Table 7.32: Pulmonary complications in Saudi homozygous sickle cell disease

Pulmonary complication	Prevalence (%)				Prevalence (%) Total adults and children
	Children	Adults		Total	
		Male	Female		
Chest infections	9.52	0	8.33	4.2	6.66
Pneumonia	42.86	8.33	25	16.7	28.9
Pulmonary function Abnormalities	0	0	8.33	4.2	2.22

Pneumonia was the most frequent finding in the children and the prevalence decreased with age. 28.9% of our total patients had suffered from peunmonia. In a group of 93 Saudi Hb SS patients followed for 277 patients years broncho-pneumonia episodes occurred 26 times.

7.3.6. The bones and joints in Hb SS

Bones and joints are frequently affected in majority of the Hb SS patients and several bone and joint defects are reported (Table 7.33). Bone marrow expansion results from increased erythropoiesis, a consequence of the chronic haemolytic anaemia, and affect the bone shape and size. The most notable effects have been seen in the shape of the skull, the vertebra, long bones and pelvic bones. These produce bossing of the forehead, gnathopathy, pigeon chest, flask shaped deformity in the long bones, `squaring' of the metacarpals and metatarsals and pathological fractures.

In addition, sickling and decrease in blood flow to the bones leads to the painful crises, dactylitis, osteomyelitis and bone and joint pains. Osteomyelitis is a frequent finding in Hb SS patients and is caused by *Salmonella typhimurium, Salmonella*, *cholera-asuis and Paratyphi* B *typhomurium*.

Bone complications encountered in Saudi Hb SS male and female adults and children are presented in Table 7.34 and discussed in the following sections.

(i) Dactylitis (Hand-foot syndrome)

Dactylitis or hand-foot syndrome is an acute painful swelling of the fingers, toes and dorsal surfaces of the hands and feet or both. It generally occurs in children and the prevalence varies from less than 1% in eastern province of Saudi Arabia to almost 80% in

Africa. Generally, it is reported in children below the age of 2 years (Table 7.35), though

Table 7.33: Bone and Joint defects encountered in homozygous sickle cell disease patients

- Avascular necrosis
    - Dactylitis (Hand-foot syndrome)
    - Avascular necrosis of:
        - ✓ Humeral head
        - ✓ Femoral head
        - ✓ Growing epiphysis
        - ✓ Face and skull
        - ✓ Mandible
        - ✓ Ribs and Sternum
        - ✓ Vertebral bodies
        - ✓ Long bone
- Osteomyelitis
- Joint changes

Table 7.34: Complications affecting bones in Saudi homozygous sickle cell disease patients*

Complications	Prevalence (%)				Preva-lence (%) total adults and children
	Children	Adults		Total	
		Male	Female		
Dactylitis	42.8	0	0	0	20
Avascular necrosis of femoral head.	9.5	41.7	25	33.3	22.2
Osteomyelitis	14.3	8.3	25	17	15.6
Bone & joint pains	90	100	100	100	95.3
Abnormal bone scan	19.0	25	50	37.5	29.0
Joint swellings	38	25	58	41.7	40
Leg ulceration	0	16.7	167	167	8.9

* Patients from Western Saudi Arabia

Table 7.35: Prevalence of dactylitis in sickle cell disease patients in different populations

SCA patients population	Prevalence (%)	Reference
African	80	Konotey-Ahulu, 1971 Lambotte, 1962
American	11	Booker et al, 1964
Jamaican < 6 month 6-12 month 13 months - 2 years	 8 24 45	Stevens et al, 1981b
Saudi Arabia Eastern Province Western Province (<14 Yrs)	 14 42.8	 Al-Awamy et al, 1991 This study

older children suffer occasionally. In the Saudi patients from the south-western province dactylitis was encountered in 42.8% of the children (Table 7.34). This was significantly different when compared to the patients from the eastern province in whom dactylitits was previously reported as low as 1% and more recently as 14% (Al-Awamy et al, 1991). The condition is associated with swelling, pain and often fever which have an acute onset and resolve in about 7 days. Recurrence is frequent. The condition results from necrosis of the bone marrow and inner cortex caused by intravascular sickling which interrupts blood flow, generates stasis, swelling and pain. Epiphysial deformities, premature fusion, and shortened deformed bones and shortened digits are revealed on radiological resolution. Cold weather precipitates the condition and seasonal variations are reported in its occurrence. Secondary infection by *Salmonella osteomyelitis* may be associated with dactylitis and are diagnosed by blood culture preparations. Treatment is supportive, by avoidance of cold, rest and analgesia.

(ii) Avascular necrosis of femoral head

Avascular necrosis of the femoral head occurs both in children and in adults though significantly more frequently in the latter (Table 7.36). The mean age of onset varies in different populations, where a mean age of 13.7 years (range 6-27 years) was reported in a Nigerian population, while in the Jamaicans, the mean age of onset was 20 years. The prevalence of avascular necrosis of humoral head also shows a significant variation in different populations. It is as high as 30% in Nigerian Hb SS patients over the age of 12 years; while in the Saudi Arabian patients from the eastern province the prevalence in the age group 10-19 years was 4.4%. In our study on 45 Hb SS patients

avascular necrosis of femoral head was present in 22.2% of the patients. Among the

Table 7.36: Prevalence of avascular necrosis of fumerol headin homozygous sickle cell disease patients from different countries

SCD in	Age group	Prevalence (%)	Reference
U.S.A.	Adults	4 - 19	- Tanaka et al, 1956 - Siegling, 1966 - Sebes and Kraus, 1983
Nigeria	< 12 yrs > 12 yrs	Nil 30	- Cockshott, 1958 - Bohrer, 1981
Jamaica	Adults upto 10 yrs	10 - 15 3 - 5	- Golding et al, 1959 - Ennis et al, 1973 - Serjeant, 1988
Saudi Arabia			
Eastern Prov.	10-19 yrs	4.4	Perrine et al, 1978
Western Prov.	< 14 yrs	9.5	This study
	15-50 yrs	33.3	
	Total 5-50 yrs	22.2	

children 9.3% had this complication, which increased to 33.3% in adults. The prevalence was more in the males compared to the females (Table 7.34).

The condition is associated with articular surface deformity and persistent pain in the hip which is relieved by resting but aggravated by walking. Damage to the articular surface and collapse of the femoral head, persistent deformity may occur if precautions are not taken to avoid weight bearing on the femoral head. Early diagnosis based on Scintigraphic techniques is vital since proper management at an early stage by avoidance of weight bearing for 3 to 6 months can arrest the damaging process and allows healing. The treatments for avascular necrosis are listed in Table 7.37.

(iii) Avascular necrosis of the humeral head

The humeral head is often affected by avascular necrosis but the condition is generally asymptomatic due to absence of weight bearing. Occasionally, the pain may be severe and persistent with restricted movement. The prevalence of avascular necrosis of humeral head varies from 2-17% in studies reported on Hb SS patients of different ethnic origins.

Diagnosis is based on radiological findings which include spotty decalcification, diffuse or patchy sclerosis and cystic areas.

The condition generally resolves spontaneously. However, cases in whom shoulder replacement was essential have been reported.

In our series of Saudi patients no patient was diagnosed as suffering from avascular necrosis of humeral head.

Table 7.37: Treatment of avascular necrosis of femoral head

Early Stage

- Avoidance of weight bearing:
  - Bed rest
  - Traction
  - Crutches

Later Stage

- Arthrodesis
- Remodelling of femoral head
- Prosthesis
- Femoral head replacement
- Total hip replacement

(iv) Involvement of long bone

Long bones are frequently affected in Hb SS patients and present as localized pain and swelling. In the children (<10 years) acute diaphysial infarction, and in the adults, a gradual marrow ischaemia and necrosis, are the main pathology behind pain and swelling.

In the older patients, progressive cortical thickening, narrowing of the medullary space and periosteal new bone formation may occur due to cortical infarction, calcification of the medullary infarcts may occur. In a few severe cases the medullary cavity may be obliterated or there is an appearance of generalized osteosclerosis.

In the Saudi patients a generalized pain in the long bones was the most frequent finding (Table 7.34). Bone scan was carried out on 45 Hb SS patients and the results are presented in Table 7.34.

(v) Avascular necrosis of other bones

Avascular necrosis affects other bones, including the skull, mandible, ribs and sternum and vertebral bodies, but these conditions are rare.

(vi) Osteomyelitis

Osteomyelitis is more prevalent in children with Hb SS than in normal children. It also affects older patients and the prevalence is higher in the males compared to the females. *Salmonella and Staphylococcus aureus* are the major infective agents and the risk of salmonella osteomyelitis is several time more in Hb SS than in normal population. Factors which seem to predispose to osteomyelitis include poor hygiene, poor nutritional status, and trauma in the form of cuts, abrasions and insect bits. The differential diagnosis of osteomyelitis from non-septic bone infarction is necessary and often difficult. The

former generally manifests a more severe clinical course, and is associated with significant radiological changes, and can be confirmed by bacteriological studies on blood cultures and/or bone aspirates. In many cases the diagnosis of osteomyelitis is suspected only when symptoms fail to respond to non-specific measures such as rest, analgesics, increased fluid intake and alkalies. Combined technetium and gallium scintigraphy has been shown to be effective in distinguishing osteomyelitis from infarction. ^{99}Tc methylene diphosphonate bone scan followed by Ga-67 citrate scintigraphy have been recommended as effective in the differential diagnosis of osteomyelitis and infarction.

In our study on Hb SS patients, the prevalence of osteomyelitis in children was 14.3%. In the adults it was 17% while the overall prevalence of osteomyelitis in the total Hb SS patients was 15.6% (Table 7.34).

(vii) Joint involvement

The joints are frequently affected and joint pain is the most frequent finding in Hb SS of almost all ages. In our patients joint pain was reported by 90% of the patients from Eastern province and 95.3% of the patients from the Western province. Joint swelling was encountered in 40% of the patients.

Joint involvement is usually secondary to the avascular necrosis affecting the articular surface, uric acid deposition leading to gout, painful crises and leg ulceration. Each of these factors are discussed later in this section.

7.3.7 Leg ulceration in Hb SS

eg ulcers are a frequent finding in the Hb SS patients from Jamaica and North America but occur at a lower frequency in Nigerian patients and no cases of leg ulcers

were identified during a study of the natural history of Hb SS in the eastern province of Saudi Arabia (Table 7.38). No specific reasons for such a wide variation in the prevalence

Table 7.38: Prevalence of leg ulceration in sickle cell disease patients in different populations

Population	Prevalence (%)	Reference
Saudi Arabia		
Eastern province	0	Perrine et al, 1978
Western province	8.9	This study
India	Rare	Bohar et al, 1963
North America	73.6	Wolfort & Krizek, 1969
Jamaica	75	Serjeant, 1964
Nigeria	5.4 - 7.5	Akinyanju & Akinsete, 1979
U.S.A. (West, Midwest South & East)	4.97	Koshy et al, 1989

of leg ulcers are yet known though it has been suggested that certain environmental factors such as zinc may play a protective role. Other factors that may influence the susceptibility to leg ulcers include the Hb F level, genotype, age, social status and geographical location. In a cooperative study of the clinical presentation of sickle cell disease, it was shown that the Hb SS, with and without one gene deletion α-thalassaemia, have the highest prevalence rate of leg ulcers. Though α-thalassaemia due to two α-gene deletion was protective against leg ulcer. Recurrence of leg ulcers was approximately 25% though significantly higher prevalence rates were reported in other studies from Africa, Jamaica and the United States. No sex differences were reported in the prevalence of leg ulcers.

The major sites affected by leg ulcers include the areas around the ankles, an area of borderline blood supply. Often the patients have a history of insect bite and trauma but several patients develop leg ulcers without any trauma. A painful area develops spontaneous, where the skin becomes hyperpigmented, undulated and necrotic lesions develop. A painful lesion is left which may heal in a few months. Another type of leg ulcers resulting from skin infarction has been reported in patients with low Hb F level.

Healing occurs on treatment and on complete bed rest. It is usually a slow process and may occur over a period of months or years. Secondary bacterial infections often occur and the organisms identified include *Staphylococcus aureus, salmonella*, beta haemolytic Staphylococcus, *Pseudomonas aeroginosa* and C. bacterium diptheriae.

In our studies in Saudi Arabia, no cases of leg ulcers were identified in the eastern province population, however, in the Western population leg ulcers developed in 16.7% of the adults (Figure 7.26). No differences were seen in the prevalence in the males and

females. Among the children no one developed leg ulcers. However, one child (age 4 years) developed an ulcer near the left ear which was not cured by various treatments used. However, when she was treated with piracetam the ulcer was completely cured within a few months.

7.3.8 The cerebro-vascular system in Saudi homozygous sickle cell disease

Complications of the cerebrovascular system listed in Table 7.39 have been identified in Hb SS patients of different ethnic origin. The young patients are most susceptible and almost 70% of the episodes occur at or before 10 years of age, while almost 83% occur by the age of 15 years.

Factors that play a role in the development of the cerebrovascular complications particularly stroke are listed in Table 7.40. Strokes result mainly from cerebral infarction in young age group, while in the adult group the major pathology leading to strokes is intracranial haemorrhage.

(i) Stroke

Stroke is a well recognized complication in the Hb SS patients. The average age of onset is around 7 years and recurrence is frequent. Though this condition has been reported in all ages, the risk in patients under the age of 20 years is reported to be almost 1.7 times more than in those over 20 years.

The prevalence of strokes varies in different populations as shown in Table 7.41. In Saudi Arabia a low frequency of strokes is encountered. In south-western Nigeria the prevalence was reported as 3% of patients admitted in hospital, while in the northern and south-western Nigeria, the prevalence was <10%. In a study on 223 patients older then 5

years the prevalence of hemiplagia was 0.9%. According to four studies conducted in

Table 7.39: Cerebrovascular complications in homozygous sickle cell disease patients

- Stroke
  - Cerebral infarction
  - Intracranial haemorrhage
- Hemiplegia
- Convulsions and seizurs
- Coma
- Stupor
- Brain stem lesions
- Visual disturbances
- Sudden loss of hearing
- Peripheral neuropathy
- Cord syndromes
- Intellectual impairment (neuropsycologic deficits)

Table 7.40: Factors affecting cerebrovascular complications

- Genotype
- Family history
- Age
- Haemoglobin level
- Hb F level
- Thrombocytosis
- Dehydration
- Hyperventilation
- Preceeding meningitis
- Fat embolism

Figure 7.26: Leg ulcer in a Saudi homozygous sickle cell disease patient

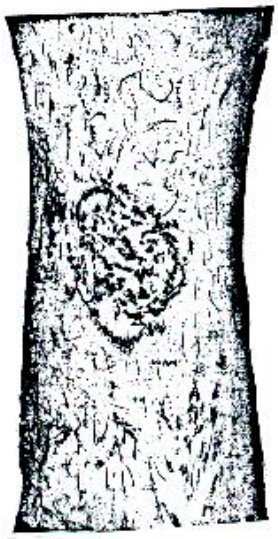


Table 7.41: Prevalence of strokes in homozygous sickle cell disease patients

Population	Prevalence	Reference
Stroke		
Britain	7.3	Brozovic & Anionwu, 1984
American	9.0	Gaston, 1987
American	24 (< 15 Yrs)	Wood, 1978
Nigeria		
- Northern	< 1	Yakuby & Werblinska, 1985
- South-eastern	< 1	Kaine, 1982
- South-western	3	Adeloye & Odeku, 1970
Saudi Arabia		
- Eastern province	0.9	This study
- Western province	9.5 (<14 yrs)	This study

America, the prevalence ranges between 7.6 - 17% and is as high as 24% in those below the age of 15 years. In our Saudi patients hemiplagia was encountered in 9.5% of the patients below the age of 14 years and in none of the patients more than 14 years of age.

The onset of hemiplagia was generally sudden, though in a few cases gradual onset has been reported. In some cases, the symptoms are transient and recovery is over a period of days or weeks, while in others the recovery is generally a slow process and recurrence is frequent (residual effects).

Other complications such as intracranial haemorrhage, convulsions, coma and stupor have been reported in Hb SS patients. Severe cerebrovascular disease often leads to coma and stupor. Powars et al (1978) reported coma following cerebral infarction in 20% Hb SS patients, while Portnoy and Herion (1972) had noted a history of coma with neurological complications in 9% Hb SS patients. Convulsions occur at a frequency of almost 12-16%.

Brain stem lesions have been reported as isolated cases. These include vertigo attacks and transient ataxia and cases of sudden hearing loss. In 105 Saudi patients followed closely for 1-7 years, deep vein thrombosis occurred in 5.7%, CVA in 13.3% and coma occurred in 4.8% of the patients. No case of convulsions or intracranial haemorrhage were identified.

(ii) Neurophysiological impairment in Hb SS patients

In an early study on Hb SS patients who did not suffer from neurologic complications, it was shown that the intellectual tests did not show any significant difference between the Hb SS patients and the normal siblings in the group studied. However, later

several studies showed that Hb SS is associated with intellectual impairment and the IQ in these patients is lower than the IQ in the normal children or the children suffering from sickle cell trait. In a well designed more recent investigation, which included tests of intelligence, constructional praxis, memory and academic learning, it was shown that significant and widespread neuropsychologic deficits are associated with sickle cell anaemia even in the absence of neurologic complications. There are a few reports of the cognitive and educational sequelae of neurologic disease in children with Hb SS. In a study by Wilimas and co-workers (1980) it was shown that children who suffer from strokes and have a decreased IQ score (45-70) after the first stroke, show an improvement in the IQ if the second stroke does not occur, while those who suffer from repeated strokes have a deficit IQ. Detailed studies of the neuropsychologic impairment in Saudi children with Hb SS were not conducted during our investigation.

(v) Priapism

A sustained painful erection of the penis is referred to as priapism. It occurs when sickling of the red cells causes obstruction of venous drainage and localized stasis in the corpora cavernosa in Hb SS patients. Priapism was first reported as early as 1934 (Diggs and Ching, 1934) and several studies later confirmed it as one of the complication of Hb SS. Several factors have been implicated in the aetiology of priapism and are listed in Table 7.42. In general, haemoglobin F level is generally low in Hb SS patients who suffer from episodes of priapism.

A few characteristics of priapism in Hb SS patients reported in literature and the methods used for treatment are listed in Tables 7.43 and 7.44. Several factors that

precipitate priapism are listed in Table 7.45. However, in most of the patients the attack may be spontaneous or may occur following spontaneous nocturnal erection. Following a

Table 7.42: Aetiological factors in Priapism

- Low Hb F level
- Psychological factors
- Infection of the urethra or urinary tract
- Prolonged erection
- Hormonal effect

Table 7.43: Characteristics of Priapism

Age of onset	5-40 Years
Prevalence	Variable Rare in some populations • 42% in < 15 years (Jamaica) • 50% in > 20 years (Jamaica)
Frequency of occurrence	1 or 2 attacks in 31% (Jamaica) Multiple attacks in 57% (Jamaica)
Duration	Single attack - severe : 24 hours Multiple attacks - milder : < 3 hours
Attack characteristics	Major attack - Severe pain in penis, abdomen and perineal area - Dysuria - Acute urinary retention - Scrotal/penile oedema - Large tender prostrate. Stuttering - Milder attack
Sexual function following severe attack	- 75% partial or complete impotence (generally older patients) - 25% normal recovery (generally younger patients)
Following stuttering	- Normal sexual function (may cause partial or or complete impotence)

Table 7.44: Treatment of priapism

- Multiple blood transfusion
- Analgesics
- Hydration
- Alkalinization
- Blood transfusion
- Stilboesterol
- Surgery
    - Direct aspiration of the corpora
    - Single or multiple incision in the corpora
    - Shunting of blood from corpora to the adjacent saphenous vein
    - Shunt between corpora cavernosa

Table 7.45: Factors precipitating priapism

- Spontaneous attack - no factors
- Following spontaneous nocturnal erection
- Sexual intercourse
- Masturbation
- Alcohol intake

severe attack several patients may become partially or completely impotent. Recovery occurs at a higher prevalence in the young patients. Treatment of severe priapism is essential at an early stage.

In our series of patients priapism was identified in only 2% of the patients. However, it may be more frequent, but due to the difficulty in diagnosis, many have been underestimated in our study.

7.3.9 The gastrointestinal tract in Hb SS

Complications affecting the gastrointestinal tract are frequent in the Hb SS patients particularly the painful crises affecting the abdomen. Other clinical syndromes include duodenal ulceration, dysfunction of the small bowel and large bowel disease.

Abdominal pain is a frequent finding in Hb SS patients. The severity and frequency of the abdominal painful crises varies in different patients and are usually more frequent in the children. In the severe episodes, localized severe pain, associated with constipation, vomiting and guarding is frequent.

Several pathological mechanisms have been implicated and include avascular necrosis of the vertebral bone marrow resulting in referred pain if compression of the nerve root occurs, enlargement of lymph nodes (mesenteric and retroperitoneal) and thrombosis in the mesenteric artery. Abdominal pain may result from cholestasis, acute cholecystitis, splenomegaly or duodenal ulcers.

Duodenal ulceration has been reported in a number of Hb SS cases and in one study the prevalence was 30.5% in Jamaican males over 25 years of age. Small and large bowel abnormalities have been reported in a few cases but the exact frequency is not

known.

In our series of Saudi patients the major abdominal complications identified included abdominal pain and gastro-enteritis. Abdominal painful crises was the most frequent abnormality. The exact frequency is not clear as some patients suffered from frequent and severe episodes, while others had mild episodes and still others did not complain.

7.3.10. The ophthalmological complications in Hb SS

Sickling process leading to vaso-occlusion and to ophthalmological complications occurs frequently in the Hb SS patients and the abnormalities identified are listed in Table 7.46. These include complications of the conjunctiva, retina choroid, the arteries and the posterior segment.

Proliferative sickle retinopathy is a frequently reported complication in the Hb SS patients. It develops in young age but the prevalence increases with age and the most optimal age for the development of proliferative sickle retinopathy was shown to be 20-34 years in patients with Hb SC disease. Factors that seem to increase the prevalence of proliferative sickle retinopathy include low Hb F level, age and mean cell volume.

During our investigation of the Saudi Hb SS patients retinopathy was identified in 3.8% of the patients. Further studies were not conducted on this aspect.

7.3.11 The immune system

Patients suffering from Hb SS have an increased susceptibility to bacterial infections which are more difficult to eradicate and thus constitute a major cause of morbidity and mortality. A higher prevalence of infections due to *Streptococcus*

pneumoniae, Haemophilis influenzae, Mucoplasma pneumoniae, Straphococcus aureus, Neissera meningitis and Salmonella species have been reported in patients with Hb SS. In

Table 7.46: Ophthalmological abnormalities identified in homozygous sickle cell disease patients

Abnormalities
1. Abnormalities of the conjunctiva 2. Abnormalities of the Anterior Segment • Anterior segment ischaemia • Sectoral iris atrophy • Hyphemas • Glaucoma • Visual loss 3. Abnormalities of the Posterior Segment • Tortuosity of major retinal vessels • Abnormalities of the perimascular and macular vasculature o Proliferative retinopathy (rare) • Central artery occlusion • Posterior ciliary artery occlusion o Choriodal infarction o Chorio retinopathy • Lesions of the optic disc • Angioid streaks • Peripheral retinal vessel disease • Peripheral retinal changes • Proliferation sickle retinopathy

early childhood severe overwhelming septicemia, meningitis and pneumonia due to *S. pneumoniae* remain the major cause of death. Salmonella species are also frequently encountered in children with sickle cell disease and osteomyelitis is more prevalent in these patients compared to normal children. After the first decade of life, infections caused by anaerobic and enteric organisms become more common.

The increased susceptibility to infection in Hb SS patients results from deficiencies of multiple host factors including defective splenic function, abnormalities in complement, immunoglobulins, leucocyte functions and cell-mediated immunity. In addition, a further contributing factor is the vaso-occlusion resulting in necrotic tissue which habours certain infections.

(i) Host defence mechanism

The spleen plays an important role in host defence and initiates the primary immunological response. It is involved in the formation of antibodies and the clearance of blood-borne bacterial organisms and foreign or damaged particles by phagocytosis. The sequestration of the sickled cells in the spleen is often increased significantly, resulting in splenic sequestration syndrome and dysfunctioning of the enlarged organ. In most serious cases, the spleen is reduced to a fibrotic nodule by repeated episodes of infarction. The resulting functional asplenia increases the risk of sepsis. In some patients splenectomy is necessary and is accompanied by increased susceptibility to infection and sepsis.

Phagocytosis plays an important role in the host defence mechanism. In patients with Hb SS defective opsonization of streptococci, staphylococci and salmonella have been reported. The attributes of immunoglobulin G and complements are called their

'opsonizing activity'. This may result either from a deficiency of serum proteins and/or an abnormality in the alternative path was of complement activation. Furthermore, the phagocytic activity of the neutrophils is highly oxygen dependent and areas where hypoxia occurs due to sickling, the killing function of the neutrophils may be markedly reduced.

Plasma immunoglobulins, IgG and IgA levels, in Hb SS patients are either normal or elevated, while IgM level are significantly lower. Thus abnormalities in immuno-globulins do not seem to be aetiologically related to the susceptibility to infection. However, splenic hypofunction has been implicated as one of the causes for defective antibody formation on response to intravenous stimulation.

In patients with Hb SS the proportion of B cells are higher and T cells are considerably lower compared to the levels in matched controls, though the absolute count of both types of lymphocytes are significantly increased. Defective cell-mediated immunity has been suggested in some studies while others have reported conflicting results.

Finally, the devitalization of the bone and gut due to repetitive vaso-occlusive crisis, saturation of the macrophage system with red cell breakdown product of chronic haemolysis and underlying splenic and hepatic dysfunction may all predispose to infections.

(ii) Common Infections in Hb SS

The common bacterial infections encountered in patients with Hb SS include pneumonia, osteomyelitis and general sepsis. Appreciable morbidity and mortality is reported to result from pulmonary diseases and infections.

(a) Pneumonia

Patients with Hb SS suffer frequent episodes of pulmonary infection and are highly susceptible to infection with *Streptococcus (Diplococcus) pneumoniae. Salmonella species, Haemophilus influenzae and Mycoplasma pneumoniae*. These patients are also prone to develop pulmonary infarction. This results from frequent congestion and stasis in the small vessels, which is caused by mechanical and viscosity changes accompanying intravascular sickling. It is often difficult to distinguish pneumonia from pulmonary infarction and the two conditions are together referred to as the 'acute chest syndrome'. Both conditions are accompanied by chest pain, fever, hypoxia, cough, infiltrate and leucocytosis.

In Hb SS patients in Jamaica, the USA and other parts of the world, pneumonia due to bacterial infection is common in children less than 5 years of age and the disease follows a fulminant course, while in adults the course of the disease is much less fulminant. On the other hand, pulmonary infarction due to intravascular sickling becomes an increasingly common cause of the acute chest syndrome in older patients. It is considered to be the commonest complication of Hb SS in all groups. Repeated clinical and subclinical infarction due to the sickle state may lead to the development of Cor pulmonale.

In Saudi Hb SS patients from eastern province, pneumonia, was encountered in 7.5%, while in the patients from western province the prevalence was 28.9% for pneumonia.

(b) Osteomyelitis

Osteomyelitis is more prevalent in children with Hb SS than in normal children. It affects patients of all age groups and occurs at a higher prevalence in the male than the female. In several studies, salmonella species have been shown to be the infective agents and the risk of salmonella osteomyelitis is considered to be several hundred times more in Hb SS than in the normal population. In some studies *Staphylococcus aureus* has been shown to be the major organism causing osteomyelitis. Additional pathogens are often isolated from pus and blood.

Environmental factors and the nutritional status of Hb SS patients seems to play a significant role in the association between salmonella and Hb SS. Among other predisposing factors, poor hygiene and minor trauma in the form of cuts, abrasions and insect bites, seem to play an important role.

The clinical manifestation of salmonella infection varies considerably. It is most prevalent during infancy and early childhood and become less so with advancing age. Multiple sites of bone involvement are common. The sites affected vary with the age of patients. The small bones of hand and feet are commonly affected in the young. While in the older patients the long bones of the arms and legs are more likely to be affected. In some patients the illness is mild and hospital admission is not necessary while others suffer from serious toxaemia and severe bone lesions with pathological fractures. The infection may become chronic.

Staphylococcus aureus is not common during the first year of life, but from then onwards affects individuals of all ages equally, being more common in the male than in the

female. Patients with Hb SS particularly those with low haemoglobin levels, often have multiple site involvement.

Furthermore, the Hb SS patients are prone to develop periodic episodes of pain in their limbs, of variable severity and duration, due to bone ischaemia, resulting from intravascular sickling and occlusion of the blood vessels, leading to infarction. In the USA, acute long bone infarction is reported to be at least 50 times more common than bacterial osteomyelitis. In the very young the painful swelling often affects the extremities, leading to severe pain and swelling of the hands and feet referred to as the 'hand-foot syndrome'. The susceptibility to develop the hand-foot syndrome varies in different populations. In Africans, it is considered as a characteristic clinical manifestation of Hb SS.

(c) Meningitis

Meningitis occurs at a higher prevalence in Hb SS patients compared with normal individuals. A high prevalence of meningitis due to *Streptococcus pneumoniae* was reported in one study in patients with Hb SS, particularly those under the age of 3 years. Later studies confirmed that pneumococcus was the most common cause of meningitis. *Haemophilus influenzae* meningitis is also encountered at a higher prevalence in Hb SS than in normal children. Other organisms causing meningitis included *N. meningitis and Escherichia coli*.

Though children with Hb SS are more susceptible to *Pneumococcal meningitis*, they are not at an increased risk from its effects. The clinical presentation and the rates of morbidity and mortality are similar to those encountered in normal children. However, recurrent meningitis and cerebrovascular morbidity are more common in patients with Hb

SS. Racial differences in susceptibility to pneumococcal infections have been reported. In a study from New York the incidence was much greater in Black children with Hb SS than in normal Black children, who in turn had a higher rate than the Whites.

In patients with SC disease or S-thalassaemia a considerably lower incidence of meningitis compared to SS disease has been encountered.

(d) Septicaemia

Patients with the sickling disorders are more prone to develop septicaemia than normal children. In the young patients, less than 5 years of age, the main causative agent is identified as streptococcus pneumoniae. The risk of *Haemophilus influenzae* septicaemia has also been shown to be greater in children with Hb SS than in the normal children. During the second decade of life, pneumococcal septicaemia becomes uncommon and an increased frequency of septicaemia due to Gram negative enteric bacteria has been reported. In the Hb SS patients septicaemia follows a fulminant course, and the progress of symptoms is rapid. It often presents with sudden fever, few prodromal features and a deceptive appearance of well-being, followed within hours by rapid, relentless, progression to shock and death. In an earlier study, children under the age of 5 years were reported to have 40-50% chance of dying of pneumococcal sepsis. However, a more recent study indicates that there has been a decrease in major morbidity due to pneumococcal septicaemia and meningitis in patients. This has been attributed to the establishment of clinical programmes that provide close medical supervision of the patient with fever and the rapid institution of parenteral antibiotic therapy.

(e) Urinary Tract Infections

In Hb SS patients, several pathological changes in the renal medulla lead to concentration defects. The scarring of the renal medulla and secretion of dilute urine can cause an enhanced rate of urinary tract infection which is often accompanied by an increased risk of pyelonephritis. The prevalence of urinary tract infection and pyelonephritis has been reported to be high in adults Hb SS patients and death from renal failure is common in adult patients with sickling disorders. Major organism contributing to the urinary tract infection are *Escherichia coli and Enterobacter klebsiella.*

(iii) Prevention of pneumococcal infection

The two major strategies adopted to safeguard the Hb SS patients against pneumococcal infection are pneumococcal vaccination and penicillin prophylaxis.

(a) Penicillin Prophylaxis

Oral penicillin prophylaxis has been shown to provide complete protection from pneumococcal septicaemia particularly in children under the age of two years. The pneumococcal vaccination must be initiated before termination of penicillin prophylaxis.

The major disadvantages with penicillin prophylaxis are the problems of compliance, emergencies of penicillin resistant strains and delay in acquired immunity to the pneumococcus.

However, the significant decrease in morbidity in the young children has provided sufficient evidence for the strong recommendation of penicillin prophylaxis.

(b) Pneumococcal vaccination

The pneumococcal vaccine has been used in several studies and proved to be of significant use in prevention of pneumococcal infection especially in the young children.

The polyvalent pneumococcal vaccine is composed of polysaccharide antigen from 23 types of pneumococci. It is generally safe and apart from erythema and mild pain at the site of injection in about 50% of the cases, severe adverse effects such as anaphylactoid reactions have been quite rare. In patients under adequate penicillin cover, pneumococcal vaccination should be given at the age of 2 years, with booster dose every two years.

(c) Haemophilus influenzae vaccination

Haemophilus influezae represents the second most common aetiologic agent of sepsis in Hb SS. It is recommended that *H. influezae vaccination* be started at 12-18 months with booster dose every two year.

(d) Routine Immunization

The routine programme of immunization against the common childhood illnesses (measles, poliomyelitis, diphtheria, tetanus, mumps and pertussis) must be maintained in all Hb SS patients.

7.3.12 Symptom free intervals in Saudi sicklers. Does pneumococcal vaccination and penicillin prophylaxis have a role?

To investigate the effects of pneumococcal vaccination and penicillin prophylaxis on the progress of Hb SS, two groups of patients (age 1-12 years) suffering from a severe clinical presentation were selected as cohorts. One group (39 patients) was vaccinated with the polyvalent pneumococcal vaccine and was given penicillin prophylaxis while the other group (54 patients) was attending a hospital where the vaccine or penicillin prophylaxis were not administered to the Hb SS patients. Retrospective analysis of the patients files was carried out for 1-5 years. The patients were assessed clinically and the frequency of hospitalization, crises, transfusions, signs and symptoms (bone pain, sepsis, osteomyelitis, meningitis, jaundice, hepatomegaly, splenectomy etc) were

recorded. Haematological assessment of the patients was carried out and differential counts were obtained. Infections were recorded in both groups and the attack rate/1000 patient years was calculated by totalling the number of years for which each patient was followed, adding the number of all attacks and calculating the attack rate/100 patient years. The results obtained in the vaccinated group were compared with the results obtained in the non-vaccinated group. The results of haematological analysis did not show any major statistically significant difference in the two groups except in WBC count which was significantly higher in the non-vaccinated group (Table 7.47). Significant differences were evident in the clinical presentation, frequency of hospitalization, crises and blood transfusion requirement in the two groups (Figures 7.27 to 7.29). The severity index in the two groups of patients is presented in Figure 7.30. In the vaccinated group the mean severity index was significantly lower. No correlation could be demonstrated between the Hb F level and the severity index in the two groups (Figure 7.31).

Though both groups of the patients were from the western province of Saudi Arabia and were suffering from a severe form of the disease, however, the vaccinated group on penicillin prophylaxis showed significant improvement in their clinical presentations. The incidence of pneumonia, meningitis and sepsis in the vaccinated group was lower and the crises-free intervals was increased. It was obvious from these results that the improved resistance against bacterial infections plays a role in lowering the severity of the disease and frequency of other complications associated with Hb SS.

7.3.13 Immunoglobulin and complement levels in homozygous sickle cell disease

Several studies have investigated the levels of immunoglobulins and complement in Hb SS patients. Inconsistent results have made it difficult to obtain a clear pattern. Studies have shown that the IgG level may be normal, elevated or low. Generally, children

have low or normal level, but adults have elevated levels. IgM level is generally lower, but IgA is generally elevated. We estimated immunoglobulin, complement C3 & C4 and properdin in sickle cell anaemia patients and compared the results with those obtained in a group of normal healthy controls. This results of our studies are presented in Table 7.48.

Table 7.47: The value of haematological parameters in the two groups of vaccinated and non-vaccinated Saudi Hb SS patients

Parameter	Non-vaccinated Group	Vaccinated Group	P
Number	54	39	-
Age mean (years)	5.55 ± 2.64	7.65 ± 3.05	-
Age range (years)	1.6 - 10.7	0.37 - 10.8	-
Hb (g/dl)	8.19 ± 1.10	8.38 ± 1.30	0.582
RBC ($x10^{12}$/l)	2.56 ± 0.53	2.72 ± 0.74	0.277
PCV (l/l)	0.21 ± 0.035	0.24 ± 0.046	<0.05
MCV (fl)	87.63 ± 6.45	87.72 ± 10.62	0.625
MCH (pg)	32.27 ± 4.33	31.48 ± 5.47	0.260
MCHC (g/dl)	37.77 ± 4.17	34.97 ± 3.95	< 0.05
WBC ($X10^9$/l)	17.82 ± 10.97	13.56 ± 4.00	<0.05
Retics (%)	19.86 ± 13.44	19.49 ± 13.44	0.205
Hb F (%)	11.09 ± 6.76	7.86 ± 5.25	<0.05
Hb A_2 (%)	3.0 ± 0.78	2.97 ± 0.68	0.860

Figure 7.27: Frequency of hospitalization, crises, transfusions, in the vaccinated and non-vaccinated SCA patients

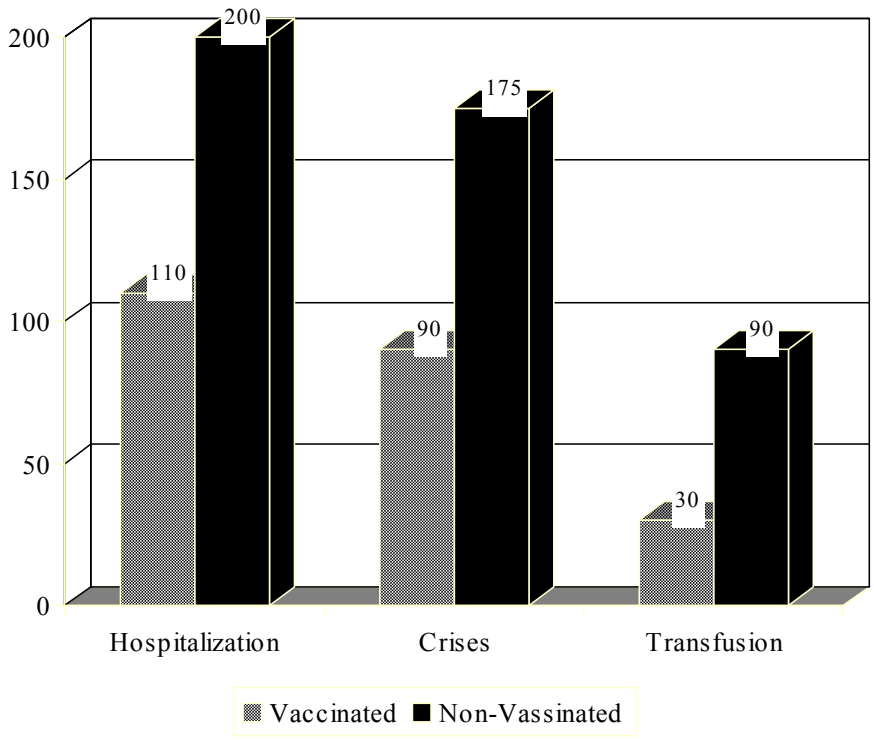


Figure 7.28: Frequency of splenomegaly, hepatomegaly, splenectomy, and jaundice encountered in the vaccinated and non-vaccinated SCA patients

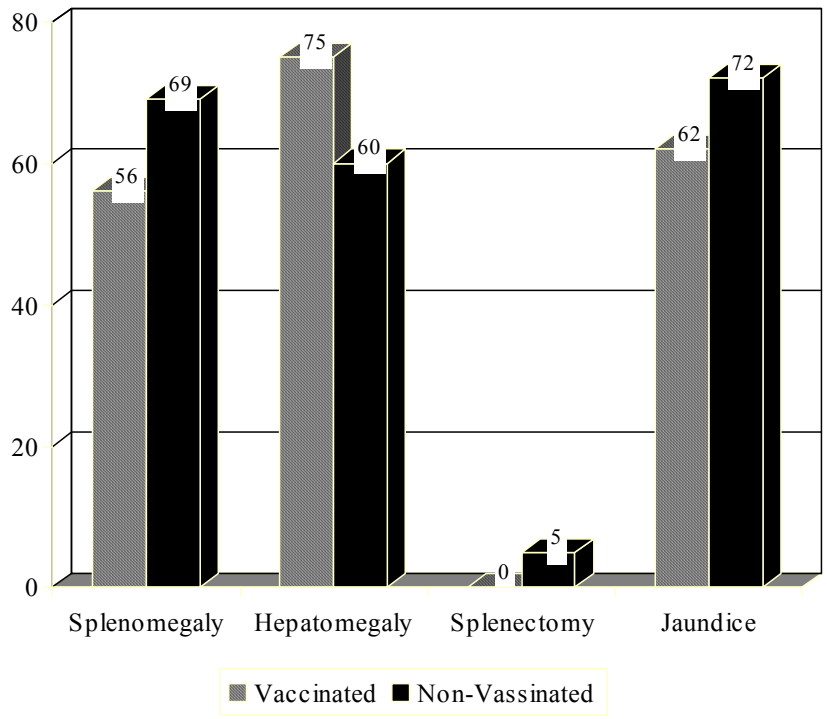


Figure 7.29: Attacks/100 patients years of pneumonia, miningitis, hand-foot syndrome, and osteomyelitis in the vaccinated and non-vaccinated SCA patients

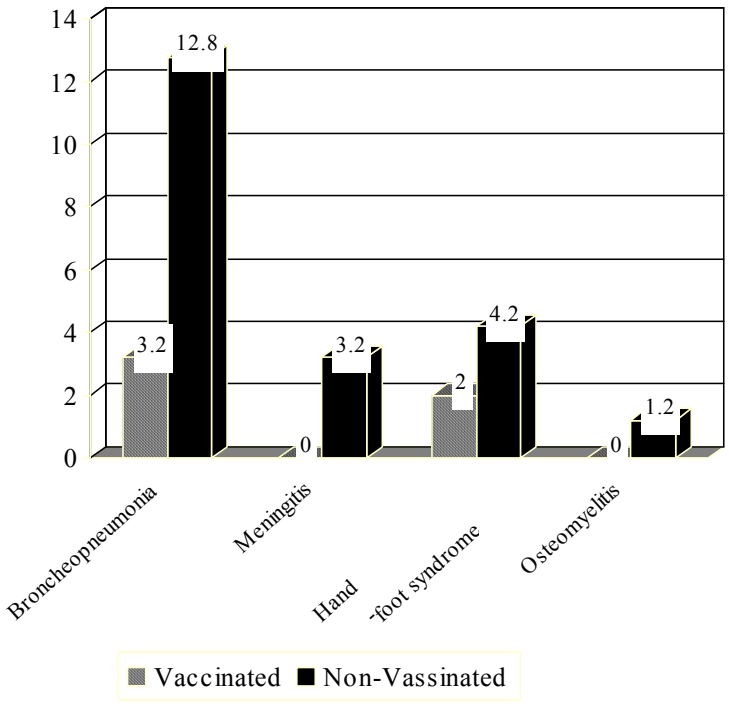


Figure 7.30: Severity Index in vaccinated and non-vaccinated SCA patients

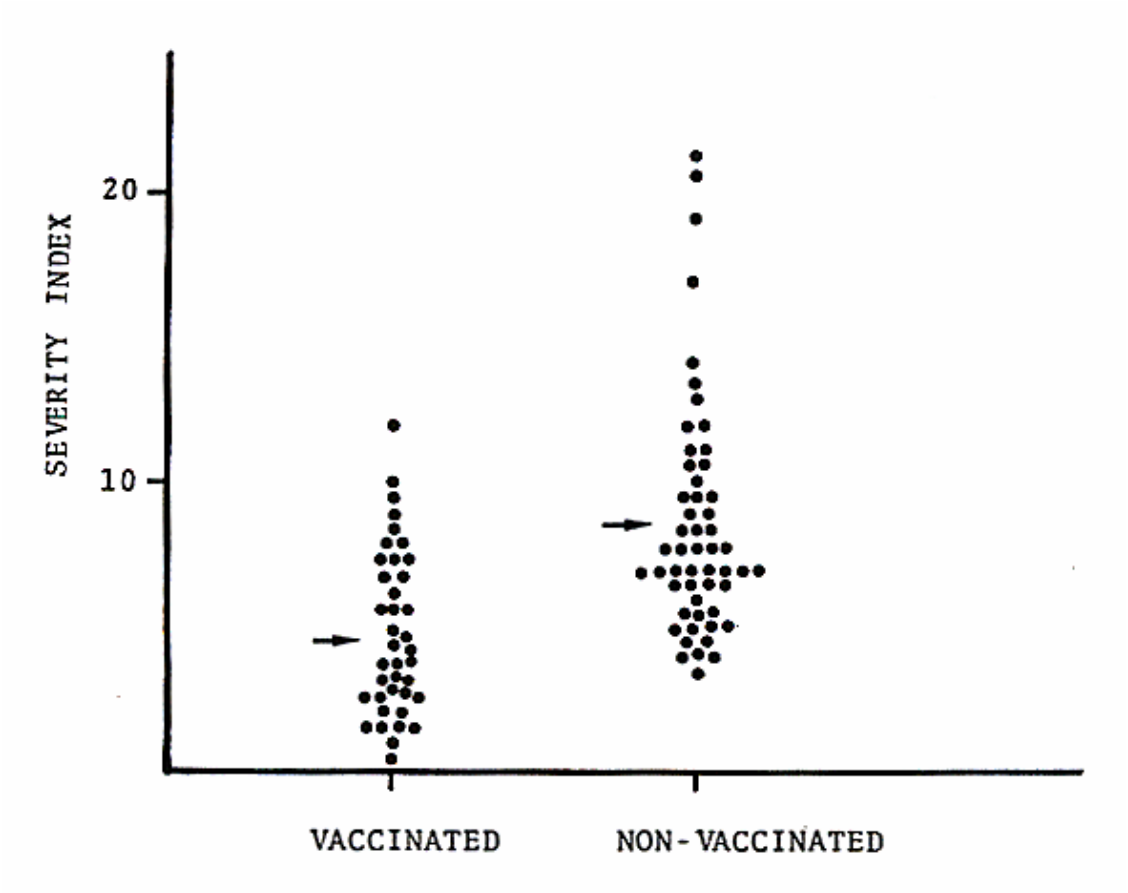
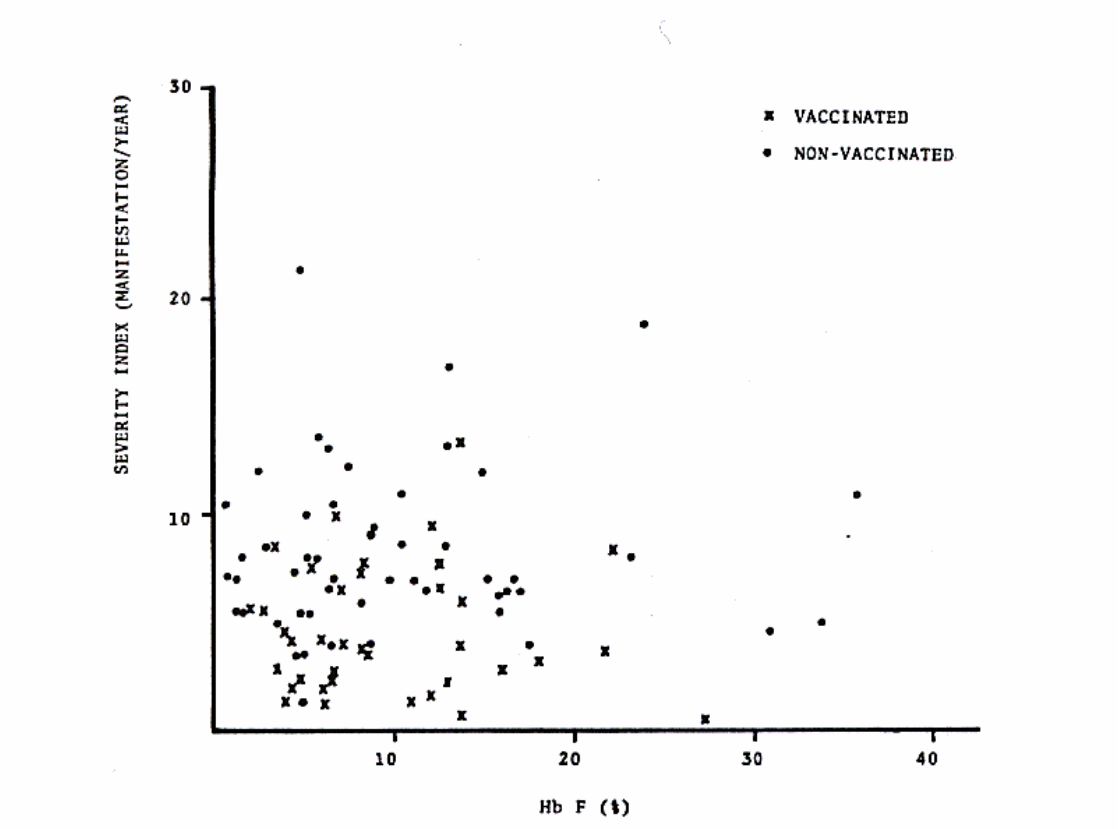


Figure 7.31: Correlation between Hb F level and severity index in vaccinated and non-vaccinated SCA patients



7.3.14. Painful crises in Saudi sickle cell disease

The steady state in Hb SS is frequently interrupted with bouts of severe pain which is a characteristic finding in the Hb SS patients. The acute attacks of severe pain in the limbs, joints, abdomen, chest or the back are often associated with fever and are referred to as the `painful crises'. These attacks are the principal cause of morbidity in Hb SS. Multiple sites may be affected and the area where pain occurs may be swollen and tender. The severity of the disease frequently determines the frequency, severity and duration of the painful crises. The pain is of different types (Figure 7.32) and the pathophysiological mechanisms leading to pain are presented in Figure 7.33. The major characteristics of the painful crises are shown in Table 7.49, which are precipitated by several factors (Table 7.50). Painful crises occurs in patients of all ages though the prevalence increases with age. The 'pain' rate is believed to be a measure of clinical severity of the Hb SS and correlates with early death in the patients over the age of 20 years.

The major pathology leading to the painful crises is not clearly understood. However, inflammatory response following ischaemia and necrosis seem to play a role. Bone marrow embolism resulting as emboli in the small vessels of the brain, lungs or kidney have been reported in a few patients.

The prevalence, frequency and duration of painful crises in the Saudi Hb SS patients during our study are listed in Table 7.51. Almost half of the patients suffered from either one or two severe attacks per year (Total 50.45%) while others had 3 or more attacks. 17.1% of the patients had never suffered from the painful crises.

Table 7.48: Haemoglobin, complement and properdin level in SCA

	Hb SS	Normal Control
IgG (g/l)	17.2 ± 5.4	11.25 ± 2.0
IgM (g/l)	1,5 ± 0.7	1.1 ± 0.4
IgA (g/l)	2.3 ± 1.3	1.5 ± 0.4
C3 (g/l)	0.62 ± 0.2	0.78 ± 0.2
C4 (g/l)	0.24 ± 0.06	0.30 ± 0.05
Properdin	31.2 ± 9.1	ND

Figure 7.32: Types of pain in sca

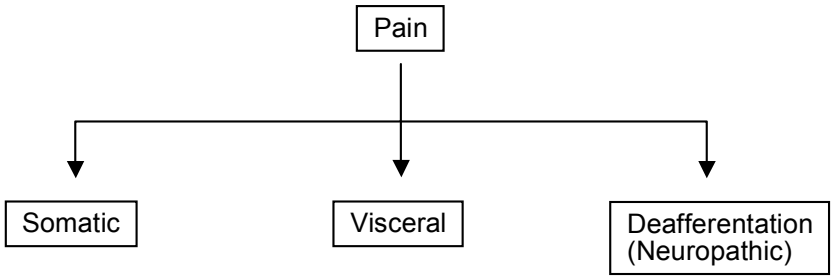


Figure 7.33: Pathophysiology of pain

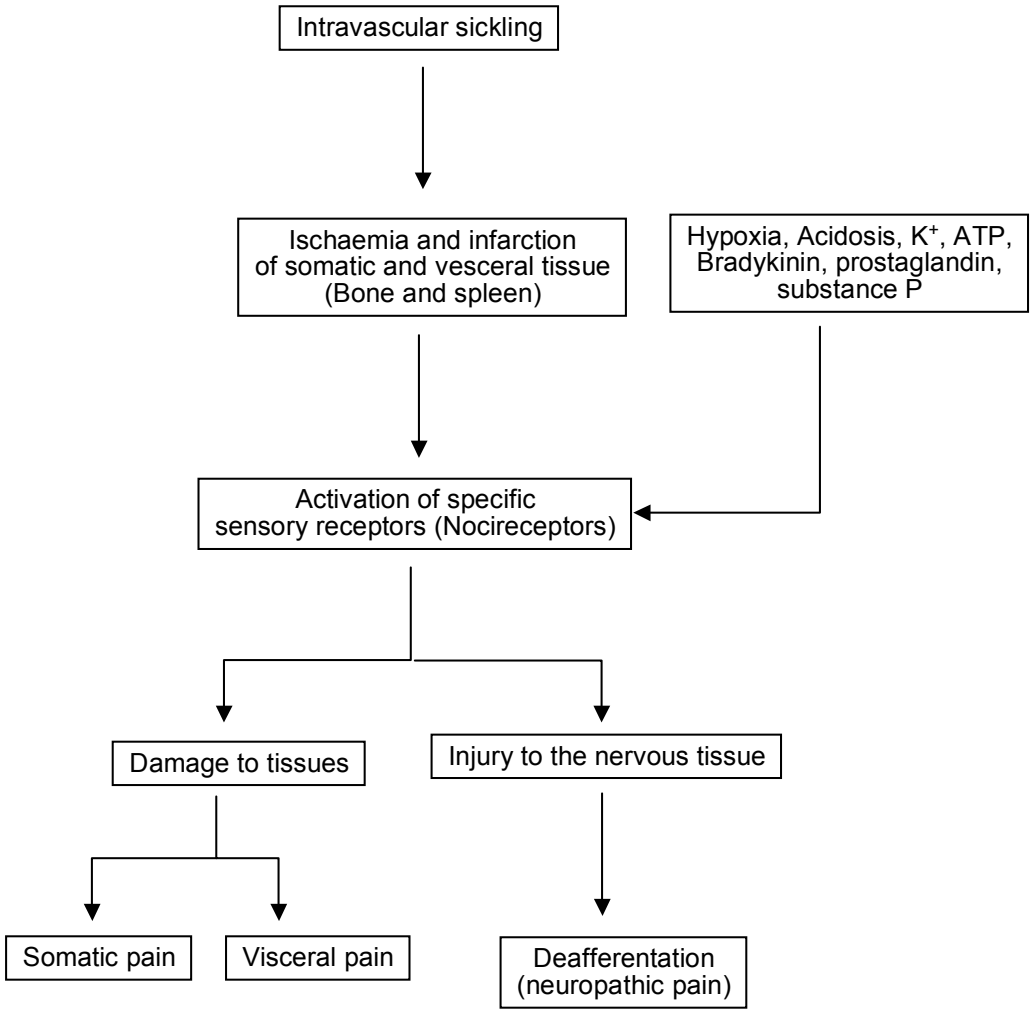


Table 7.49: Characteristics of painful crises in sickle cell disease

Frequency

- Variable: Nil to frequent severe attacks
- Shows geographical differences
- Affected by genotype

Areas affected

- Abdomen
- Chest
- Long bones and joints
  - Ankles
  - Shoulders
  - Knees
  - Elbows
  - Wrists

Severity

Mild to severe

Duration

Few minutes (5-10) to days and weeks

Age

Almost nil in young children. Increases with age. Less frequent after 30 years.

Associated symptoms

- Fever
- Passage of dark urine
- Acute urinary retention
- Swelling and tenderness of affected areas

Table 7.50: Factors precipitating painful crises

- Cold
- Fever
- Acidosis
- Dehydration
- Intracellular Hb S concentration
- Infections
- Hypoxia
- High altitude
- Stenous exercise
- Diureses
- Emotional stress
- Pregnancy

Table 7.51: Painful crises in Saudi homozygous sickle cell disease (Hb SS)*

		Frequency
•	Total Frequency:	82.9%
•	No. of attacks/year	
	0	17.14
	1	20.95
	2	29.5
	3	14.3
	4	9.5
	5	5.7
	6	1.9
	7	0.95
•	Duration:	Variable

* in Hb SS patients from Western Province

Haematological and relevant biochemical parameters were estimated in 23 Saudi Hb SS patients during the painful crises and compared to the results obtained during the steady state. The results are presented in Table 7.52. The interpretation of the haematological events is difficult since the painful crises is associated with infections and dehydration and the patients are generally on some form of treatment. The haemoglobin level was slightly reduced while the white cells, reticulocytes and total bilirubin level were increased. Except for MCHC no other parameters showed any statistically significant change. This finding confirms the earlier finding reporting a reduction in haemoglobin level during painful crises and an increase in the reticulocyte count during the crises.

Several studies have been directed to the study of changes in the red cell rheological properties during the painful crises. Red cell deformability was shown to decrease, while the dense cells increased. In a recent report of Ballas and Smith (1992) it was shown that the painful crises occurs in two distinct phases. During the first phase the pain escalates, the red cell deformability decreases and the number of dense cells increase. In the second phase the pain ameliorates, the red cell deformability increases and the number of dense cells decrease.

After the painful crises, the restoration of the rheologic properties of the red cells to baseline values may be delayed for a long time and during this period the recurrence of the painful crises may be frequent. In some patients the steady state is restored within a short period of time while in others it may be longer than a month. Factors that improve red cell deformability also decrease the frequency of the painful crises. These include associated α-thalassaemia and hydroxyurea treatment.

Table 7.52: Haematological parameters and total bilirubin level during the steady state and crises in Sickle cell disease (Hb SS) patients

	RBC ($x10^{12}$/l)	Hb (g/dl)	PCV (l/l)	MCV (fl)	MCHC (g/dl)	MCH (pg)	Retic (%)	WBC ($x10^{9}$/l)	T. Bil. (μmol/l)
Steady state	3.19± 0.8	9.5± 1.5	0.27± 0.05	78.9± 26.2	35.6± 2.3	30.6± 4.6	6.4± 4.0	11.97 ± 8.2	35.4± 22.0
Crises	3.13± 0.7	8.6± 1.5	0.26± 0.04	80.3± 23.3	33.6± 2.0	27.9± 5.0	9.7± 5.4	14.0± 5.6	85.8± 66.9
P	0.825	0.085	0.571	0.880	0.039*	0.132	0.137	0.448	0.082

- No. of children investigated during study state and crises = 23
- Type of crises = Vasoocclusive
- Type of treatment received
    - Blood transfusion (13/23) 56/5%
    - Intravenous fluid (23/23) 100%

*Statistically significant

(i) The treatment of painful crises

Painful crises with a severe presentation generally requires hospitalization. The treatment involves the removal or treatment or avoidance of the precipitating factor e.g. treatment of infections with antibiotics or avoidance of stress and exercise (Table 7.53). The fluid balance is restored by infusion of intravenous fluids (normal saline, dextrose, saline/ dextrose mixture). Both intravenous and oral routes may be used. To ameliorate the pain various analgesics have been used in different studies (Table 7.53). It is recommended to discourage the use of addictive preparations in order to avoid dependance of the patients on these drugs. Protocol used for the treatment of Hb SS in our patients are presented in Table 7.54.

7.3.15. Growth and development in Saudi homozygous sickle cell disease patients

The state of chronic anaemia, associated with other complications leaves an affect on the normal growth and development in Hb SS patients. In addition, depending on the social status of the patients, environmental factors such as diet and nutrition, hygienic state and medical care, further influences the development in these patients. A list of factors that result in altered growth and development in Hb SS patients is presented in Table 7.55. Major growth and development abnormalities reported in Hb SS are presented in Table 7.56.

(i) Growth and Physical Development

At births no significant differences are reported in the length and weight of the newborn Hb SS compared to normals. As the child with Hb SS grows the growth and physical development slows and differences are obvious as early as during the 1st year of

life. In a well designed study from Jamaica, the differences in the mean weight and height

Table 7.53: Treatment of painful crises

1. Treatment and avoidance of precipitating factors

2. Restoration of fluid balance.
   - Intravenous infusion
   - Oral intake

3. Analgesia
   - Acetaminophen
   - Paracetamol
   - Morphine

4. Antisickling agents
   - Piracetam
   - Hydroxyurea
   - Others

5. Limited exchange transfusion

Table 7.54: Protocol for the treatment of painful crises - Recommended in Saudi Arabia

- Analgesics:
  - Acetaminophen
    - Adult: 0.3-0.6g Q4H; PO
    - Children: 8 mg/kg/dose; Q4H; PO
  - Codein*
    - 1 mg/kg/dose; Q4H; PO
- Hydration
  - i.v. + oral
    - Children: 5% dextrose + 0.225N saline
    - Adult: 5% dextrose + 0.45N saline
- Treatment of infections
- Avoid exposure to cold
- Patient reassurance
- Blood transfusion
- Antisickling agents (e.g. piracetam)

*Given in sufficient doses and around the clock.

Table 7.55: Factors affecting the growth and development in sickle cell disease (Hb SS) patients

- State of chronic anaemia
- Severity of Hb SS disease
  - Hb F level
  - Associated thalassaemia
- Social status
  - Diet habits and nutrition
  - Hygeinic condition
  - State of clothing
  - Public health measures
  - Medical care.
- Iron status of the body
- Endocrine functions
- Micronutrient intake
  - Zinc level
- Protein intake
- Vitamin status
  - Folic Acid

Table 7.56: Retardation of growth and development of sickle cell disease (Hb SS) patients

Height	
In children:	Reduced
In adults:	Normal
Weight	
In children:	Reduced
In adults:	Reduced
Skeletal development	Retarded
Sexual development	
Puberty	Delayed
Age of menarche	Delayed
Infertility	Common
Secondary sexual characteristics	Retarded
Gonadal function	Retarded
LH	Retarded
FSH	Retarded
Testosterone	Retarded
Spermatogenosis	Delayed

became significant in comparison with the normal children from 20 months of age in boys and 12 months in girls. In other studies the mean height were generally reduced in the childhood. In the girls the deficit seems to be more than in the boys. The weight increase with age is more retarded compared to the height increase and the Hb SS patients generally have a thinner body build. In a study of natural history in the Eastern Province population marked individual variability was noted in height and weight (Al-Awamy et al 1991). Studies in adults have shown greater mean height in Hb SS patients compared to normal controls, this gives a typical body habitus in Hb SS patients which is characterized by long limbs and a decreased upper to lower segment ratio. Other abnormalities in the skeletal development result in narrow pectoral and pelvic girdles, increase antero-posterior chest diameter and lesser circumference. In addition, bone age is retarded in the adolescent Hb SS patients.

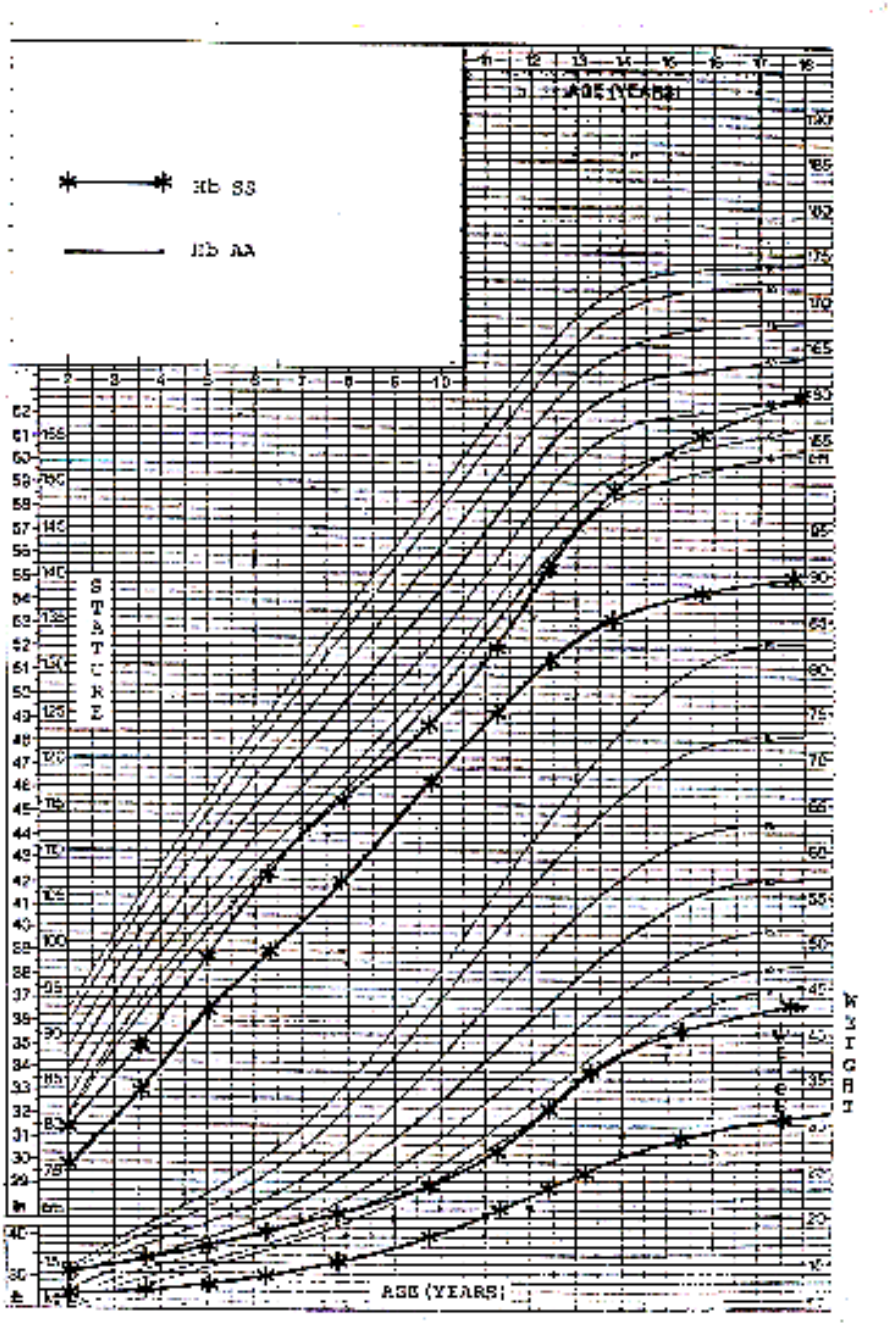
In our study, all of the Hb SS patients under the age of 15 years had decreased growth and height, both in the male and female group. Figure 7.34 plot the results of our Hb SS patients and shows the significantly lower weight and height in these patients. Lower weight remained throughout adulthood and majority of the adult patients had lower than normal weight and small stature.

(ii) Sexual development

The development of the sexual characteristics and onset of puberty is generally delayed in the Hb SS patients. Menarche is delayed and variation is obvious in patients from different populations. Alleyne et al (1981) reported the age of menarche as 15.4± 1.7 years, while Graham and coworkers (1986) reported 16.1 ± 1.9 years compared to 13.1 ±

1.7 years in normal controls (Alleyne et al, 1981). The prevalence of infertility is higher in

Figure 7.34: The height and weight range in Saudi Hb SS patients



Hb SS patients compared to normal controls.

The gonadal functions are generally reduced and a decreased in the level of luteinizing hormone (LH) and follicle stimulating hormone (FSH) have been observed in these patients in some studies, while in other studies elevated LH and FSH level after stimulation studies have suggested that partial hypothalamic-hypogonadism defect occurs in Hb SS patients. We estimated LH and FSH in Hb SS patients and found that compared to the age matched controls the values were either normal or even elevated (Discussed later in Endocrine Section). These results show that Saudi Hb SS patients (particularly those from the western province) are generally small and have a low body weight and small stature. Even after reaching puberty and as adolescent they often look so small that they keep attending the paediatrics clinics.

Though several factors may contribute to the delay in growth and development one of these factors may be the plasma zinc level.

7.3.16. Zinc level in Saudi homozygous sickle cell disease

Zinc is an essential nutrient for humans and animals and is required for normal growth, brain development and brain function. Normal population with dietary Zn deficiency show a delayed growth and puberty and this has lead to the speculation that zinc deficiency may be related to the short stature, hypogonadism and delayed puberty commonly encountered in the Hb SS patients. Zinc deficiency has been reported in adult Hb SS patients in the plasma, hair and red blood red cells. However, a few studies have challenged the finding as they did not find any Zn deficiency in the Hb SS patients. The mechanism which produces Zn deficiency is not well understood, though it has been

suggested that the state of chronic haemolysis in the Hb SS patients produces a subsequent loss of Zn from the RBCs. Higher urinary loss of zinc have been confirmed. Several mechanisms have been proposed which may lead to the crises

but the exact mechanism is not known.

We investigated plasma zinc level in the Saudi Hb SS patients and our results are presented in Table 7.57. No significant differences were found in the plasma Zn level in the Hb SS, Hb S heterozygotes and the normal control group, thus suggesting that plasma Zn level may not be a factor involved in delayed growth and development in the Hb SS patients.

7.3.17 Iron status of Saudi sickle cell disease

Generally the Hb SS patients do not suffer from iron deficiency. There is iron released as a result of excessive haemolysis of the red cells and is available for reutilization. In addition, the anaemic state often results in an increased intestinal absorption of iron thus leading to either normal or increased iron stores particularly in the children. In addition, some patients need blood transfusions for the management of the complications and this results in increased iron stores in the body. However, studies on patients suffering from severe form of the Hb SS have shown that they often develop iron deficiency. This may be due to decreased iron intake, or loss of blood due to epistaxis,

haematuria or peptic ulcers.

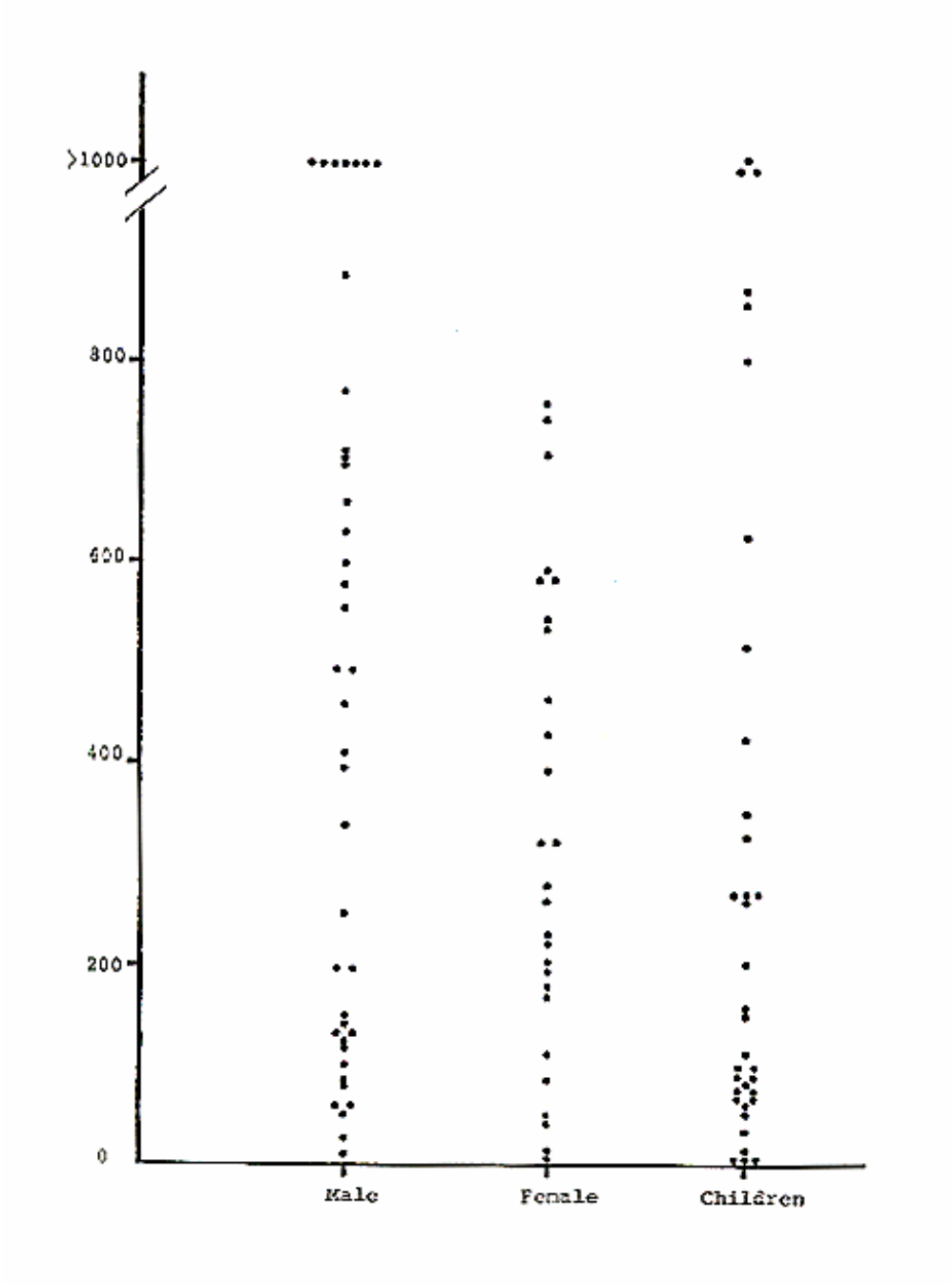
A useful test of the body stores iron is by estimation of serum ferritin level. Using this method we determined the iron status in Saudi Hb SS patients. The results are presented as Figure 7.35. There were 60.0% patients who had elevated ferritin level

indicating iron overload, 36.7% had normal body iron stores and 3.63% suffered from iron deficiency

Table 7.57: Plasma zinc level in Saudi homozygous sickle cell disease patients compared to normal controls

Group	Zinc (mmol/l)		P
	Male	Female	
Hb SS	14.8 ± 7.4	13.2 ± 2.6	> 0.1
Hb AS	13.5 ± 2.5	13.2 ± 2.4	> 0.1
Hb AA	14.2 ± 2.7	13.2 ± 2.6	> 0.1

Figure 7.35: Serum ferritin level in Saudi Hb SS patients



7.3.18. Pregnancy in Saudi sickle cell disease

Pregnancy may or may not be associated with complications in the sickle cell disease patients and geographical differences are obvious. Patients from the eastern province of Saudi Arabia do not show increased prevalence of any maternal or fetal complications. On the other hand, reports from other cases showed increased prevalence of complications affecting the maternal health and the fetal outcome. The major complications which are reported to occur at a higher prevalence in the pregnant Hb SS are listed in the Tables 7.58 and 7.59. However, a wide variation is reported in the prevalence of complications. The patients from the eastern province of Saudi Arabia suffer from a mild disease and this is also reflected in their eventless pregnancies. Patients from western province, showed more complications such as low fertility, spontaneous abortion, perinatal death, low birth weight babies and suffered from severe anaemia requiring frequent transfers. Though further studies are required to investigate in detail the maternal and fetal outcome in these patients and to obtain the frequency of these abnormalities in the Hb SS patients.

More care is required in the management of pregnant Hb SS patients. These are listed in Table 7.60. It is becoming quite obvious that with better management and proper care the frequency of complications during pregnancy in Hb SS are reducing quite significantly.

7.3.19. Vitamin E level in Saudi sickle cell disease

Vitamin E, a fat soluble antioxidant, is known to stabilize the red cell membrane