CRISIS AT THE KENYATTA NATIONAL HOSPITAL.

INTRODUCTION.

Patients with sickle cell disease (Hbss) commonly suffer from painful crises and haematological crisis. Painful crisis is characterised by musculoskeletal or abdominal pain attributed to the long jam sickled erythrocytes in small blood vessels. Bone and pulmonary infarction, renal disfunction, priapism, leg ulcers and a variety of neurological sequelae are well known complications of associated tissue anoxia, thrombosis and necrosis.

Accelerated anaemia due to Red Blood Cell Sequestration or hyperhaemolysis may complicate painful crisis but haematological crisis typically appear separately and are due to transient depression of bone marrow (1, 2, 3, 4).

Infection and not crisis is the most common cause of death particularly in children (5, 6, 7, 8, 9). The frequency of infection in hospitalised patients with sickle cell disease has led to the dual hypothesis that these patients are unduly susceptible to infections and that infection commonly precipitates crisis (10, 11, 12, 13, 14). While no infection is found with

majority (1, 15), subclinical infection has been postulated on the basis of infection in other members of the family at the time of crisis in siblings or simultaneous crisis in affected members of a family (16, 17, 18). Support for fever induced crisis is provided by the frequency of crisis following febrile transfusion reactions (13), and by increased sickling associated with pyrexia of typhoid immunisations in patients with sickle cell trait (19).

Also prevention of febrile disease by regular doses of long acting penicillins and chloroquine reduced clinical crisis and improved haematological picture in African children (20).

There are however very few convincing reports of crisis associated with proven bacterial infection especially in developing countries. However documented infection does not always induce crisis (1, 15), thus the actual risk or relative importance of bacterial infection in the causation of frequent crisis or early death is unknown (22).

It is with these facts in mind that the author undertook to carry out this study with the following aims and objectives.

AIMS AND OBJECTIVES.

To establish the types of bacterial infections in childre in sickle cell crisis and the distribution of these infections.

To establish the age distribution of patients in sickle cell crisis.

MATERIALS AND METHODS:

The study was carried out at the Kenyatta National Hospital in-patients services which comprises the paediatric observation ward, wards 7 to 10 and the Block III of the Infectious Disease Hospital. The study was done over a nine month period July, 1982 to March, 1983.

The criteria for selection of patients into the study were:-

1. All patients proven by citrated Acetate Paper Electro-phoresis to be homozygous for sickle cell disease presenting in clinical crisis. The haemoglobin electrophoresis was either done in a previous admission or in the haematology clinic of the hospital, but this was however repeated in all the patients on admission.

2. All children in sickle cell crisis who present with a probable bacterial infection aged 12 years and below. The age was ascertained from the parent or guardian on interview or on production of a birth certificate whenever this was possi

3. Patients were admitted into the study on Mondays, Wednes and Fridays of every week during the study period. Every child seen for each particular day was included.

4. Patients who had not been previously diagnosed to be suf fering from sickle cell disease and gave a history of blood transfusion within the last three months were excluded from

the study. ..../

5.   All patients proven to have malaria infection on admission and during the study were excluded from the study.

6.   All patients who had received anti-biotic therapy from a peripheral hospital before admission to the hospital were excluded from the study.

The author then interviewed all the parents or guardians of the children and carried out a systematic physical exa-mination on all the children. An informed consent was obtained from all the parents or guardians accompanying the patient for the child to be included in this study. A written consent was obtained from the Ethical Committee of the Hospital.

The following investigations were performed on all the children :

I.   A venepuncture was performed to obtain a total of 12 ml of venous blood . The skin at the site of venepuncture was cleaned with sterile swabs soaked in 70% alcohol. Dry disposabl 20 cc syringes and 23 gauge syringes were used for this procedur The needles were changed between venepuncture and innoculation of blood into the culture transport media bottles. 5 ml of bloo was innoculated into each of the bottles; one for aerobic cultur containing Thiol Dextrose Phosphate broth and one for anaerobic cultures containing sodium Thioglycollate. These were then sent immediately to the Microbiology Laboratory of the Hospital.

Standard Methods were used for bacteriological cultures and
sensitivity testing, by a microbiologist   (41, 42).   Three
sets of blood cultures were obtained within the first 24 hours
of admission.

II.   The remaining 2 ml of blood was sent to the Haematology
Laboratory in a sequestrated bottle. A haemogram using a
coulter counter machine was performed; a haematologist did
a peripheral blood film for white blood cell differential
count; reticulocyte count; erythrocyte sedimentation rate,
haemoglobin electrophoresis and malaria parasites using
standard haematological methods (43, 44).

III.   A clean catch urine specimen was obtained in all children
on admission. The vulva or glans penis were cleaned with sterile
swabs soaked in normal saline. For females the vulva was cleaned
twice in the antero-posterior direction and finally wiped with
dry sterile swabs. Paediatric adhesive urine collectors were
then taped onto the external genitalia. In older children the
above procedure was demonstrated to the parent and the patient
and were then asked to provide the urine specimen thereafter.
The urine was sent in a sterile bottle to the Microbiology
Laboratory within 30 minutes of collection. The urine was
analysed for protein, sugar, red blood cells, pus cells and
a culture and sensitivity testing was performed for all
urine specimens. Standard methods were used (41, 42).

<u>The following investigations were done</u>

<u>on patients in whom the clinical presentation necessitated</u>

<u>these to be done.</u>

I.   Throat swabs using sterile fresh wet serum swabs.
These were taken in all those children who were found to
have purulent pharyngitis and/or tonsillitis on examination
of the throat.   The tongue of the child was depressed with
a wooden tongue depressor and without touching the buccal
mucosa or tongue the serum swab was rotated deeply around
the pharynx and tonsils.   These were immediately sent to the
Microbiology Laboratory for bacteriological cultures using
Standard Methods (41, 42).

II.   A stool specimen was collected in those children who
presented with diarrhoea as the main and only presenting
complaint.   This was sent in a sterile plastic bottle for
bacteriological cultures.

III. A lumbar puncture was done in those children who presented
with features of meningitis on clinical examination.   The
cerebrospinal fluid was sent to the Microbiology Laboratory
in a sterile cerebrospinal fluid bottle for culture and
sensitivity using standard methods.   Another sample was
sent to the Chemical pathology laboratory in a fluoride bottle
for sugar and protein estimation.   (41, 42).

IV. Chest radiographs were done in all cases of pneumonia and specific bone radiographs were done in cases of suspected osteomyelitis. A radiologist interpretation was sought in all these cases.

The author then categorised these patients into the various tupes of clinical crises according to the classification of Rolant Scott (34).

RESULTS

There were a total of 40 patients in this study. There were 28 males and 12 females. 31 (77.5%) of the patients were of the Luo Ethnic group;.6 (15%) were Lukhya while the Giriama, Kamba, and Kisii accounted for 1 case each (2.5%).

AGE DISTRIBUTION.

The majority of the patients were in the age group 4 - 6 years in which there were 17 patients (42.5%) (Table I).

TABLE I. AGE DISTRIBUTION OF THE 40 PATIENTS

AGE (YEARS)	NO. OF PATIENTS	%
0- 3	10	25.0
4-6	17	42.5
7-9	10	25.C
10-12	3	7.5
TOTAL	40	100.0

CLINICAL DIAGNOSIS AND BACTERIOLOGICAL DATA.

The commonest reason for hospitalisation was respiratory tract infections accounting for 20 of the 40 patients (50%). Pharyngotonsillitis accounting for 10 and pneumonia for the other 10 (Table II).

There were a total of 18 bacteriologically positive cases. There were 9 positive cases from the 10 cases of pneumonia while 3 positive cases of the 10 patients with pharyngotonsillitis (Table II).

The three cases of meningitis also had pneumonia and the same organisms were isolated from blood and cerebrospinal fluid in each of the patients. The distribution of the Clinical diagnosis and bacterial   organisms is shown in Table II.

TABLE II. DISTRIBUTION OF THE 40 PATIENTS ACCORDING TO
CLINICAL DIAGNOSIS AND OF THE VARIOUS
ORGANISMS ISOLATED.

CLINICAL DIAGNOSIS	NO. OF PATIENTS	%	ORGANISMS ISOLATED.
PHARYNGOTONSILLITIS	10	25.0	2 STAPH. AUREUS 1 STREP. PYOGENES
PNEUMONIA	10	25.0	3 STREP.PNEUMONIA 2 STAPH. AUREUS 2 SALM.TYPHIMURIUM 1 STREP. PYOGENES 1 KLEBSIELLA
SEPTICAEMIA	8	20.0	1 SALM.TYPHIMURIUM
OSTEOMYELITIS	4	10.0	2 STAPH. AUREUS 1 STREP. PNEUMONIA
*MENINGITIS	3	7.5	*2 STREP.PNEUMONIA *1 KLEBSIELLA
BACILLARY DYSENTERY	1	2.5	1 SHIGELLA SONNEI
OTITIS MEDIA	1	2.5	-
UTI	1	2.5	1 E. COLI
PYOGENIC AXTHRITIS	1	2.5	-
IMPETIGO	1	2.5	-
TOTAL	40	100.0	21

* The 3 cases of Meningitis also have positive blood cultures

There were 10 positive cases in the age group 4-6 years and 4 in the age group 0-3 years (Table III).

TABLE III   AGE DISTRIBUTION OF THE 18 POSITIVE CASES.

AGE (YRS)	NO.OF +VE CASES	NO. OF -VE CASES	TOTAL
0-3	4	6	10
4-6	10	7	17
Over 7 yrs.	4	9	13
TOTAL	18	22	40

From this table there is no statistical significance in the distribution of the organism for the three age groups, $(P > 0.05)$.

Of the 18 positive cultures 12 of these (66.7%) were from blood and the remaining were either from throat swabs, stool or urine (Table IV).

TABLE IV.   DISTRIBUTION OF THE SPECIMENS AND ISOLATED ORGANISMS.

SPECIMEN	NO. OF PATIENTS	%	ORGANISMS
BLOOD	12	66.7	5 STREP. PNEUMO 3 3 STAPH. AUREUS 2 SALM. TYPHIMURIUM 1 STREP. PYOGENES 1 KLEBSIELLA
THROAT	3	16.7	2 STAPH. AUREUS 1 STREP. PYOGENES
STOOL	2	11.0	1 SALM. TYPHIMURIUM 1 SHIGELLA SONNEI
URINE	1	5.6	1 E. COLI
TOTAL	18	100.0	18

The gram positive organisms accounted for 12 (66.6%) of the cases while the gram negative organisms accounted for the rest (33.4%). The streptococcus pneumonia and staphylococcus aureus accounted for 27.8% each; followed by salmonella typhimurium 16.65%; streptococcus pyogenes 11% while klebsiella, E.Coli and Shigella accounted for 5.55% each.

CRISIS DISTRIBUTION:

Thrombotic crisis accounted for 24 of the 40 patients (60%). The distribution according to crisis and age is shown in Table V.

TABLE V.   AGE DISTRIBUTION OF THE 40 PATIENTS.
                        ACCORDING TO CRISIS

AGE YRS	THROMBOTIC	MIXED	HAEMOLYTIC	APLASTIC	TOTA
0-3	7	2	1	0	10
4-6	8	4	2	3	17
7-9	6	2	2	0	10
10-12	3	0	0	0	3
TOTAL	24	8	5	3	40

HAEMATOLOGICAL PARAMETERS

The haematological parameters of all the 40 patients have been devided according to crisis (Table VI).

(a) Haemoglobin

The mean haemoglobin level was 7.41 g/dl for thrombotic crisis patients; 5.49 g/dl for mixed crisis, 5.62 g/dl and

The means and standard deviations are shown in Table VI.

(b)   Total white cell count:

The overall mean white cell count was 17700 per cu mm. The means and standard deviations for the various types of crisis are shown in Table VI.

(c)   Erythrocyte Sedimentation rate.

This is elevated in all types of crisis but not higher than 10 mm/Hr.

(d)   Reticulocyte Counts:

There was reticulocytosis of between 7% and 10% in all types of crisis except for aplastic crisis where there is a reticulocytopenia.

(e)   Polymorphonuclear Leucocytes:

In all the types of crisis there was a polymorphonuclear leucocytosis as shown in Table VI. The absolute counts are all greater than 10,000 per cu mm except for patients in aplastic crisis. The absolute mean average for the 40 patients was 11,310 per cu mm.

TABLE VI.

HAEMATOLOGICAL PARAMETERS OF THE 40 PATIENTS ACCORDING TO CRISIS (MEANS AND STANDARD DEVIATIONS).

CRISIS	Mean Hb g/dl		Mean $\angle$ WBC x 10^3/cu mm		Mean $\angle$ ESR mm Hr.		Mean Retic %		Mean Polys $\cdot$ %	
	Hb	SD	WBC	SD	ESR	SD	Retic	SD	Polys	SD
THROMBOTIC n = 24	7.41	1.16	20.20	5.26	28.9	15	6.58	0.58	66.7	12.69
MIXED n = 8	5.49	1.62	15.58	3.08	19	8.56	8.62	1.85	67.25	6.39
HAEMOLYTIC n = 5	5.62	1.46	16.86	2.00	16.2	9.01	9	1	58	10.93
APLASTIC n = 3	3.86	0.42	10.06	3.48	15	8.66	2	0	48.67	26.83
STATISTICAL SIGNIFICANCE $\exists X^2$ test	$P < 0.01$		$P < 0.01$		$P > 0.01$		$P < 0.01$		$P > 0.01$	

From this table we see that there is significant statistical
difference in all the types of crisis in the level of haemoglobin,
white blood cell total counts and reticulocyte counts but no
statistical significance in the erythrocyte sedimentation rates
and polymorphonuclear leucocytes among the types of crisis.

DISCUSSION AND REVIEW OF THE LITERATURE

Sickle cell disease is prevalent among the Negro population of the world. In Kenya it is found among the Luo and Luhyia ethnic groups living around Lake Victoria as evidenced by the tribal distribution shown in the results of this study. Its also found among the Arabic Kinsmen of the Coast viz the Giriama. A few cases are found among the Kamba and Kisii tribesmen, but with the increasing intermarriage this is bound to spread to other tribes as generations pass by.

This study was carried out in Nairobi which comprises a mixed ethnic society and the findings may not portray the same picture that would be seen if this study were carried out in a rural settin in the Western Region of Kenya if given similar facilities. The findings of this study may also be modified by a better socio-economic status of the Nairobi Urban population that was selected with a better income and sanitary environment than the rural population that is found in the Western region of the country where majority of the children with sickle cell disease normally reside and thus prone to overwhelming and fatal infections. This is made even worse by the distant health institutions and lack of adequate facilities for diagnosis and drugs.

A controlled study could not be carried out for this study for various reasons. First, is the absence of an appropriate control in that stable state sickle cell patients would not be useful as no bacterial organisms would be obtained for comparisons and even the sickle cell disease. Children not in crisis with probable bacterial infection would not make an ideal control group because

crisis does not change the organisms in the environment and
differentiation between /crisis and infection without crisis is
infection with
so diffuse that it would practically be not possible to under-
take without intermixing, although this would appear theoretically
easy.

Secondly proof of bacterial infection as a precipitant of
crisis has not been documented biophysically or biochemically
and it would be futile to attempt this in the absence of appro-
priate facilities. But it would suffice to comment on the relation-
ship between bacterial infection and crisis from the bacteriolo-
gical,haematological and clinical evidence of presence of infection
in these children in the absence of other known causes as dehy-
dration, malarial infestation and other forms of stress.

The yield of positive blood cultures and other cultures in
this hospital is relatively low. It is reported as 60-80% ac-
cording to the annual returns of the Department of microbiology.
This influences the results of this study directly; as 45% of
the patients were bacteriologically positive. Another factor
which accounts for the low positivity of the cultures is the
widespread use of antibiotics in the surrounding health centres
for minor ailments before seeking treatment at this Referral
hospital. Although an attempt was made to exclude all children
who had some form of antibiotic therapy before admission, there
is no guarantee as to how genuine the parents were in answering
to the author's question on this. There is usually a tendency
of parents to withhold this kind of information from hospital
personnel for reasons that are not very clear.

Bacterial infections are a leading cause for hospitalisation of patients with sickle cell disease especially in the developing countries   (14), when malaria is excluded. Of the 40 patients in this study 18 had bacteriological positive cultures and the remaining 22 were negative on various cultures nevertheless had clinical and haematological evidence of presence of bacterial infection and indeed in those with pneumonia and Osteomyelitis radiological findings were consistent with pyogenic infection. Further evidence of bacterial infection is shown by remarkable improvement of all these patients when antibiotics were given. This is in keeping with studies elsewhere (2, 3, 36). Buchanan et al Studied leucocyte counts in children with sickle cell disease both in steady state and in crisis with bacterial infections and he found that the absolute polymorphonuclear leucocyte counts were more than 10,000 per cu mm in those with bacterial infection and this has been the finding in this study too, in which the average count was 11310 per cu mm. Although no band or stab counts were done in this study, the therapeutic response plus the absolute polymorphonuclear leucocytosis of more than 10,000 per cu mm highly suggest pyogenic infection in these culture negative patients.

The commonest reason for hospitalisation in this study was pneumonia and pharyngotonsillitis and the commonest organisms isolated were streptococcus pneumonia and staphy loccus aureus which were equally prevalent. Barret Connor   (22) found that the streptococcus pneumonia was the single most common organism isolated in these patients and that pneumonia was the commonest reason for hospitalisation for children with sickle cell disease.

This has also been found by many other workers (23, 37).

The distinction between pulmonary infarction and pneumonia
is radiologically difficult but clinically and by haematological
indices this can easily be made especially when coupled with anti-
biotic response of the radiological changes in patients with
pneumonia, (11, 15, 48).

Osteomyelitis is another common reason for hospitalisation
for patients with sickle cell disease and salmonella osteomyelitis
occurs with increased frequency when compared to normal popula-
tion. Workers elsewhere have found salmonella organisms being
the commonest causative organism for osteomyelitis in children
with sickle cell disease (22, 24, 25). In this study there was
no case of salmonella osteomyelitis but salmonella typhimurium
was isolated in three patients with septicaemia and pneumonia.
The three cases with osteomyelitis in this study were due to
staphylococcus aureus (2 cases) and streptococcus pneumonia (1 case)
which is consistent with findings in the normal population. How-
ever its a known fact that even among sickle cell disease patients
staphylococcus aureus and streptococcus pneumonia are the commonest
organisms but the frequency of salmonella osteomyelitis is com-
paratively higher than in the general population. (49)

Meningitis was found in three of the patients in this study.
It has been found to be relatively common in other studies.
Robinson et al (39) found that the pneumococcus was responsible
for 87% of all the meningitis cases in his study among sicklers
and the remaining were due to staphylococcus aureus and Haemophi-
lus influenza. In this study the pneumococcus was responsible for

two of the three cases and the third case was due to klebsiella.
These patients all had concurrent pneumonia and same organisms
were isolated from the blood. However only small numbers of
meningitis are found in most studies. (26, 39, 50) It should
however be noted that the pneumococcus is relatively rare at the
age below 2 years but Robinson found the contrary in children
with sickle disease. The two cases in this study with pneumoco-
ccal meningitis were in the 4 - 6 year age group.

The question of prophylactic antibiotics especially penicillins
(long acting) as is the case with antimalarials cannot easily be
answered from this study since pneumococcus was responsible for
5 out of the 18 cases (27.8%). From this therefore prophylactic
penicillin would not be justified and the use of appropriate
antibiotics based on culture and sensitivity would be ideal.
However a study carried out in Mulago Hospital Kampala (20)
showed that these patients under 6 years of age followed for
10 months or longer on both long acting penicillin and chloroquine
prophylactically, had a significant low rate of dactylitis and
a higher average haemoglobin level than those patients on
placebo. However the role of the long acting penicillin is
not yet clear since some organisms are not sensitive to peni-
cillin but further work on this subjects is needed.

The majority of patients in this study were below 6 years
of age accounting for 67.5% of all the patients. Most of these
patients were however 4 - 6 years old (42.5%). This is unlike
other studies (33) where most cases are reported to be under 2
years. This is not the case in this study probably because
most of the children die within the first two years and what
we are seeing are the survivors of whom a few may live upto
adolescence and adulthood.

Thrombotic crisis was found to be most common crisis
accounting for 60% of the patients and was the commonest
crisis in all age groups. This was followed by the mixed
crisis, haemolytic and lastly the aplastic crisis. No case
of sequestration crisis was encountered in this study whether
this is because of its rarity or because they usually succumb
before they arrive to hospital is not easy to say. This pattern
was also seen when only the 18 positive cases were considered
separately.

In this study respiratory infections accounted for 50% of
the patients and of these 60% were found to be bacteriologically
positive. Respiratory infections accounted for 66.7% (12 cases)
of the 18 bacteriologically positive cases.

From all this we can deduce that infection probably has a
part to play in the initiation of crisis in patients with sickle
cell disease and that there must be immunological derangements
in these patients. Bacteria are usually prevented from invading
the body by a normal integument. When this system fails bacteria
are introduced into the blood stream where they are taken up
partly into the Reticuloendothelial system (liver and spleen)
and phagocytes in the capillaries of the various organs especially
the lungs. The organism may multiply in these foci leading to a
bacteraemia. Once the phagocytes have ingested the bacteria
antigens are passed along the Reticuloendothelial system which
recognises the antigens as foreign and initiate the production
of antibody. The bactericidal activity of serum against gram
negative organisms depends on antibody, complement and lysozymes.
While these are bactericidal factors in serum too for gram
positive organisms, the main factors are phagocytosis in the

presence of opsonins (specific antibody, complement and other
heat labile factors).

Evidence for defective integument as a major disease
mechanism in the bacterial infection of sickle cell anaemia
is lacking. It has been proposed that the increased susceptibi-
lity to Salmonella septicaemia results from pathology secondary
to sickling in the gastrointestinal tract but this has never
been demonstrated (24). There is normal gastric secretion which
is responsible for enteric organism defense (28). Patients with
sickle cell disease have an overload of Kupfer cells with Red
Blood cells breakdown products as well as increased incidence
of cirrhosis and this is important in some patients with bacte-
raemia. The liver acts as a filter for bacteria. The spleen
is important in host defences. It provides an anatomical site
for bacteria as well as a slow sinusoidal circulation through
a bed of macrophages capable of clearing bacteria. In young
patients with sickle cell disease the spleen is usually large
as a consequence of erythrophagocytosis and trapping of sickled
cells. Later in life the spleen is virtually destroyed by
repeated infarcts and fibrosis and thus absent or reduced splenic
clearance occurs and thus becomes an inactive biological filter
for particles (33).

Laboratory evidence of impaired splenic function in
haemolysis reviewed by Kay, Gill and Hook in 1967 in a study
in mice demonstrated increased susceptibility to Salmonellae
in haemolysis with or without anaemia (25).

They concluded that erythrophagocytosis by Reticuloendo-
thelial system interferes with capacity of the cells to kill
bacteria. This is supported by increased incidence of sal-
monellosis in other states where there is chronic haemolysis
(malaria, bartonellosis) and in other conditions involving
the Reticuloendothelial system (schistosomiasis, lymphoma,
Gauchers disease). (51, 52, 53, 54).

However, splenectomised children have increased suscep-
tibility to the pneumococcus especially when they are under
4 years of age. Pyogenic organisms (Pneumococcus, B -haemophilus
influenza) usually invade through the respiratory tract. Initial
defences occur without antibody by surface phagocytosis (27).

When despite this mechanism, the blood barrier is penetrated,
pneumococci may be phagocytosed by polymorphonuclear leucocytes
lining the blood vessels of the lungs and the Reticuloendothelial
system by surface phagocytosis (again without antibody), and
later by enhanced phagocytosis in the presence of opsonins.

In patients with sickle cell anaemia subclinical pulmonary
thrombi, fluid filled alveoli and congestion could afford an
excellent focus for bacterial multiplication and at the same
time impair surface phagocytosis. Further phagocytosis by
alveolar macrophages is impaired at reduced oxygen tension,
patients with sickle cell anaemia have intrapulmonary shunting
and reduced arterial pO_2 (29). In addition Winkelstein and
Drachman have demonstrated deficient heat labile serum opsonizing
activity for the pneumococcus but not for Salmonella in the
serum of 12 of the 14 children with sickle cell anaemia
(12) in their study. Thus it would appear that multiple

factors favour the development of pneumococcal infection in
sickle cell anaemia. Since more than one host defense factor
is impaired in this population one could anticipate increased
susceptibility to other bacteria in addition to pneumococcus and
salmonella. This possibility was suggested by the data of Eeckels
et al (30) and supported by Barret-Connor (22). With age most
susceptibles are either removed from the population or other
defence mechanisms replace the known defects in bacterial
immunity.

These observations do not explain the marked difference in
susceptibility within the populations of patients with sickle
cell anaemia. No other abnormalities of bacterial immunity
have been demonstrated. Patients with sickle cell anaemia
have levels of haemolytic complement serum immunoglobulins
and antibody response to Salmonellae vaccines comparable with
normal persons (26, 31, 32).

CONCLUSIONS:

1.   Bacterial infection is a common cause of hospitalisation
of patients with sickle cell disease. 45% of the cases in this
study were positive on culture and the remaining had ample
clinical, radiological and "therapeutic response" as evidence
for bacterial infection.

2.   68% of the cases were under 6 years of age and the greatest
risk of life threatening bacterial infection was common in these
patients and 78% of the 18 positive cases were under 6 years
of age. Cram positive bacteria were more prevalent (66.6%)
than gram negative organisms. The commonest organisms were
streptococcus prenmonia and staphylococcus aureus which were
equal in occurrence.

3.   The commonest reason for hospitalisation of the 40 patients
was respiratory infections (pneumonia and pharyngotonsillitis)
accounting for 20 of the 40 cases. Clinical pneumonia was not
difficult to differentiate from pulmonary embolism on clinical,
radiological and haematological findings together with a
remarkable response to therapy · of these patients to antibiotics
clinically and radilogically.

4.   10% of the cases were found to have Osteomyelitis but none
of these cases were due to Salmonella species. Staphylococcus
aureus and pneumococcus were causative in 50% and 25% respectively
of the 4 cases, one case was negative on culture. Salmonella
typhimurium was however responsible for 3 of the cases who presented
as septicaemia.

5.   Although no definite causal relationship has been clearly
shown in this study but the fact·that 45% were positive on cultures
and the presence of clinical, radiological and haematological
features suggestive of pyogenic infection is corroborative evidence
of bacterial infection as the possible precipitating factor in the
causation of the crises (in the absence of clinical malaria).
However biochemical studies on the Red blood cell are necessary
to establish the role of bacterial infections in causation of crisis

6. Thrombotic crisis is the commonest type of crisis. 24 of the 40 patients were in this crisis 13 of which were positive on bacterial cultures. No case of sequestration crisis was found.

7. As would be expected in this country 90% of the patients were the Luo and Lukhya ethnic groups who occupy the Nyanza and Western Provinces of Kenya.

8. The total mean absolute white cell count was over 17,000/cu mm (average) for the 40 patients with an average mean polymorphonuclear leucocyte count of more than 64% in the majority of the cases. The absolute mean polymorphonuclear leucocyte count was 11,310/cu mm (average) which is highly suggestive of presence of pyogenic infection in these patients including those who were culture negative.

RECOMMENDATIONS:

1. More research is required in the field of bacterial infections in patients with sickle cell disease especially in this country in reference to:

    (a) incidence of various bacterial organisms and malaria in patients with sickle cell disease.

    (b) a controlled study on the haematological parameters in patients with sickle cell disease both in stable state and in crisis due to whatever cause, especially for bacterial induced crisis.

    (c) A similar study to the one undertaken here by carried out in one of the hospitals in Western Kenya involving a large number of patients with a control if possible.

2. There is ample evidence to indicate greater susceptibility

of patients with sickle cell disease particularly to **pneumococcal**
and salmonella infections. A controlled study is necessary to
establish what roles prophylactic penicillin (long acting)
would play in reducing bacterial induced crisis and improving
the haemoglobin level in these patients. This type of prophylaxis
is already being given for malaria using paludrine or chloroquine.

3. All patients of the Luo and Lukhya ethnic groups should
have a sickling test and haemoglobin electrophoresis carried
out when they present to hospital with anaemia and bacterial
infection before they are transfused especially in infants
and younger children.

4. Genetic counselling should be attempted for all parents of
children with sickle cell disease and for all sickle cell
disease adolescents especially regarding marriage and child
bearing.

5. The levels of G6PD should be estimated in children with
sickle cell disease especially those in haemolytic crisis.

ACKNOWLEDGEMENT

To the Staff of the Paediatric In-Patient Wards for their
co-operation during the period of study.

To the Laboratory staff of both the Haematology and
Microbiology Departments for their co-operation in carrying out
all the respective investigations which have been the corner-
stone of this study.

To my supervisor Dr. Julius Meme whose special interest
and guidance during the study period and in the final write-
up made the study a success.

Last but not least to my wife Mary and Uncle Mathias Amake
for the typing and photocopying of the script.

To the Staff of the Department of Paediatrics and my
Colleagues for the constructive criticism when I presented
this paper to the Department.

To the Statisticians of the Medical Research Centre for the
Statistical analysis of the results. ..../27

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P R O F O R M A

BACTERIAL INFECTIONS AND SICKLE CELL DISEASE

Date .... I.P. No. ....

Name of patient...............................

Sex: .... Age .... Tribe ....

Type of crisis: ....

Clinical diagnosis: ....

RESULTS:

1.   Haemoglobin Electrophoresis:

2.   Haemogram   - Hb:

                  - WBC Count

                  - Differential

                  - ESR

                  - Reticulocyte Count:

3.   Blood cultures:

4.   Urine cultures:

5.   Stool cultures:

6.   Throat Swab cultures:

7.   Radiological findings - Chest X-ray

                              - Others