THE RADIOLOGICAL FEATURES OF SICKLE CELL DISEASE AS SEEN AT KENYATTA NATIONAL HOSPITAL

A dissertation submitted in part fulfilment for the award of the degree of master of medicine (Diagnostic Radiology) of the University of Nairobi.

by

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DECLARATION

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

Signed.

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

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CONTENTS

Dedication

This work is dedicated to patients who have sickle cell disease.May the art of science continue to supplement the efforts of your families and improve the quality of your lives further.

Acknowledgement

I wish to thank all the staff in the Haemotology clinic, particularly Drs J.N. Owade and S.E.N. Waweru, whose co-operation and guidance made this study possible. I also thank the staff in the X-ray department, particularly Mrs J.Gachau and Mrs M. Njuwe who tirelessly took the radiographs.

I thank Prof. Howland who encouraged me during the initial stages of the study. I am very grateful to Prof. Ebel, Dr. Wachira and Dr. Adamali for assisting me in interpretation of the radiographs. I am particularly indebted to my supervisor Dr. Adamali for the guidance and advice throughout the study period and during the final write up.

I sincerely thank Miss Margaret Omotto for a neat secretarial work.

Finally, I acknowledge the understanding and co-operation of my dear wife Pamela.

Abbreviations and Symbols

ϵ	-	Epsilon
γ	-	Gamma
δ	-	Delta
β	-	Beta
α	-	Alpha
ζ	-	Zeta

HbF	-	Fetal haemoglobin
HbA	-	Adult haemoglobin
SCD	-	Sickle cell disease
KNH	-	Kenyatta National Hospital

Figures

SUMMARY

A total of 32 patients with sickle cell disease who attend haematology clinic were seen and sent for radiologic examinations for skull, chest, spine, pelvis and hands. These were all outpatients of whom 19 were females while 13 were males with age range from 1 year 9 months to 24 years.

25 patients (78%) had no gross complication. One patient had healing leg ulcer while three (9.4%) patients had recovered from osteomyelitis. Avascular necrosis of the epiphysis was seen in 3 patients.

The change in bone texture attributed to sickle cell disease was seen in all the body regions examined and in the young patients this was remarkable in the hands. The pelvis had least pronounced changes in the bone trabeculea. The chest x-ray showed heart enlargement in 30 patients (93.7%). This was the single most common radiologic feature.

INTRODUCTION

Haemoglobin inheritance obeys the classic Mendelian Laws. Separate genes govern inheritance of each of the haemogoloin subunits:- $\alpha, \epsilon, \beta, \gamma, \delta, \zeta$. A haemoglobin molecule contains 4 haem molecules and 4 polypeptide chains of the globin. The polypeptide chains are in two pairs of identical chains, hence designated $\alpha_2, \beta_2, \gamma_2$ etc.

ϵ and ζ are only found in embryonic haemoglobin. Genes for ζ and α chains are on chromosome 16 while ϵ, γ, δ, and β genes occupy adjacent loci on chromosome 11. β , α, and γ chains inheritance is governed by 2, 4 and 4 genes respectively (9).

Until 3 months of intrauterine life the fetus contains haemoglobin Gower which has $\alpha_2\epsilon_2$, ϵ_4 and $\zeta_2\epsilon_2$ and haemoglobin Portland designated $\zeta_2\gamma_2$. This is replaced by haemoglobin F which has $\alpha_2\gamma_2$. Haemoglobin F constitutes 70 - 90% of total haemoglobin at birth but this falls to 10% or less at 4 months. HbF constitutes 0.5 - 1% of total haemoglobin in some children upto 10 years. Most non-pregnant women of reproductive age have small amounts of HbF of upto 0.9%. 20% of women show a small temporary rise in HbF during early pregnancy. This rises to 2-3% of total haemoglobin and persists during and following pregnancy in 1-2% of women. Fetal haemoglobin is replaced by adult haemoglobin and 97% of total haemoglobin in an adult is Haemoglobin A composed of $\alpha_2\beta_2$ and 3% is haemoglobin A_2 composed of $\alpha_2\delta_2$ (11).

Common haemoglobinopathies are β chain variants and 90% of abnormal haemoglobins are single amino acid replacement (9).

The α polypeptide chain has 141 amino acids while β chain has 146 amino acids. The number and sequence of amino acids are genetically determined (11). Morphological abnormality of sickle cell disease was first described by Dr. Herrick in 1910. Further studies were undertaken thereafter by various scientists linking this defect to the observed physiological changes mainly in oxygen and carbondioxide transport and resultant plasma pH. It was not until

1949 that Hb electrophoresis done by Paulin et al showed the differences in haemoglobin molecules in sickle cell anaemia and sickle cell trait. The molecular abnormality in haemoglobin S where valine replaces glutamic acid at position 6 of the β chain was first described by Ingram in 1957 (4). Sickle cell disease is transmitted as autosomal dominant condition (18). However, Haemoglobin polymer formation which leads to sickling does not occur in heterozygous AS state until haemoglobin oxygen saturation falls to 40% and below (11). In homozygous state this occurs at normal oxygen tension of venous blood. Red blood cells sickling and aggregation in small vascular channels form microthrombi or thrombi which interrupt circulation and cause infarction.

Sickle cell disease is systemic and the primary abnormality is in the red blood cells. Sickling and haemolysis lead to reduced life span of the red blood cells.

THE PATHOLOGIC BASIS OF RADIOLOGICAL CHANGES IN SICKLE CELL DISEASE

Bone Changes in Sickle cell disease were first described by Graham in 1924 and the radiologic skeletal changes were first described by Le Wald in 1932 (29).

Bone changes in sickle cell disease are due to

(i) hyperplasia of bone marrow

(ii) Infarction

(iii) Infection

(iv) Bone reaction to these processes (16)

Erythrocytic, granulocytic and megakaryocytic series contribute to bone marrow hyperplasia. This leads to thinning of the cortex, widening of the medulla and cavities or intertrabecular spaces due to bone resorption. Hypercellularity together with infarction reduce the number of trabeculae. New bone formation on the few remaining trabeculae make them appear coarse (10, 22). Connective tissue replaces some of the destroyed trabeculae and the overall bone density is reduced.

Cessation of blood flow due to thrombosis causes infarction (1). Infarcts may occur in the medulla, epiphysis or the cortex. The sequelae of infarcts depend on vascular network. Large infarcts in areas supplied by end arteries have relatively poor prognosis compared to small infarcts in areas with collateral circulation. The sickle cells in the bone marrow may aggregate in the sinusoids causing hypoxia and cell injury perceived as bone pains. A small bone marrow infarct is dissolved by proteolytic enzymes and cleared by phagocytes. New blood vessels and marrow cells are formed and the trabeculae is restored. Large infarcts with poor collateral circulation develop fibrosis which appear as cystic areas but these may calcify.

In children under 5 years old, bone marrow necrosis manifest in small bones of the hands and feet where hypoxia is maximal (1). Fat and marrow embolism may follow marrow infarction, particularly in the vertebrae and more commonly in pregnancy (30).

Occlusion of end arteries at joints lead to infarction of subchondral bone with collapse in weight bearing joints or fragmentation. A sector of the epiphysis is usually involved but it may be multifocal.

In the long bones infarction is usually generalized. Periosteal new bone formation gives bone within bone appearance. Involvement of metaphyseal end arteries affects the growth cartilage hence bone growth and maturity. This is particularly seen in dactylitis. The central part of the metaphysis is most commonly affected while perforating metaphyseal vessels offer alternative supply to the periphery (Fig. 1). The differential growth results in conical, triangular or rhomboid epiphysis (16). Early fusion of epiphysis may occur as a result of infarction causing shortening (16).

Focal necrotic lesions of long bones may be seen in central shaft portion supplied by nutrient artery and in the intermediate zones between bone ends supplied mainly by periosteal blood vessels (Fig. 2).

In young children periosteum is loosely attached and may separate from cortex following focal infarction, and cortical bone death occurs as blood supply is detached. Decalcification follows and subperiosteal new bone gives bone within bone appearance.

In the skull a characteristic finding is wide diploe and thin or absent outer table. The inner table is also thin. This is clinically evident as frontal or parietal bossing. The trabeculae appear coarse. 5% of patients show hair-on-end appearance. (16)

Fig 1

Blood supply to growing bone

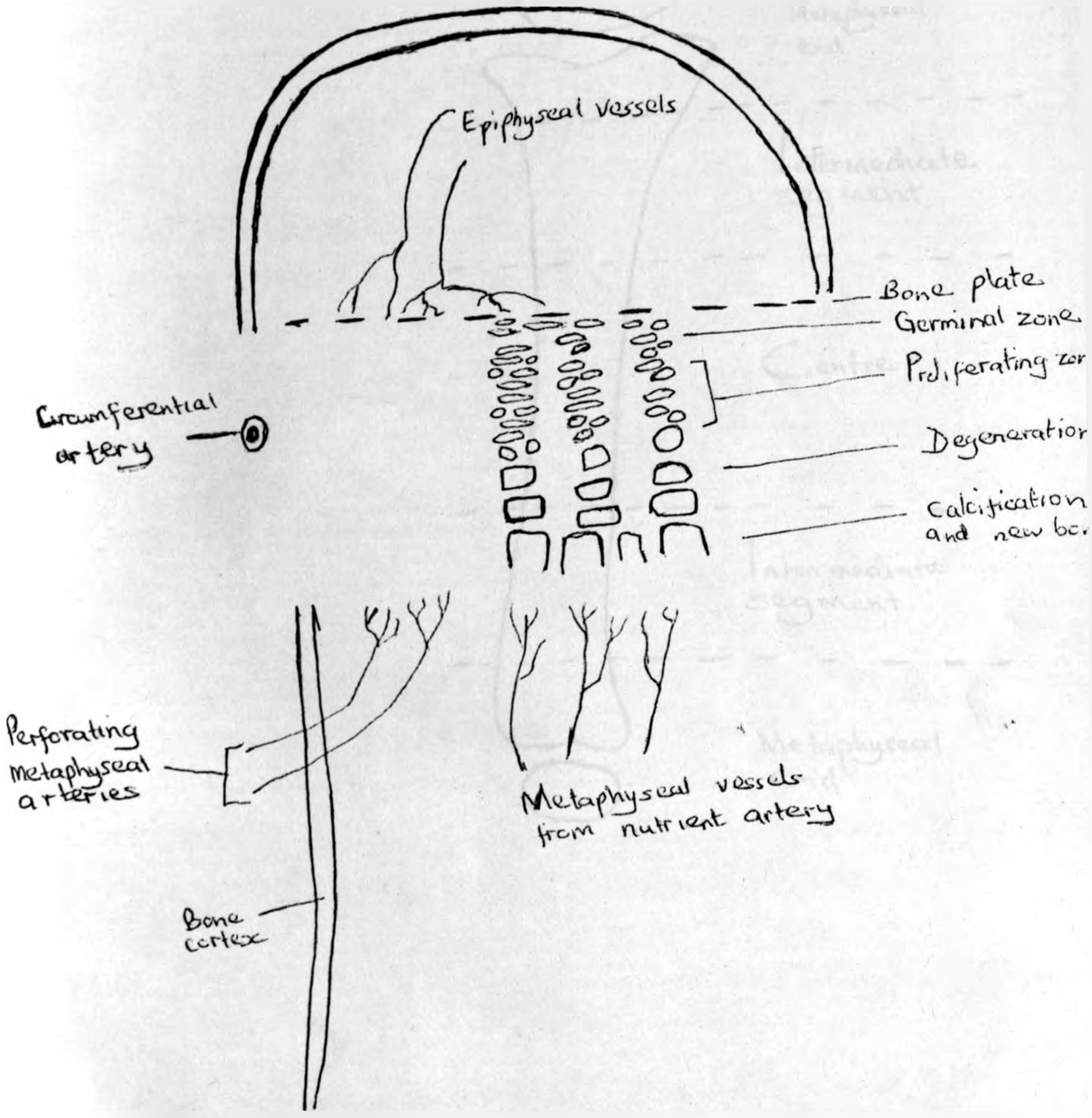
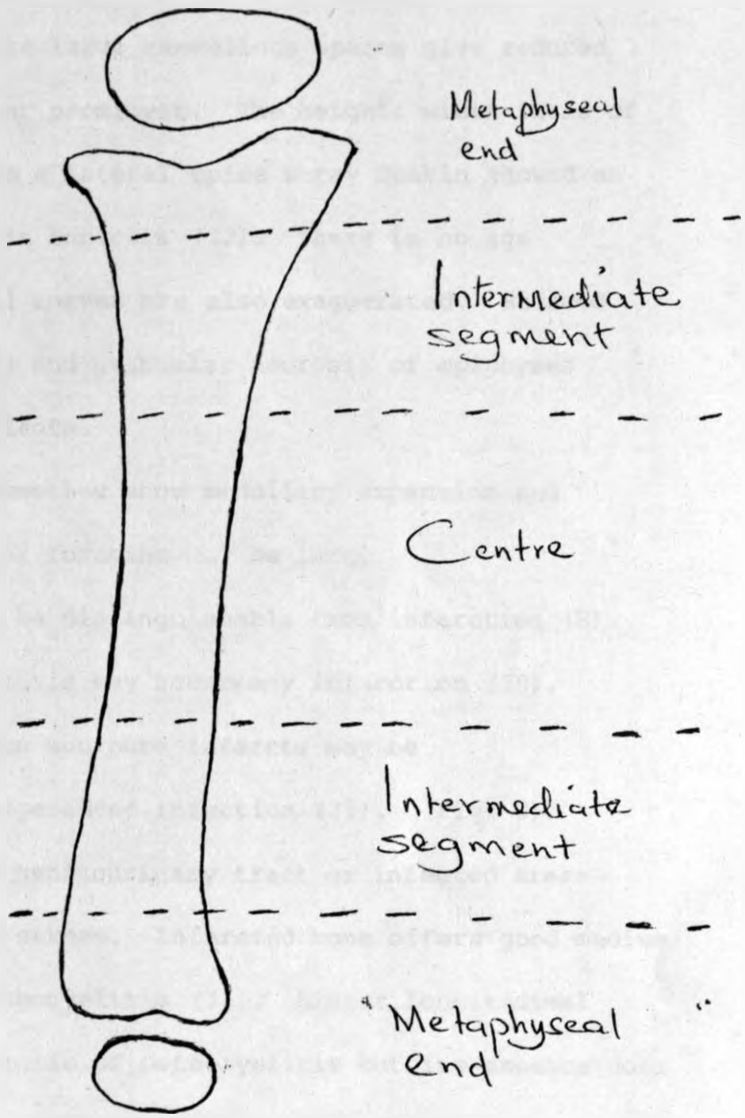


Fig 2

Bone segments

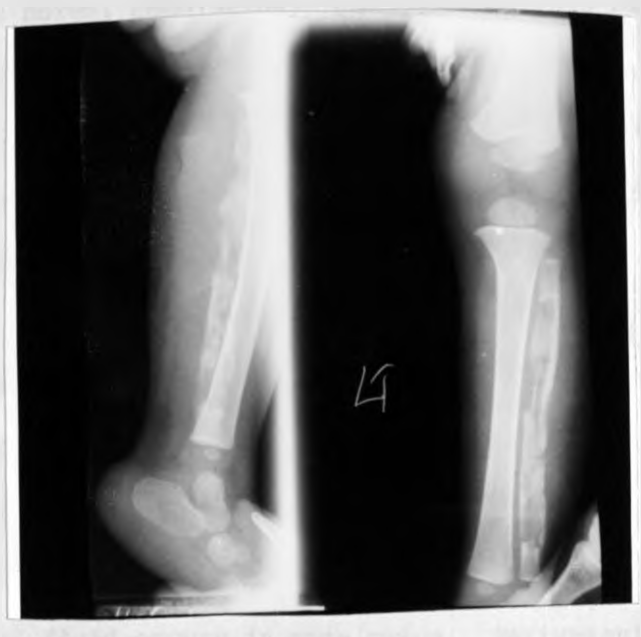


The vertebrae are usually flat or biconcave and have vertical trabeculae. The central cupping or fish vertebrae is due to poor central circulation where there is stasis resulting in defective growth. The margins have better blood and oxygen supply and less stasis or sickling hence grow faster than central portion (1). The large cancellous spaces give reduced bone density and trabeculation appear prominent. The height: width ratio of vertebral bodies is increased and on a lateral spine x-ray Henkin showed an average ratio of 1:1.45 with 1:1.2 in controls (22). There is no age variation in the ratios. The spinal curves are also exaggerated. Reduced vertebral body height, kypholordosis and avascular necrosis of epiphyses result in reduced height of the patients.

The tubular bones of the extremeties show medullary expansion and thinning of the cortex. The vascular foramina may be large.

Bone infection may not always be distinguishable from infarction (8). Severe pain, high fever and leucocytosis may accompany infarction (30). Infection commonly follows infarction and pure infarcts may be indistinguishable from those with superadded infection (31). (Fig. 3). Microthrombi in gastrointestinal or genitourinary tract or infected areas permit entry of bacteria into blood stream. Infarcted bone offers good medium in which bacteria thrive causing osteomyelitis (31). Linear longitudinal intracortical fissuring is pathognomonic of osteomyelitis but its absence does not exclude osteomyelitis (10, 31). Sequestrum is rare in sickle cell patients with osteomyelitis (16). Abbreviated digits frequently follow dactylitis.

Fig 3



Clinical or radiological features or both may not always distinguish infection from infarction or infarction with superadded infection. Needle aspiration for laboratory examination may be indicated to make this distinction.

Heart enlargement occur earlier than bone changes (31) and is the commonest finding in sickle cell disease (30). The heart appears globular. Plethora in the lungs is due to chronic anaemia and the resultant haemodynamics (23). Pulmonary hypertension with enlarged main pulmonary artery may occur in the young and adults (16).

The spleen is large in early life but becomes atrophic due to repeated infarction. Calculi in the biliary tract is more common in sickle cell disease than normal population. Due to haemolysis bile pigments are in high concentration leading to biliary stone formation (29, 31). There is high incidence of renal papillary necrosis in homozygous sickle cell patients (27).

Fat and marrow emboli following bone marrow infarcts may lead to infarction in the lung, kidney, brain, heart, spleen, adrenal and pancreas (30).

In the brain, focal infarcts are common in cortical grey mater. Blood is shunted into venous channels due to obstruction in capillaries. Thrombi may extend from capillaries to subarachnoid veins, dural and lateral sinuses. Subarachnoid spaces become engorged and extravasation of red blood cells into cerebrospinal fluid occurs in some cases. Perivascular haemorrhages followed by necrosis may occur. Meningeal artery may be closed by retrograde thrombosis. Brain atrophy with distortion of the cortex and dilated ventricles follow healing (1)

In older patients the haemopoietic red marrow is limited to axial skeleton and proximal parts of humeri and femora. As myelofibrosis occurs the infarctive episodes cease and sclerosis and calcification predominate over hyperplasia, hence the bone marrow narrows and the cortex is irregularly thickened particularly in the endosteal aspect (1).

Appropriate imaging modality is a prerequisite for elucidating these pathological processes of sickle cell disease. Conventional radiography, computed tomography and radionuclide scanning are adequate in the majority of cases. Intravenous urography is necessary for renal changes and ultrasound for showing abdominal complications particularly calculi.

AIMS AND OBJECTIVES

1. Assess radiological changes in SCD at KNH.
2. Evaluate the influence of regular medical review and management on radiological features.
3. Assess the age of patient and any relationship with degree of radiological changes.
4. Evaluate the single examination showing most radiological changes in the various ages.
5. Assess the incidence of avascular epiphyseal necrosis.

Case Material and Method

This is a prospective study done between May 1990 and January 1991. The patients were seen at haematology consultant clinic and radiological examinations were done at the X-ray department, both at Kenyatta National hospital. This clinic is conducted weekly on Monday mornings.

In this study sickle cell patients with Hb electrophoresis SS or SF were included. 32 patients were studied. 13 of these were males while 19 were females with the age range of 1 year 9 months to 24 years.

These are stable patients and they attend the clinic for review and evaluation aimed at promoting and maintaining stable health status. Periodic haemograms are taken to assess haematologic status, particularly when clinical findings are not satisfactory.

The patients are maintained on daily doses of folate and proguanil. Other specific conditions or complications are given appropriate attention whenever they arise.

X-ray examinations done included lateral skull view, lateral thoracolumbar spine, postero-anterior chest view, antero-posterior pelvis xray and postero-anterior hand views.

The standard technique as outlined by K.C. Clark (15) were used for the examination of the various regions of the body.

The film sizes used were 10" x 8" (24 x 20) 12" x 10" (30 x 24cm) 14" x 14" (35 x 35) and the radiographs were interpreted with the assistance of consultant radiologists.

A sample of the questionnaire used in this study is given in the Appendix.

RESULTS

Table 1

District Distribution

District	No. of patients
KISUMU	3
SIAYA	11
SOUTH NYANZA	4
KAKAMEGA	7
BUNGOMA	3
BUSIA	3
NAIROBI	1
TOTAL	32

Kisumu, Siaya, and South Nyanza districts are in Nyanza province. These districts are inhabited by the Luo tribe mainly.

Kakamega, Bungoma and Busia districts are in Western province which is predominantly inhabited by the Luhya tribe.

These two provinces are neighbours in Western Kenya.

One child of Nubian origin traced his ancestry to Kibera in Nairobi.

Age distribution Tables

Table 2.0

Age range 1 year 9 months to 24 years

Age	Number of patients
Under 5 years	13
5 - 12 years	10
13 - 24 years	9
Total	32

Table 2.1

Under 5 years: Age	Number of patients
upto 2 years	3
upto 3 years	4
upto 4 years	4
over 4 years	2
Total	13

Table 2.2

Age group 5 - 12 years

Age	No. of patients
5 - 7 years	4
8 - 10 yrs	3
over 10 years	3
Total	10

Table 2.3

Age group 13 - 24 years

Age	No. of Patients
13 - 15 years	4
16 - 18 yrs	1
19 - 21 yrs	2
22 - 24 yrs	2
Total	9

Table 3

Age of the patients at the time of diagnosis

Age	No. patients
Below 6 months	9
6 months - 1 year	13
1 - 2 years	7
over 2 years	3
Total	32

Two patients were diagnosed at the age of 2 months and one of these patients had lost 6 elder siblings due to sickle cell disease (mother). Two other patients were diagnosed at 3 months. These are the patients diagnosed at the youngest age. The patients who were over 2 years old at the time of diagnosis were 2½yrs, 4 years, and 14 years old. The patient diagnosed at 14 years is now 19 years. She was well until her first presentation and subsequent diagnosis.

Table 4

Family occurence

Number of Siblings affected	No. of Patients
No sibling affected	20
The only child	4
1 sibling affected	5
2 siblings affected	1
3 siblings affected	1
6 siblings affected	1
Total	32

The affected siblings had died except one family in which both the affected children were attending the clinic.

Table 5

Transfusions since birth

Number of transfusions	No. of Patients
None	10
1	9
2	3
3	5
> 3	2
> 10	2
Don't Remember	1
	32

9 out of 10 patients who had not been transfused were below 6 years. 7 of these were below 5 years. One was 19 years. Out of 9 patients who had been transfused once, 3 were less than 5 years, 4 were between 7 - 10½ years, two were 13 years old. Two patients transfused over 10 times were 23 and 24 years old.

Table 6

Hospital admission in the last one year

Number of admissions	Number of patients
0	10
1	15
2	6
Don't remember	1
Total	32

Chronic osteomyelitis of the humerus was the indication for admission in one patient. One patient had gastroenteritis, one patient had meningitis, one patient presented for the first time with acute abdomen. Two patients had bronchopneumonia. Thrombotic crises was responsible for the rest of the admissions. Blood slides in these patients were negative for malaria parasites.

Table 7

Complications

Complications	No. of patients
None	25
Leg ulcer	1
Osteomyelitis	3
Avascular epiphyseal necrosis	3
Total	32

Table 8

Clinical findings

Symptoms	No. of patients
No complaint	6
Sore throat	10
Coughing/Sneezing	7
Swelling of digits	4
Epistaxis	2
Headache	2
Dizziness	2
Joint pains	6
Stiff shoulder joint	1
Swelling of neck	1
Left hypochondrial abdominal pain	6

All the patients had history of recurrent fever, swelling of wrists and hands, ankle and feet with joint pains on and off.

Table 9

Clinical findings contd.

Signs		No. of Patients
Pallor	absent	3
	mild	16
	moderate	9
	severe	4
Jaundice	present	19
	absent	13
Tonsils	enlarged	27
	Normal	5
Cervical hymphadenopathy		1
Leg ulcer		1
Abdomen	Normal findings	19
	Splenomegaly	6
	Hepatomegaly	6
	Hepatosplenomegaly	1
Splenomegaly	2cm	1
	4cm	1
	6cm	4
	10cm	1
Hepatomegaly	1cm	2
	2cm	1
	3cm	1
	5cm	1
	6cm	2
Heart Sounds:		
	Systolic murmur	4
	Normal heart sounds	28

Table 10

Laboratory findings

Range of Haemoglobin: 4.6 - 9.3 gm%

Hb	Patients
less than 6gm%	5
6 - 8 gm%	12
more than 8gm%	11
untraced results	4
Total	32

Table 11

Haemoglobin electrophoresis

Hb electrophoresis	No. of patients
HbSF	26
HbSS	6
Total	32

Radiological findings

Table 12

Lateral skull view

Width of diploic space: Range 4 - 14 millimetres

Width in millimetres	No patients
4- 5	10
6 - 7	6
8 - 9	9
10 - 11	4
12 - 13	2
14	1
Total	32

Table 13

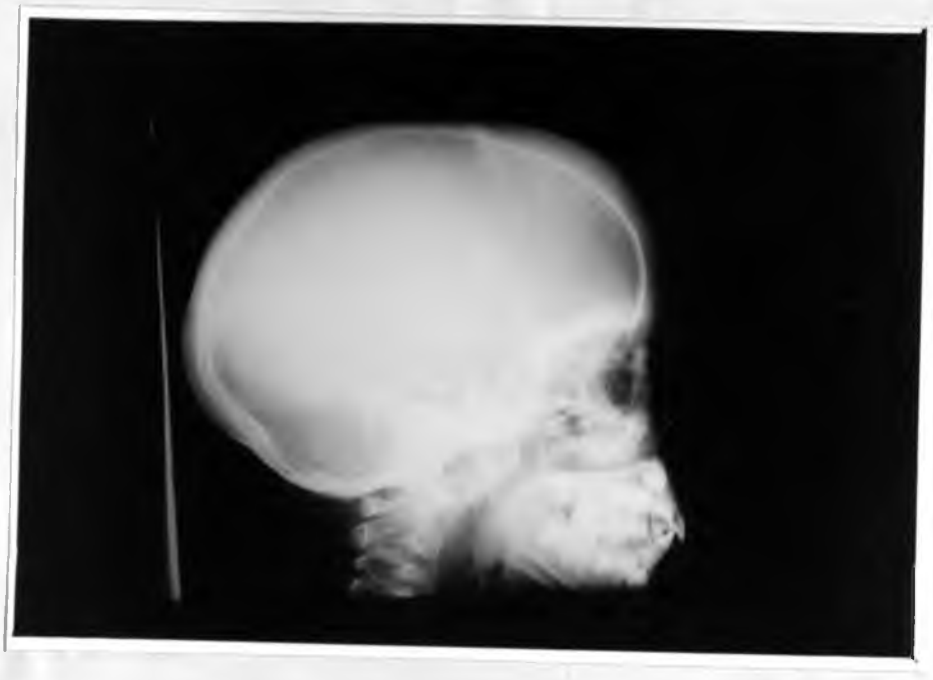
Trabecular appearance

Normal	15
Coarse	17

9 patients with normal trabecular were less than 5 years old.

3 were between 5 and 12 years old while the other 3 were between 13 and 24 years old.

Fig 4



This is a 7 year old girl with sickle cell disease. Note the wide diploe, thin inner table, absent outer table and post-nasal space soft tissue shadow due to enlarged adenoid.

Table 14

Adenoids measurements

Measurement in millimetres	No. of Patients
5 - 9	3
10 - 14	8
15 - 19	11
20 - 24	5
25 - 29	2
30	1
Not measured	2
Total	32

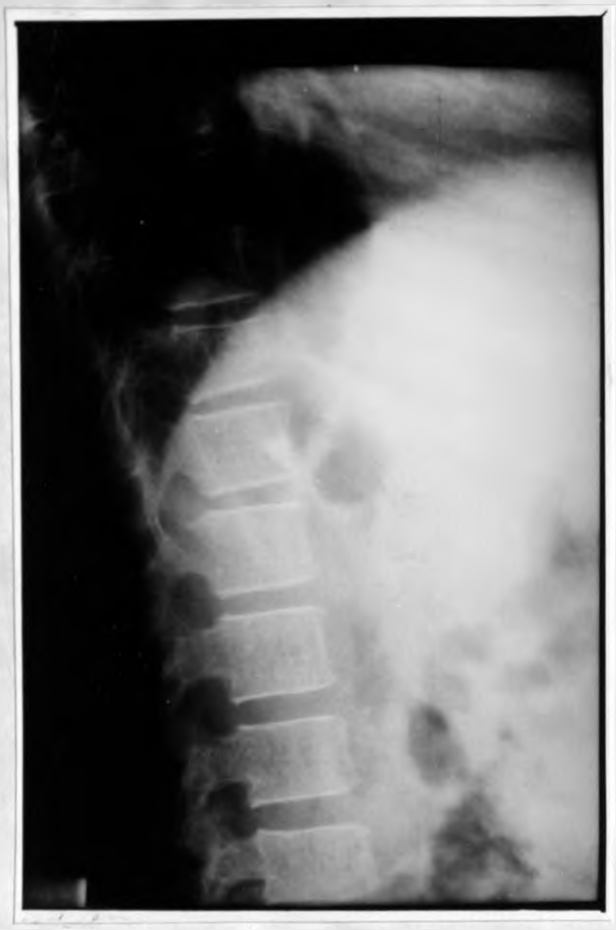
The line of measurement was the anterior margin of foramen magnum to posterior margin of hard palate. (17) Two radiographs were not satisfactory for this measurement.

Table 15

Lateral thoracolumbar spine

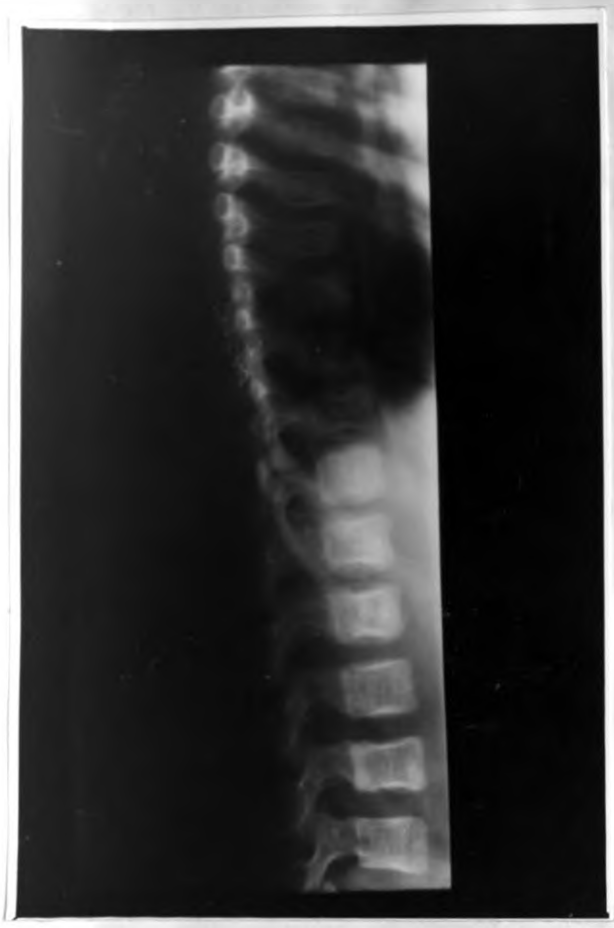
Radiologic Sign	below 5 years		5-12yrs		13-24 yrs	
	n = 13	%	n = 10	%	n = 9	%
Osteopenia	11	84.6	7	70	6	66.7
Coarse trabeculae	8	61.5	8	80	7	77.8
Predominant vertical striations	7	53.8	10	100	6	66.7
Fish vertebrae	1	7.7	2	20	4	44
Step depression	1	7.7	2	20	2	22
Bone within bone appearance	1	7.7	3	30	4	44
Anterior Vascular notching	6	46.2	5	50	1	11
Vertebral body Height: Width ratio	1:1.5		1:1.48		1:1.4	

Fig 5



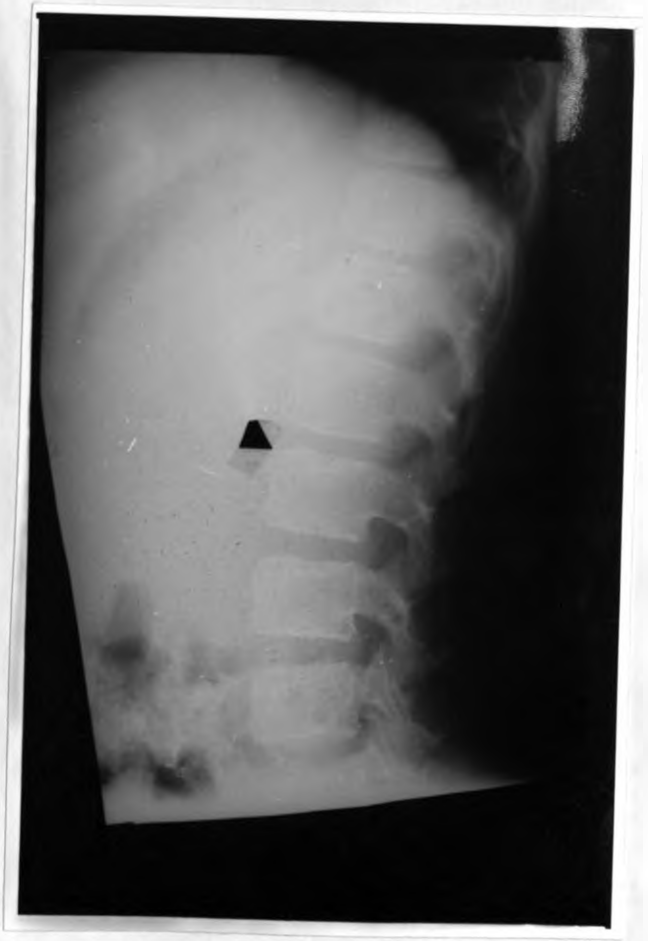
The spine of 19 year old patient with sickle cell disease. The trabecular pattern appears coarse with vertical striations. This patient did not have cupping of the vertebrae.

Fig 6



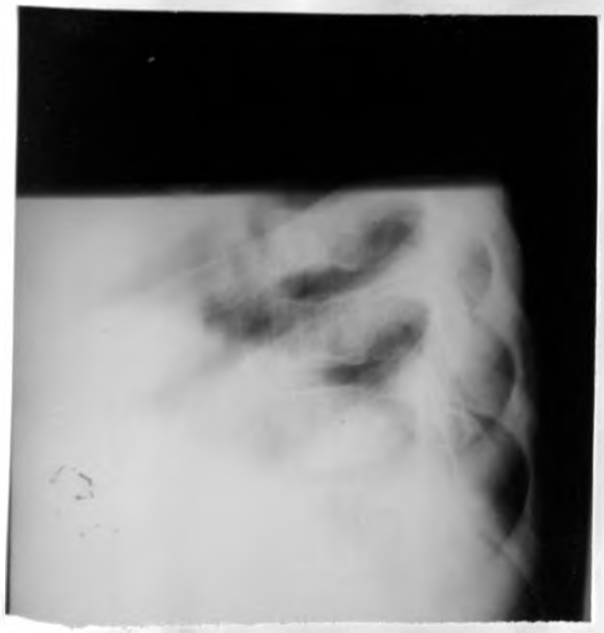
4 year old patient with fish vertebrae and anterior notching of vertebral bodies

Fig 7



13 year old patient with step depression in the vertebral bodies

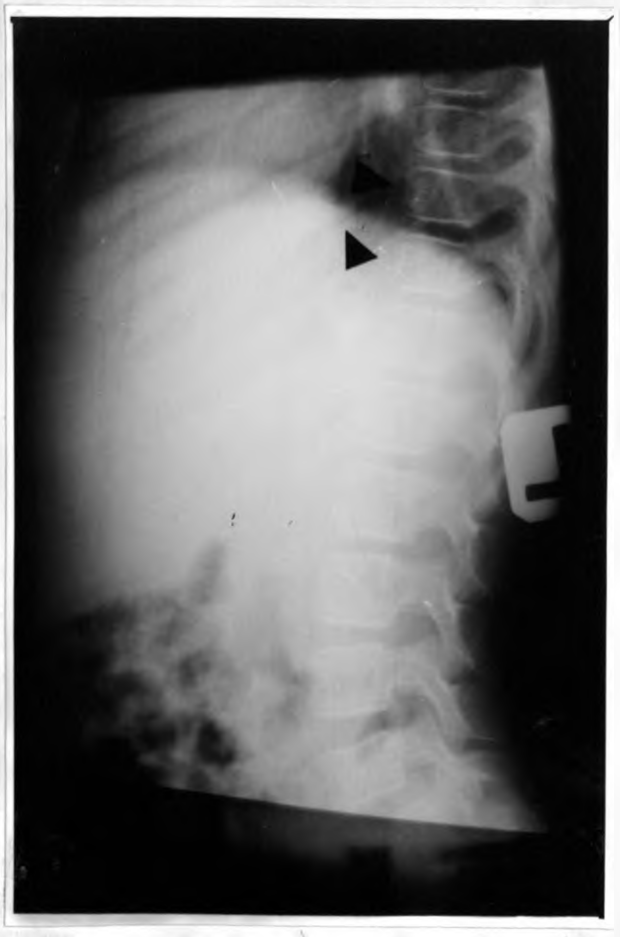
Fig 8



10 year old female patient

with cod fish vertebrae

Fig 9



9 year old patient

Note the anterior vascular

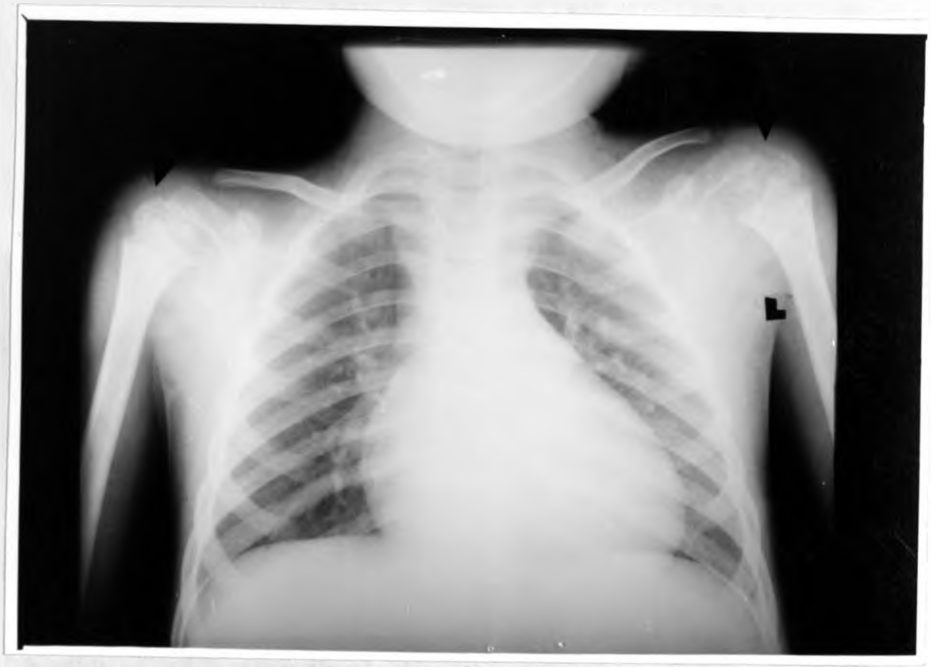
Impression on vertebral bodies

Table 16

Chest X-ray

	below 5yrs		5-12yrs		13-24yrs	
Findings	n = 13	%	n = 10	%	n = 9	%
Cardiomegaly	12	92	10	100	8	88.9
Cardiothoracic ratio (average)		56		60		55
Increased pulmonary vessels	3	23	5	50	5	56
Shoulder joint lesion	1	7.6	0	0	0	0
Coarse trabeculation in ribs	4	30.8	3	30	6	66.7

Fig 10



4½ year old male child with stiff shoulders
Note fragmentation of the humeral epiphyses
bilaterally. The heart is enlarged.

Table 18

Hands

findings	below 5 yrs n = 13	%	5 - 12 yrs n = 10	%	13 - 24 yrs n = 9	%
Coarse trabeculae	6	46	4	40	1	11
Wide Medulla/thin cortex	11	84.6	10	100	0	0
Growth lines	3	23	1	10	2	22
Prominent nutrient foramina	1	7.6	0	0	2	22
Growth disturbance/Early						
Epiphyseal fusion	0	0	1	10	1	11
Cystic areas (cavities)	0	0	2	20	1	11
Skeletal maturity Carpal bones	Normal		Normal		-	

There was no patient with periostitis. Thinning of the cortex is more marked in the 1st metacarpal and more extreme in the younger patients. Two patients had early fusion of the epiphysis with shortening of affected bone: One patient 5 years 4 months old had early fusion of 5th metacarpal with resultant bone shortening. The other patient was 13 years old with early fusion of right 1st metacarpal epiphysis and short proximal phalanx of the index finger with conical epiphysis. This patient had bilateral double epiphysis of 2nd metacarpal: an incidental finding (Figs 13, 14).

Table 18

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findings	below 5 yrs n = 13	%	5 - 12 yrs n = 10	%	13 - 24 yrs n = 9	%
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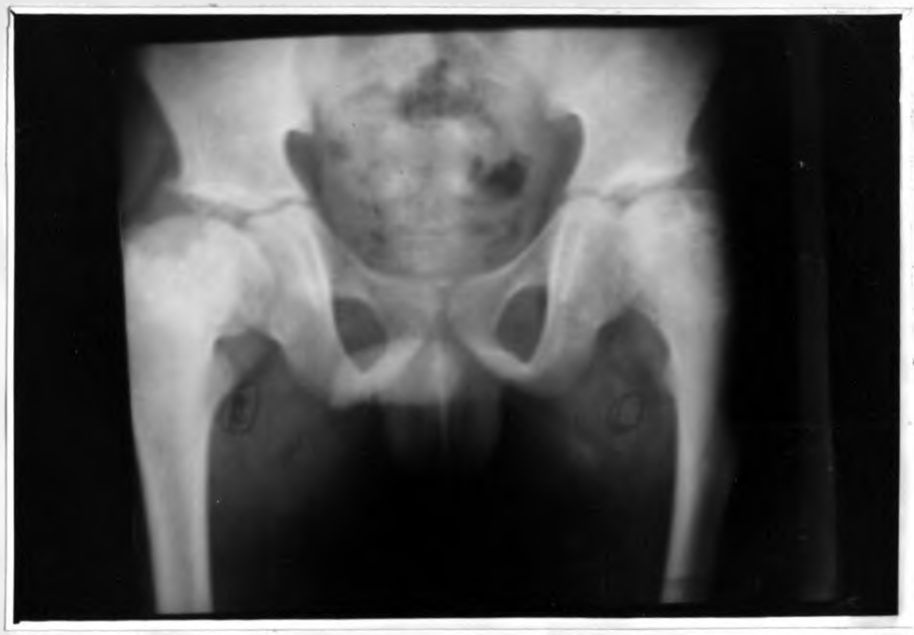
Table 17

Pelvis

Radiologic sign	below 5 yrs		5 - 12 yrs		13 - 24 yrs	
	n = 13	%	n = 10	%	n = 9	%
Coarse trabeculae	6	46	5	50	2	22
Avascular hip necrosis	0	0	1	10	1	11

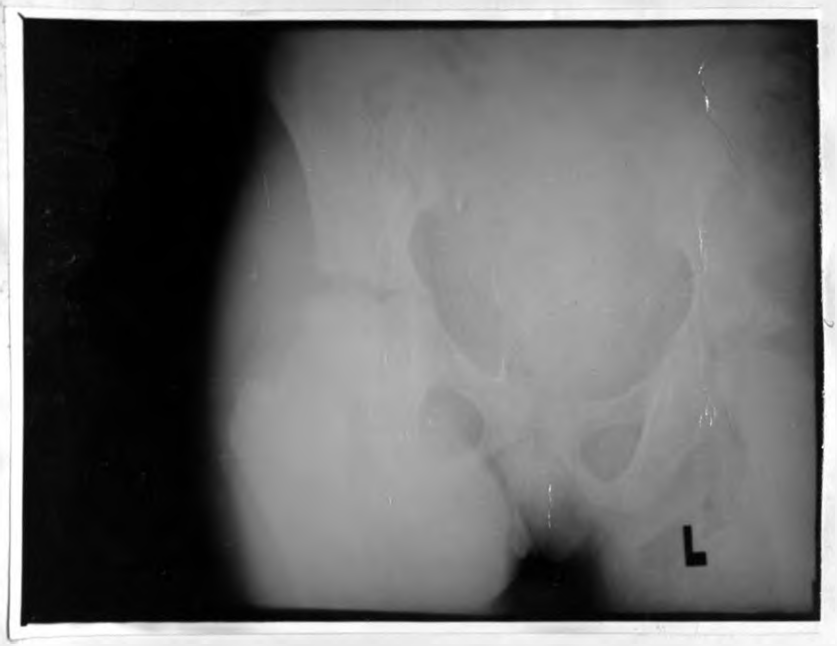
One 10 year old girl had grade 4 avascular necrosis of the right capital femoral epiphysis. One male patient 13 years old had bilateral avascular necrosis of the capital femoral epiphyses: Grade 3 on the right and grade 2 on the left.

Fig 11



13 year old male patient with
flattening of both femoral epiphyses

Fig 12



10 year old female with total avascular necrosis of the left femoral epiphysis.

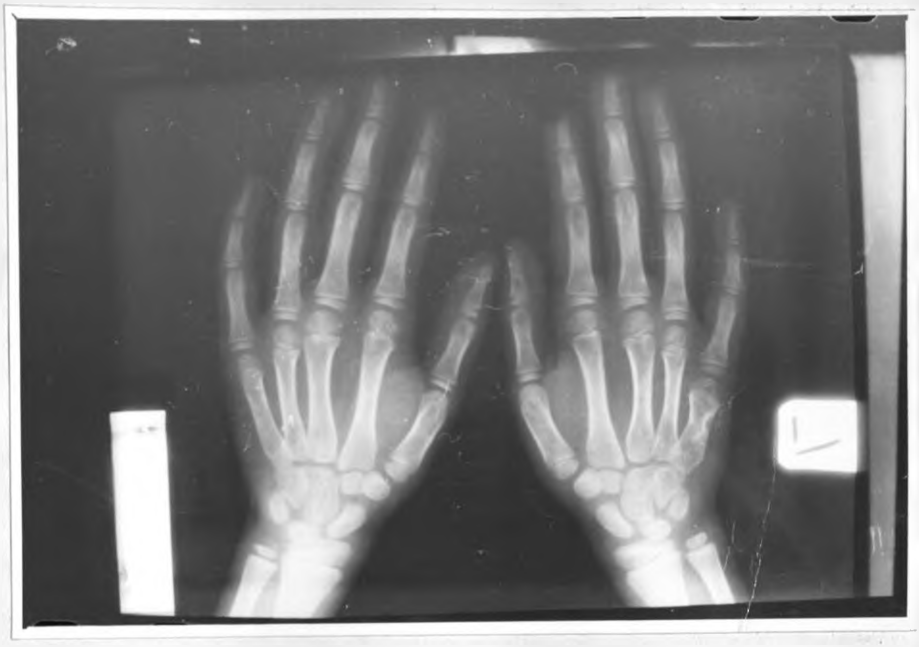
Table 18

Hands

findings	below 5 yrs n = 13	%	5 - 12 yrs n = 10	%	13 - 24 yrs n = 9	%
Coarse trabeculae	6	46	4	40	1	11
Wide Medulla/thin cortex	11	84.6	10	100	0	0
Growth lines	3	23	1	10	2	22
Prominent nutrient foramina	1	7.6	0	0	2	22
Growth disturbance/Early Epiphyseal fusion	0	0	1	10	1	11
Cystic areas (cavities)	0	0	2	20	1	11
Skeletal maturity Carpal bones	Normal		Normal		-	

There was no patient with periostitis. Thinning of the cortex is more marked in the 1st metacarpal and more extreme in the younger patients. Two patients had early fusion of the epiphysis with shortening of affected bone: One patient 5 years 4 months old had early fusion of 5th metacarpal with resultant bone shortening. The other patient was 13 years old with early fusion of right 1st metacarpal epiphysis and short proximal phalanx of the index finger with conical epiphysis. This patient had bilateral double epiphysis of 2nd metacarpal: an incidental finding (Figs 13, 14).

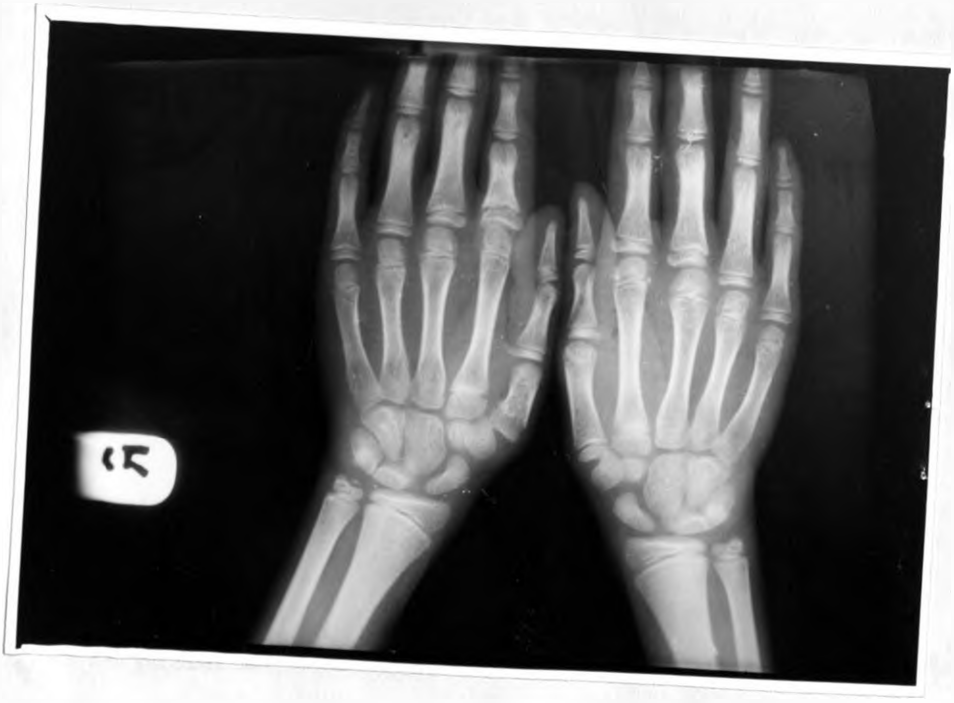
Fig 13



5 year 4 month old female

Note short left 5th metacarpal with irregular medial cortex.

Fig 14



13 year old male patient. Note the short right first metacarpal with fused epiphysis, short proximal phalanx of right index finger. Double epiphyses of the 2nd metacarpals bilaterally was incidental finding.

DISCUSSION

Sickle cell disease is mainly prevalent in Western Kenya amongst the Luo and Luhya communities (26, 35).

In this study all except one patient were from these communities. This particular exception is from Nairobi which is a cosmopolitan city. It was observed that the patients or their parents are fairly informed about their medical condition and therefore showed good compliance. Almost in all cases the parents, particularly mothers were young and had a good command of English indicating reasonable educational background. The patients in the older age groups were equally fluent. These ones were attending the clinic alone. This level of awareness facilitated communication and data collection. It was noted among some young mothers that fear of similar outcome in subsequent pregnancy existed. A few requested for arrangements to have prenatal examination and diagnosis.

In this study the diagnoses in most patients were made by the time they were 2 years. However, in one patient the diagnosis was made at 14 years. Kraft describes an extreme case in which diagnosis was made at 43 years and the oldest patient diagnosed at 62 years (24).

25% of the patients had at least one member of the nuclear family having had or having sickle cell disease. In these families the affected sibling(s) had died except in one family. However, apart from these 1st degree relatives there was no extended or wider family incidence of the disease known to these patients or their parents. The parents said they first became aware of this disease when their children developed medical problems and were not aware of other relatives with a similar ailment.

Follow-up of patients is fairly streamlined and these patients are reviewed at least once every 3 months. This is done at the haematology consultant clinic.

This ensures adequate information on how the patient is doing in general and early detection and treatment of complications or intervening diseases. It also conveniently enables the patients to keep stock of the prophylactic drugs without going through the long queues of other outpatient departments. However, these patients are advised to seek medical attention immediately they experience some unusual medical problem. Although most patients take heed to this advice, a few situations were encountered where the patient had developed a febrile illness a few days to the clinic appointment day and the mother treated him or her with chloroquin with favourable outcome. The family is therefore part and parcel of management of sickle cell disease and the parents particularly mothers are willing to go the extra mile to protect the affected children from any situation that may jeopardize their state. In the short period, it was noted that mothers need reassurance in what activities are safe for the child including playing with other children, travelling or school curriculum. Only two patients were brought by their fathers and their concern is not different.

It was also noteworthy that these patients or their parents have confidence in this clinic. Although some do not stay in Nairobi on regular basis they travel from their homes to attend the clinic when they are due. Occasionally they come later after their appointment date.

The general physical appearance of these patients was good. There was really no evident features of chronic ill health and one had to go through clinical examination to elicit the attending signs. 31% of the patients had not been admitted to hospital in the preceeding one year and only 18% had been admitted twice. Although thrombotic crises appeared to be the commonest reason for admission, malaria could be predisposing to the crises and the patients are started on antimalarial drugs before they reach the hospital.

The incidence of complications was 21.8%, of these 3% was due to chronic lower leg ulcer which was just healing at the time of examination. This was one patient who was the oldest in this series - 24 years old. Avascular

humeral epiphyseal necrosis was found in one patient and avascular hip necrosis in two patients. Avascular epiphyseal necrosis of humerus and femur accounted for 9%. Tanaka et al found an incidence of 12% in their series (30). Pneumococcal meningitis has been noted to have higher incidence in children with sickle cell disease as compared to Haemophilus influenza in other children. Although one patient in this series had been admitted and treated for meningitis, bacteriological report was not available.

6 patients (18.8%) attended the clinic on the appointment date but had no complaints. Respiratory symptoms of sore throat and coughing were the commonest accounting for 31% and 21% respectively. Headache and dizziness was reported by only two patients, 23 and 24 yrs old.

Some degree of anaemia is common while jaundice was not as commonly noted in this series. Whereas only 3 patients did not appear anaemic, 13 patients (40%) had no clinically observable jaundice. Tonsils are apparently enlarged in a significant proportion of sickle cell patients, as 84% had enlarged tonsils. This indicates an immunological effect sickle cell disease may have on the patients. One patient also had marked enlargement of the cervical lymph nodes. This may also be due to immune status.

Out of 7 patients with splenomegaly 4 were under 10 years but two had splenomegaly of 6cm below subcostal margin in mid-clavicular line at 13 and 23 yrs. Although functional ability of the spleen was not evaluated, this showed that there are exceptions to splenic size with age.

Although hepatomegaly was also seen in 7 patients only one patient had hepatosplenomegaly. There were no clinical features of cardiac failure and hepatomegaly in these patients could have been due to other manifestations of sickle cell disease or just as a result of haemopoietic process.

Systolic heart murmurs mimicking mitral incompetence was noted in 4 cases (12.5%). Hyperdynamic state of the circulation has been attributed to this cardiac finding.

In this series the haemoglobin concentration of 4.6 - 9.3gm% was slightly lower than that observed by Chanarin of 6-10gm% in stable sickle cell patients (12). However, the average Hb level in the two populations may be variable and other factors like nutrition and intercurrent infections may be contributory.

Most of the patients had persisting haemoglobin F, but the percentage of HbF was not given hence proportion not shown. The youngest patient with HbSS was 3½yrs male child.

The features examined on the lateral skull radiograph include the width of the diploe, the trabecula pattern in the vault and the size of the adenoid.

The width of the diploic space was wide in all the patients. The outer table was commonly absent while the inner table appeared thinned in many patients. In this series sclerotic changes on the skull was not observed. This may still develop in later ages. The trabeculae appeared coarse in 53% of the patients. 23.5% of these were under 5 years. 41% were between 5-12 years and 35.5% were between 13 and 24 years. There was no patient who had hair-on end appearance. This has been reported to be 5% in other studies (16). Caffey observed that skull changes are seen more frequently after the 5th year of life (30). In this series widening of the diploe appears in all the ages while the trabeculae was normal in the majority of the patients under 5 years (69%), leaving 30.7% with some changes in the trabeculae appearance. In the 5-12 years age group, 70% had coarse trabeculae while in the 13-24 year age group 66% had coarse trabeculae. The overall observation therefore is that the trabeculae is more commonly coarse in older patients even though the diploic space is wide in all age groups. Punched out lesions simulating multiple myeloma as described by Carroll (30) or thickening of calvarium giving ground glass appearance described by Golding (30) was not seen in this series. These may still develop in these patients as age advances.

The adenoids measured using Eller's method in lateral skull x-ray (17) was enlarged in even older patients. This finding and the enlarged tonsils may have the same immunologic basis and present with upper respiratory tract symptoms.

In the lateral thoracolumbar spine xray, the common radiologic features in all age groups were osteopenia and coarse trabeculation. Diffuse osteosclerosis as described by Moseley and Manly was not a feature in the age groups covered (30). Flat or fish vertebrae was a less frequent finding (Table 15) particularly in the young patients. The disc is biconvex between the involved vertebrae (1). Step depression which is almost pathognomonic (32) was seen in only one patient (7.7%) under 5 years, 2 patients (20%) in the 5-12 year age group and 2 patients (22%) in the 13-24 years age group.

Vascular notching on the anterior aspect of the vertebral bodies is a usual finding in young children. In this study the notching was pronounced in some patients and was present in almost 50% of patients under 12 years. (Table 15). It was observed in only one patient above this age. The increased haemodynamics and resultant pulsations against the bone is the most likely cause of increased and prolonged appearance of notching of the vertebral bodies.

The vertebral body height: width ratio appeared increased and the figures obtained compared well with those of earlier authors (22). Although an upright posture would be expected to further increase the ratio, the ratio obtained in this series did not appear to have a significant association with age. Henkin observed that the ratio does not vary with age (22). In this series the ratio was actually slightly higher in the younger age group.

Heart enlargement occurs before the skeletal manifestations of sickle cell disease (Macht & Roman). (30)

Legant and Ball observed that cardiac enlargment is the most frequent abnormality is sickle cell patients (19, 30).

In this study, cardiac enlargment was the most common significant finding on chest radiograph. Almost all patients had cardiomegaly regardless of the age (Table 16). The cardiomegaly is however, not so gross as seen in most intrinsic cardiac lesions. There is no strict specific cardiac chamber involvement. The appearance is that of mild generalized cardiomegaly (Fig. 10).

The pulmonary vessels were increased in a significant proportion of patients above 5 years affecting just over 50% of these patients (Table 16). However only 3 patients or 23% of the patients under 5 years had increased pulmonary vascular markings on chest film. These cardiopulmonary features are attributed to chronic anaemia and resultant increase pulmonary blood flow (23).

The skeletal changes in the chest radiograph were observed in the ribs and humerus only. Rib trabeculation was coarse in 66.7% of patients between 13-24 years, while only about 30% in patients below 13 years. This finding suggests significant haemopoetic functions of the ribs in older sickle cell patients, where as tubular bones of the extremeties contribute significantly to haemopoietic requirement in earlier ages.

Only one patient had humeral epiphyseal pathology. This represents about 3% of the patients examined. This humeral epiphyseal fragmentation is less common compared to hip epiphyseal avacular necrosis (6).

Infarction of the scapula is symmetrical in sickle cell disease (10). There was no scapular lesion observed in this series. Pulmonary infarction described particularly in Haemoglobin S-C patients (6) was not seen. Pulmonary bone marrow embolization or subsequent pulmonary infarction was not evident in these chest radiographs.

X-ray of the pelvis had least suggestive features of sickle cell disease and except for those cases with avascular necrosis of capital femoral epiphysis the degree of trabecula changes may not raise any suspicion. Hip necrosis was found in 2 patients (6.25%). This incidence is less than that

found by Tanaka et al which was 12% (6, 33). These patients were 10 and 13 years respectively. Only the 10 year old female patient had hip symptoms which had been present for 2 years. The 13 year old patient had no hip complaints. Moseley et al observed that radiological appearance may not have any correlation with clinical severity (25). The age of onset of avascular hip necrosis appears to be earlier than stated by earlier publications (16, 20).

Chung observed complete recovery in patients with avascular necrosis (14) and he suggested conservative or orthopaedic management of either high osteotomy of McMurray or hip replacement. In this series "NO WEIGHT BEARING" management was not applied and the 10 year old female patient had no visible left femoral capital epiphysis.

The appearance of hand radiograph is suggestive of haematological condition particularly in the young patients. Coarse trabecular and wide medulla are characteristic features of sickle cell disease in young patients. Bone marrow hyperplasia appears to be the dominant process in the bones of the hand before puberty. Two patients also had growth disturbance resulting in shortness of affected bones. Growth plate involvement in infarction may be followed by early fusion of epiphysis resulting in abbreviated digits. Dactylitis is also frequently followed by short digits (16).

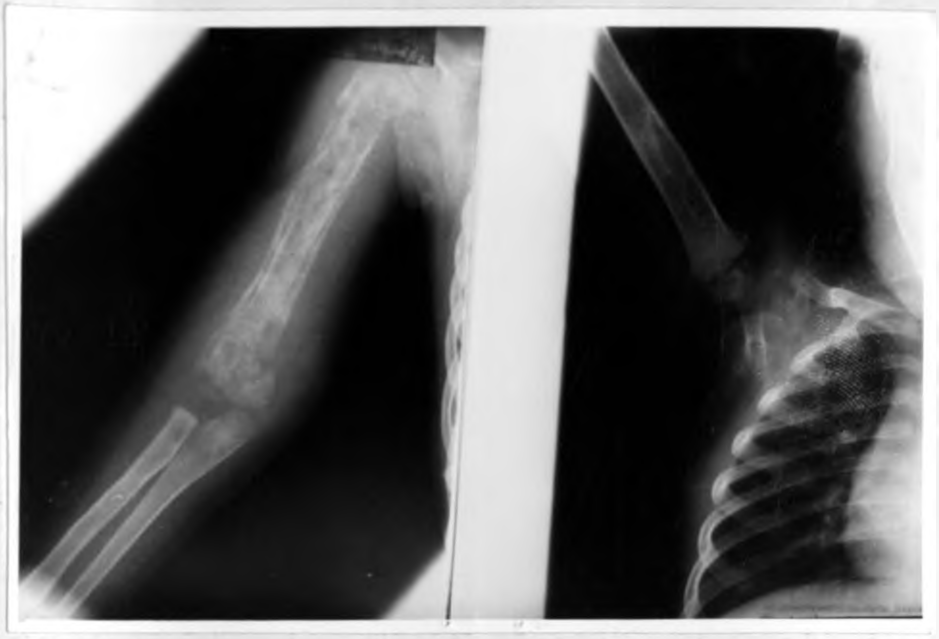
The radiological manifestations of sickle cell disease have no definite age distribution. However the radiological signs in the hands are more pronounced in the young patients under 13 years, in this study. After 13 years the bones of the hands appear almost normal except those with specific residual effects like growth disturbances.

On the other hand bone changes in the skull were more pronounced after 5 years. The size of the adenoid and width of diploe may give a clue before 5 years. The spine also shows more definite changes after 5 years. The skull and spine examination are therefore likely to show characteristic changes after 5 years.

The bone structure in the pelvis appeared least suggestive of haemapoietic disturbance and examination of the pelvis is only rewarding where specific abnormality as avascular necrosis of hip has occured.

Chest examination shows cardiomegaly in all ages. This generalized cardiomegaly may be the only feature and it is too non-specific to be diagnostic.

Fig 15



26.12.89 3.12.90

This is a 3½ year old patient who was admitted to an orthopaedic ward with osteomyelitis one year earlier. SCD was diagnosed thereafter. The humerus appears almost normal thereafter following treatment.

In this study the overall radiologic features had no correlation with clinical features or Haemogram findings. The features described in literature were commonly also observed in these patients who have close medical follow-up. Growth retardation and delayed skeletal maturation attributed to folate deficiency (16) was absent. Haris stress growth lines were however seen in 18.8% of the patients. This may be due to preceeding crises or intercurrent infections.

CONCLUSION

Laboratory diagnosis is definitive for sickle cell disease. Clinical assessment and regular review of each patient is mandatory in promoting the health of sickle cell patients. This however does not eliminate complications and emergence of any complication should be dealt with promptly and aggressively. Prompt effective management of infection or avascular necrosis is likely to revert to normal. The skeletal changes due to hyperplasia persist even in stable patients with optimal medical management but do not appear to be of any clinical significance.

Recommendations

1. Early diagnosis of complications and immediate institution of remedial therapy. Non-weight bearing should be encouraged in early avascular necrosis.

2. Skeletal complications need radiographic follow-up to confirm recovery following treatment.

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Name: ..... Unit No: .....

Age: ..... X-ray No: .....

Age at Diagnosis: ..... Home District: .....

No. of Siblings with SCD: .....

Complaints: .....

.....

Findings on Examination: .....

.....

No. of admissions in last 1 year: .....

Reasons: (1). Anaemia

(2). Infection (a). Malaria
(b). staphylococcus
(c). No specific organism isolated

(3). Bone pain

(4). CCF

(5). Crisis

(6). Others (specify) .....

Number of crisis in last 1 year: .....

Complications attributed to SCD: (1). Leg ulcers
(2). Arthropathy
(3). Osteomyelitis
(4). Necrosis of femoral epiphysis
(5). Others (specify) .....
.....

Number of transfusions given: (1).
(2).
(3).
More than 3 times .....
.....(specify)

Hb: .....

Sickling Test: .....

Hb electrophoresis: .....

Radiological Features: Skull X-ray .....

.....

.....

Thoracolumbar spine .....

.....

.....

X-ray pelvis .....

.....

.....

X-ray hands and wrists .....

.....

.....

Chest x-ray .....

.....

.....

Others: .....

.....

.....

.....