Table 7.58: Complications encountered during pregnancy in homozygous sickle cell disease (Hb SS) patients

- Increased severity of anaemic state:
  - Hepatic sequestration
  - Splenic sequestration
- Increased frequency of acute chest syndrome
- Increased episodes of bone pain
- Pre-eclamptic toxaemia
  - Hypertension
  - Albuminuria
  - Oedema
- Increased prevalence of urinary tract infections
- Increased prevalence of spontaneous abortion
- Increased prevalence of natural death

Table 7.59: Fetal outcome in pregnant sickle cell disease (Hb SS) patients

- Recurrent fetal loss
- Increase prevalence of spontaneous abortions
- Increased prevalence of still birth
- Increased prevalence of neonatal death
- Low birth weight

Table 7.60: Management of pregnant homozygous sickle cell disease (Hb SS) patient

- Regular antenatal care
- Intra-uterine fetal growth monitoring
- Dietary supplementation
  - Folic acid
  - Iron
- Partial exchange transfusion

and protect against oxidative damage during oxidative stress. It functions as a free radical scavenger or a structural stabilizer of the red cell membrane bilayer. There is evidence of membrane lipid peroxidative damage in sickle cells which may play a role in formation of irreversibly sickled cells. There is increased accumulation of an end product of lipid peroxidation i.e. malonyldialdehyde, which seems to be responsible for the membrane damage. The lipid peroxidation is reduced in presence of vitamin E. There is evidence that in sickle cell patient the vitamin E level is significantly reduced and thus may fail to protect the membrane damage in the Hb SS patients. The exact mechanism which leads to the reduction in the vitamin E level in these patients is unclear. Either there is an increased utilization of vitamin E or there is an decreased intake.

In a more recent study, it was shown that the plasma vitamin E level were not different in the Hb SS patients compared to the controls. A significant negative correlation was shown between the MCHC and vitamin E level and between vitamin E and total haemoglobin. It was stated that the levels of vitamin E was dependent on the degree of anaemia and low vitamin E may contribute to cellular damage in individuals with Hb SS.

We estimated plasma vitamin E level in 58 Saudi Hb SS patients using HPLC. The results were compared to the results obtained in 49 age and sex matched normal controls and are presented in Table 7.61. The major vitamin E subtype in all patients was α-tocopherol. Other subtypes i.e. β-tocopherol and γ-tocopherol were present only as traces. The level of vitamin E was significantly lower in the Hb SS patients compared to the other two groups. Further detailed studies are required to determine the possible benefits of vitamin E supplementation in these patients.

Table 7.61: Vitamin E level in Saudi homozygous sickle cell disease patients

Group	No. investigated	Vitamin E	P
Hb SS	58	20.2 ± 13.7	< 0.001
Control (Hb AA)	49	72.6 ± 29.2	

7.3.20. Haptoglobin levels in Saudi sickle cell disease

Haptoglobin is a plasma protein, with a specific function of binding and transporting free haemoglobin, released from the red cells upon their haemolysis, to the reticuloendothelial system where the haemoglobin-haptoglobin complex is removed from the circulation. Thus haptoglobin is considered as a suicidal protein. The estimation of plasma haptoglobin level is considered as a reliable parameter to show an increased rate of red cell haemolysis. As the level of free haemoglobin increases in plasma the level of haptoglobin decrease. Thus a positive correlation exists between the haptoglobin and total haemoglobin level in red cells.

We investigated plasma haptoglobin in 68 Saudi Hb SS patients and compared the results with those obtained in age and sex matched normal non-anaemic controls (Table 7.62). The haptoglobin level was significantly low in Hb SS patients investigated indicating

haemolysis in these patients.

7.3.21 Riboflavin level in Saudi sickle cell disease

Riboflavin is a water soluble vitamin and functions as two coenzymes i.e. flavin adenine dinucleotide (FAD) and flavin adenine mono nucleotide (FMN). These coenzymes are essential for the activity of several enzymes and hence are required for the normal metabolism in the body. Riboflavin is a constituent of milk, grains, legumes and beans. Deficiency of riboflavin has been frequently encountered and has been related directly to the milk consumption. Children of low socio-economic status, teenagers and adolescents and pregnant lactating females are particularly prone to develop riboflavin

deficiency. Thus poor dietary habits and the stages of rapid growth are some of the factors

Table 7.62: Haptoglobin level in Saudi homozygous sickle cell disease patients and controls

	No. investigated	Hepatoglobin (g/dl)	P
Hb SS	68	< 0.1	< 0.001
Control (Hb AA)	68	1.8 ± 0.73	

that result in riboflavin deficiency (Ten State Nutrition Survey, 1968, 1970).

In an attempt to investigate the riboflavin status of children suffering from homozygous sickle cell disease, we conducted this study on 73 children. The prevalence of riboflavin deficiency was significantly higher in the Hb SS patients ($P < 0.05$) compared to the normal Hb AA individuals (Table 7.63). The riboflavin deficient and non-deficient individuals were grouped separately and the haematological parameters were determined, to estimate if there were any specific haematological abnormalities in the riboflavin deficient individuals, in both Hb SS patients and normal controls. The results (Table 7.64) showed no statistically significant differences in the haematological parameters in the riboflavin normal and deficient group.

The signs and symptoms in the Hb SS patients with and without riboflavin deficiency were calculated (Table 7.65) and showed that only the frequency of pain in bones and joints was significantly higher in Hb SS patients with riboflavin deficiency, while hepatomegaly was higher in patient without riboflavin deficiency. All other signs and symptoms occurred at about the same frequency.

The higher prevalence of riboflavin deficiency in Hb SS could be due to a combination of causes. Firstly, these children generally have a poor apetite and often suffer from gastrointestinal disorders which influence the amount of food consumed. Secondly, the food intake may be affected by recurrent infection and haematological crises. Thirdly, since the metabolism in these children is always under a stressful state due to excessive turnover of the red cells, thus depleting the riboflavin, the need for riboflavin may be higher in these children, and finally, the socio-economic status of the families and the

excessive burden generated due to a chronic illness in the family may influence the

Table 7.63: Prevalence of riboflavin deficiency in Saudi homozygous sickle cell disease patients compared to normal controls (Hb AA)

Population	Number investi-gated	Age	No. of riboflavin deficient	Prevalence (%)	P
Sickle cell disease (Hb SS)	73	5.5±3.3	30	41.1	<0.05
Normal (Hb AA)	86	6.2±3.0	14	16.3	

Table 7.64: Haematological parameters in sickle cell disease patients and normal children with and without riboflavin deficiency

Parameter	Hb SS patients			Normal controls		
	Without riboflavin def.	With riboflavin deficiency	P	Without riboflavin def.	With riboflavin deficiency	P
RBC ($X10^{12}$/l)	3.2 ± 0.91	2.9 ± 1.03	0.579	4.5 ± 0.39	4.4 ± 0.65	>0.1
WBC ($X10^{9}$/)	13.9 ± 7.80	14.2 ± 5.59	0.139	9.4 ± 2.97	9.37 ± 3.89	>0.1
Hb (g/d)	8.48 ± 1.37	8.4 ± 1.39	0.922	12.0 ± 1.2	12.0 ± 1.8	>0.1
PCV (/)	0.23 ± 0.044	0.22 ± 0.054	0.316	0.35 ± 0,036	0.35 ± 0.053	>0.1
MCV (f)	79.8 ± 11.1	82.0 ± 9.40	0.462	77.5 ± 6.1	80.3 ± 6.7	>0.1
MCH (pg)	27.6 ± 5.39	30.5 ± 5.90	0.665	26.7 ± 2.4	27.4 ± 2.5	>0.1
MCHC (g/d)	36.3 ± 2.90	38.3 ± 6.20	0.0007*	34.4 ± 1.08	34.1 ± 0.86	>0.1
Hb A_2 (%)	3.2 ± 1.09	3.18 ± 1.09	1.000	2.8 ± 0.30	2.8 ± 0.30	>0.1
HB F (%)	11.4 ± 6.66	11.4 ± 7.44	0.604	0.8 ± 0.25	0.8 ± 0.25	>0.1
GR activity without FAD	116.7 ± 67.20	86.2 ± 36.0	0.0076*	130.2 ± 33.1	96.2 ± 28.3	<0.05
GR activity with FAD	122.6 ± 71.1	139.3 ± 59.1	0.414	138.2 ± 32.9	137.1 ± 32.1	>0.1
AC value	1.05 ± 0.05	1.61 ± 0.20	0.0001	1.07 ± 0.077	1.46 ± 0.20	<0.05

Statistically significant; Hb SS = Sickle cell disease

Table 7.65: Signs and symptoms in Saudi homozygous sickle cell disease patients with and without riboflavin deficiency

Signs and Symptoms	Sickle cell disease patients with riboflavin deficiency (%)	Sickle cell disease patients without riboflavin deficiency (%)	P
Pain in bone and joints	(14/16) 87.5	(15/27) 55.5	< 0.05
Pallor	(15/16) 93.75	(23/27) 85.28	< 0.05
Abdominal pain	(11/16) 68.75	(15/27) 55.5	< 0.05
Crises Vasoocclusive Long bone	 (8/16) 50.0 (3/16) 18.75	 (10/27) 37.0 (4/27) 14.8	 < 0.05 < 0.05
History of hospitalization	(15/16) 93.75	(23/27) 85.8	< 0.05
Blood transfusion	(12/16) 75.0	(14/27) 51.85	< 0.05
Jaundice	(5/16) 31.25	(7/27) 25.9	< 0.05
Lymphoadenopathy	(9/16) 56.25	(9/27) 33.3	< 0.05
Hepatomegaly	(5/16) 31.25	(19/27) 70.37	< 0.025
Splenomegaly	(5/16) 31.25	(16/27) 59.25	< 0.05
Angular stomatitis	(0/16) 0	(0/27) 0	1.0

dietary habits of the Hb SS patients.

It may be concluded from these results that the Hb SS patients may differ in their recommended daily allowance (RDA) compared to the normal children and may have higher demands for some nutrients. Deficiency of these nutrients would have a further adverse affect on the health of children and thus it is essential to stress the need for complete and balanced diet with dietary supplementations to prevent nutritional deficiencies.

7.3.22. Uric acid level in Saudi homozygous sickle cell disease

Uric acid is the end-product of purine metabolism in man and is derived from the catabolism of nucleic acids. Some uric acid is also produced during the synthesis of nucleotides. In addition to this endogenous uric acid, almost 33% of the uric acid present in the body is derived from the diet. The uric acid circulates in the blood as urates and is excreted mainly through the kidney. About one-third of the daily loss of uric acid is through the digestive tract, in secretions and exfoliated cells.

The normal excretion of the urate in the kidney requires a normally functioning kidney. Altered renal tubular function and increased production of urates due to excessive purine catabolism or excessive protein intake may lead to the state of hyperuricaemia. Several studies have shown that hyperuricaemia occurs in Hb SS patients. Hyperuricaemia and secondary gout are also expected in Hb SS patients due to the increased turnover of red blood cells which is almost 6-8 times greater than in normal individuals. In a study conducted on 64 patients (15-66 years old) it was shown that urate concentration in the serum of Hb SS patients, was dependent on renal urate clearance and on creatinine

clearance. The relation between serum urate and creatinine clearance was abnormal in these patients. Renal urate clearance is a major determinant of serum urate in Hb SS patients. On the other hand, it was shown that serum urate concentration has no relation to urate production judged by daily urinary urate excretion, nor to haemoglobin or reticulocyte count, suggesting that hyperuricaemia in Hb SS is not closely related to increased bone marrow activity.

We estimated plasma uric acid level in male and female adults and children from the eastern province suffering from Hb SS. Other parameters measured in these patients included the total haemoglobin level, haematocrit, reticulocyte count, blood urea level and creatinine level. The level of uric acid, urea, creatinine of the patients compared to the results obtained in normal healthy adults and children are presented in Table 7.66. The distribution of these parameters are shown in Figure 7.36 and 7.37. and the correlation between age and uric acid level is presented in Figure 7.38 and Table 7.67.

In this study on the eastern province patients, the prevalence of hyperuricaemia among the sickler was only 4.44%. No patient with gout was encountered. This is significantly low when compared with a prevalence of 25.5% with elevated uric acid levels reported in a group of Nigerian children with sickle cell disease. In this population, it was shown that during bone pain crises the uric acid was elevated but reverted to normal upon recovery from the state of crises. In patients with renal damage, hyperuricaemia due to decreased renal excretion, becomes a prominent feature. Since kidneys that are chronically exposed to hyperuricaemia may develop nephrolithiasis, it has been emphasised that though hyperuricaemia may be mild to moderate in patients with Hb SS disease, however,

regular monitoring is essential as the interstitial deposition of uric acid may consequently result in further renal parenchymal damage. Deterioration of renal

Table 7.66: Uric acid, urea and creatinine level in adults and children male and female Saudi homozygous sickle cell disease patients and normal controls

Parameter	Group	No.	Haemoglobin phenotype		
			SS	AA	P
Uric acid (μmol/l)	Adults				
	Male	14	356.2± 86.0	342.9± 74.7	>0.1
	Female	11	235.0± 46.8	272.0± 43.2	>0.05
	Children				
	Male	14	290.1±57.3	259.5± 68.9	>0.1
	Female	6	245.0±104.6	235.1± 58.3	>0.1
Total		45	293.4±87.0	285.3± 74.3	>0.1
Urea (mmol/l)	Adults				
	Male	14	3.99 ± 1.07	5.11 ± 1.14	< 0.05
	Female	11	3.54 ± 0.87	3.98 ± 1.17	>0.1
	Children				
	Male	14	3.62 ± 1.44	4.03 ± 1.14	>0.1
	Female	6	3.62 ± 0.97	4.28 ± 1.49	>0.1
Total		45	3.73 ± 1.11	4.40 ± 1.26	<0.05
Creatinine (μmol/l)	Adults				
	Male	14	77.93 ± 15.2	87.78 ± 16.2	>0.1
	Female	11	66.90 ± 28.4	81.00 ± 29.0	>0.05
	Children				
	Male	14	60.50 ± 22.90	85.43 ± 30.35	<0.05
	Female	6	66.28 ± 25.6	58.00 ± 13.87	>0.1

Total		45	68.24 ± 23.0	81.40 ± 13.87	<0.05

Figure 7.36: Distribution of uric acid in sickle cell anaemia patients (SS) and normal individuals (AA). The arrow points to the mean value

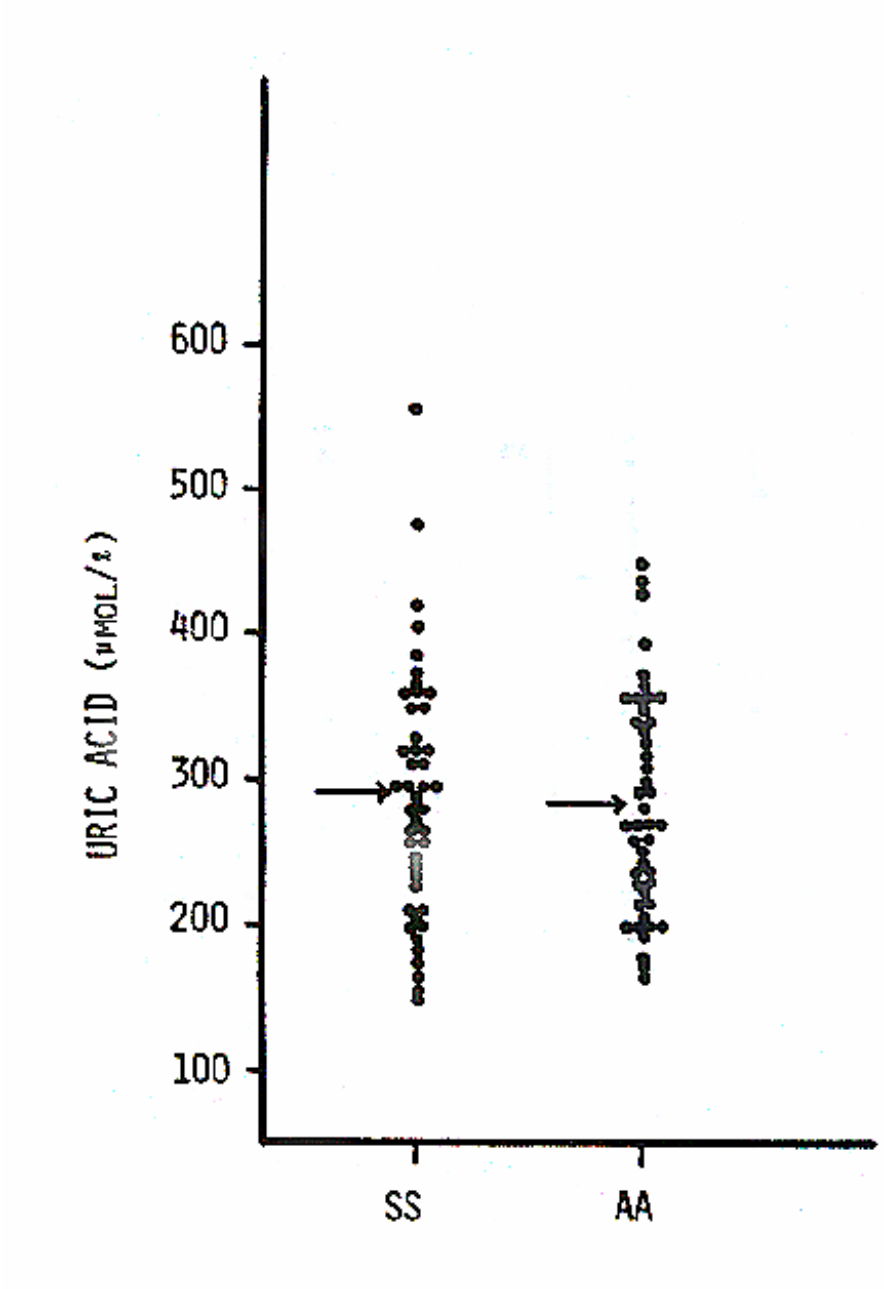


Figure 7.37: Distribution of urea and creatinine in sickle cell anaemia patients (SS) and normal individuals (AA). The arrow points to the mean value.

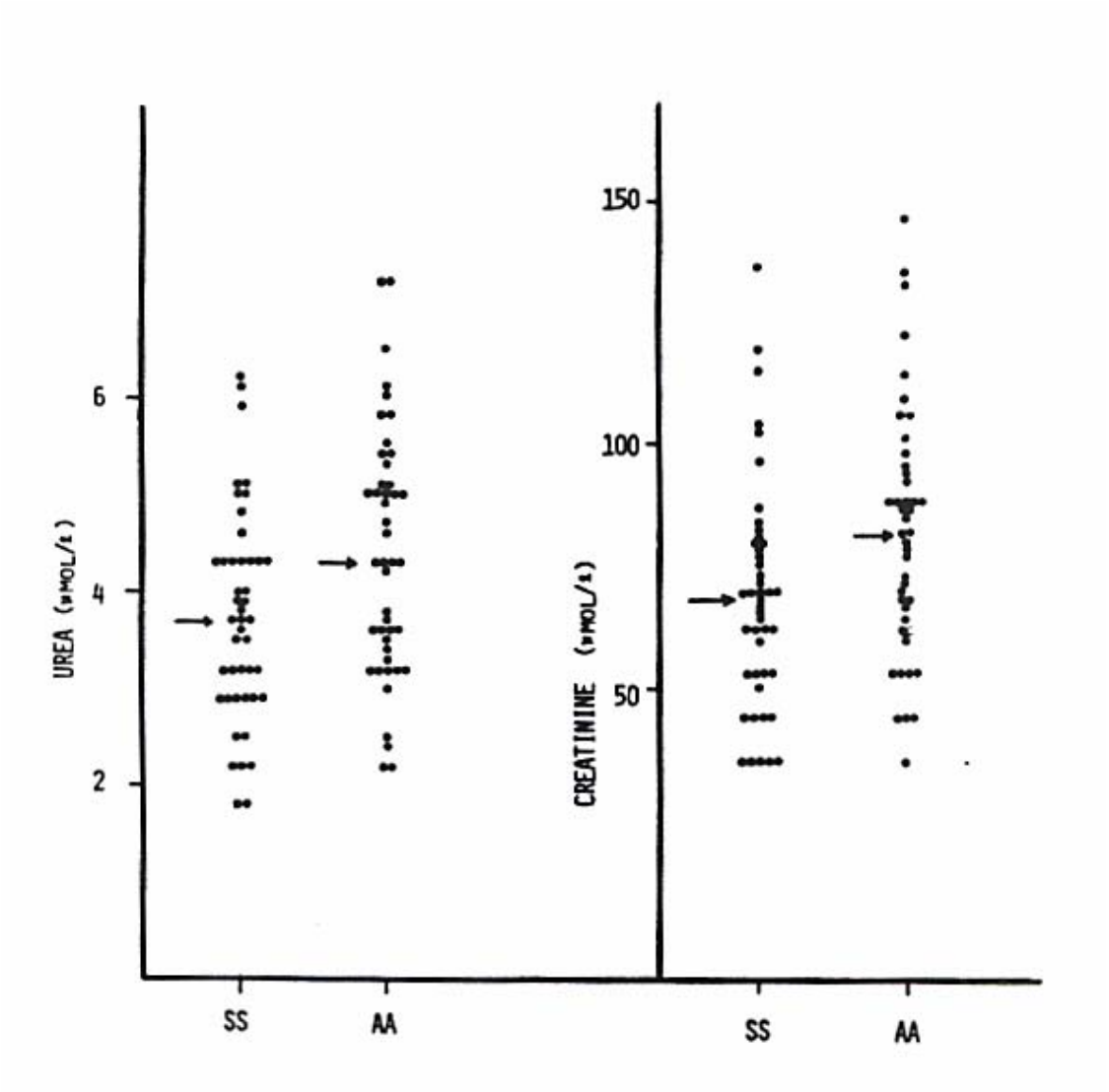


Figure 7.38: Distribution of uric acid in relation to age in normal (-) and sickle cell anaemia (x) patients.

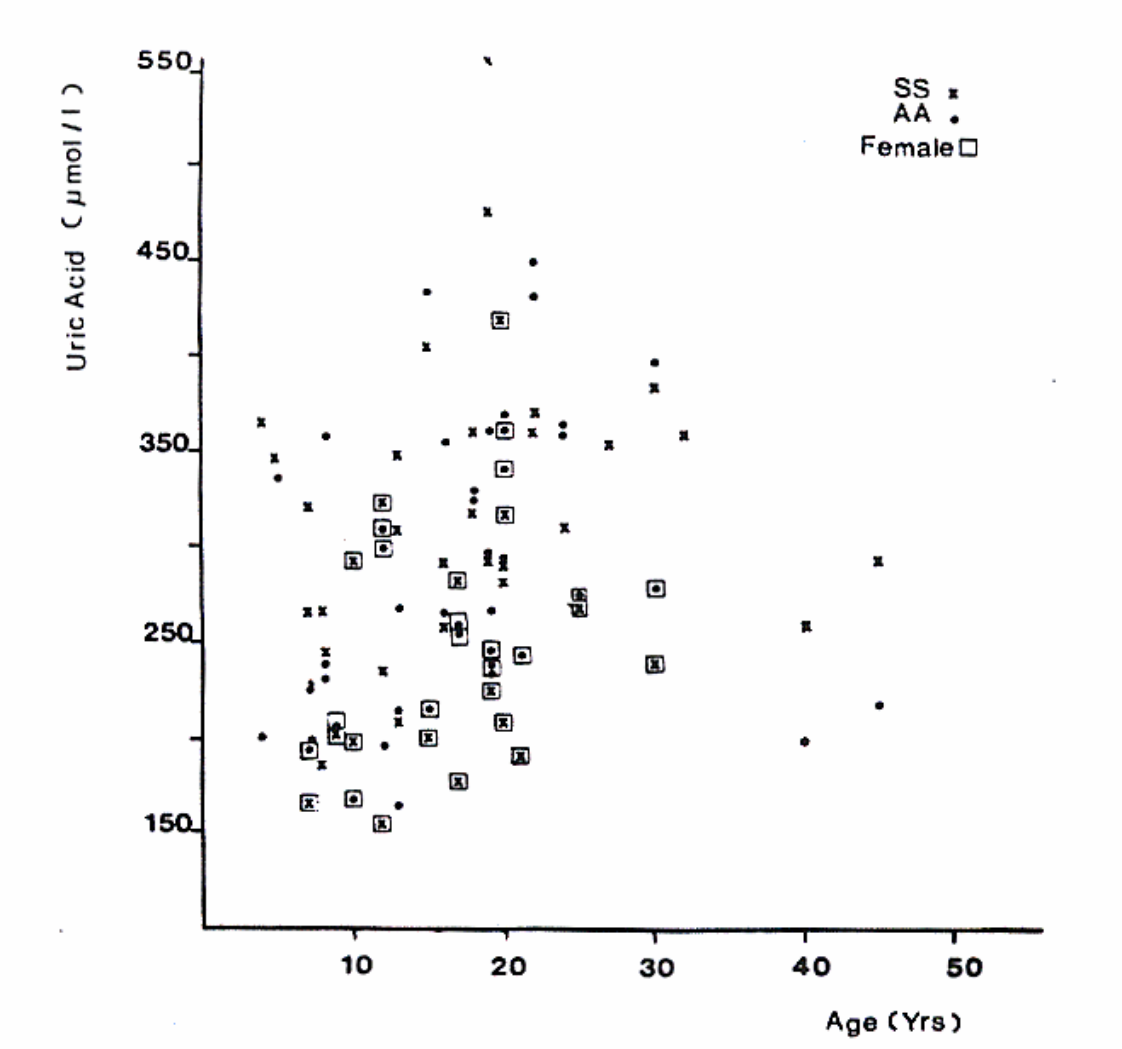


Table 7.67: Regression analysis and correlation coefficient between uric acid and creatinine level and age in normal and Hb SS patients

Correlation between age and	Hb Phenotype	r	Intercept	Slope	P
Uric Acid	SS Total population	0.194	253.63	1.905	< 0.001
	- Male	0.231	289.74	2.24	< 0.001
	- Female	0.332	179.64	2.777	< 0.001
	AA Total Population	0.214	251.42	1.858	< 0.001
	- Male	0.163	274.33	1.361	< 0.001
	- Female	0.469	192.16	4.023	< 0.001
Urea	SS Total population	0.027	3.694	0.003	> 0.10
	- Male	0.060	3.759	0.007	> 0.10
	- Female	0.126	3.826	-0.017	> 0.10
	AA Total Population	0.168	4.060	0.024	< 0.001
	- Male	0.354	3.885	0.044	< 0.001
	- Female	0.333	5.395	-0.070	< 0.001
Creatinine	SS Total population	0.321	54.837	0.804	< 0.001
	- Male	0.569	51.24	1.03	< 0.001
	- Female	0.0431	70.572	-0.186	> 0.01
	AA Total Population	0.223	69.486	0.641	< 0.001
	- Male	0.194	76.141	0.446	< 0.001
	- Female	0.338	46.234	1.737	< 0.05

function with age, probably as a result of parenchymal damage, has been reported in homozygous Hb SS patients.

The Saudi population of the eastern province generally presents with a mild clinical picture. One of the factors contributing to the amelioration of the clinical manifestations is reported to be the elevated haemoglobin F (Hb F) level which extends the red cell life span and correlates inversely with reticulocyte count. It is possible that due to a longer red cell life span in Saudi Hb SS patients, the nucleic acid turnover is less and hence the uric acid level is not significantly more than that in normal individuals.

On the other hand, the results of this study show that age and sex are important modulating factors of the uric acid level. In the overall normal and Hb SS population a positive correlation is found between uric acid level and age ($P<0.01$) (Table 7.67). A significant difference is also obtained in the uric acid level between adults and children and between males and females ($P<0.01$).

The levels of blood urea and creatinine were significantly lower in the overall Saudi Hb SS patients compared with the values in controls. The decrease in urea level may be a consequence of liver dysfunction and the decrease in serum creatinine may be due to the reduced muscle mass in these patients. This conclusion is in line with a study investigating the effect of dietary nitrogen on urinary excretion of non-protein nitrogen in sickle cell patients. It was reported that creatinine excretion was lower and this was attributed to the smaller physical stature of these patients. In addition to liver dysfunction and reduced muscle mass, diet also influences the plasma urea and creatinine level. Since diet and muscle mass were not controlled during this study, further investigations are

necessary to study the possible contribution of these variables to the level of biochemical parameters. There are reports of renal dysfunction in Hb SS involving an inability to concentrate the urine normally, resulting in elevation of serum creatinine and urea. In order to access the renal function in sickle cell disease patients from Saudi Arabia, it is essential to conduct further studies that include the determination of renal clearance of uric acid, urea and creatinine in these patients.

In conclusion, this study on Saudis has shown a slight increase in the uric acid level and a decrease in the level of urea and creatinine in patients with Hb SS compared with the controls. This study also shows that the increase in uric acid level is considerably lower in the Saudi Hb SS patients compared with the results reported for other populations. It is essential that further detailed investigations including clearance studies, are conducted to determine the renal function in these patients. In the light of our studies and those of others, regular monitoring of uric acid level in Hb SS and treatment of hyperuricaemia may provide a measure to minimize renal damage particularly in older Hb SS patients.

7.3.23 Proteins C&S in Saudi Hb SS

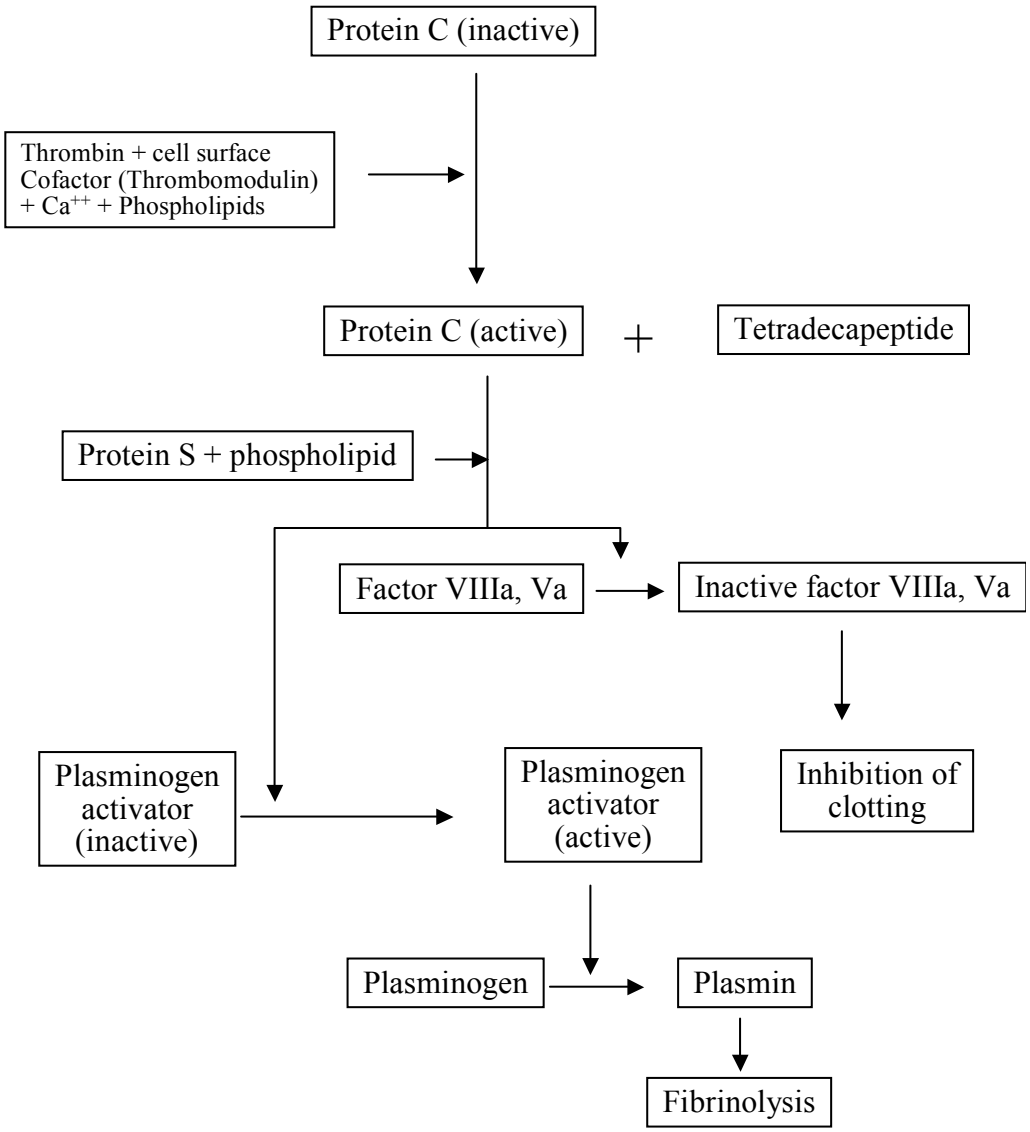
Proteins C&S are vitamin K dependent protein which contains several γ-carboxyglutamate residues, bind Ca^{++} and have an anticoagulant activity. Protein C is synthesized as a zymogen in the liver and circulates in the blood. It is converted to the active molecules by a Thrombin (T) - Thrombomodulin (1:1) complex in the presence of phospholipids and calcium. Unlike thrombin, this complex has a significantly higher affinity for the activation of protein C and a lower activity for fibrinogen, factor-V and platelet activation.

The activation of protein C to active protein C (APC) involves cleavage of a single peptide bond and release of a tetradecapeptide (Figure 7.39). In this activation the protein S plays an essential role, where it acts as a cofactor and potentiates the anticoagulant function of protein C. In serum, almost 60% protein S occurs in the bound form where it is bound to C4-binding protein and the rest almost 40% occurs free.

In the anti-coagulation process the activated protein C inactivates factor Va and VIIIa and is believed to activate the plasminogen activation, thus stimulating fibrinogen activity. This process requires both protein S and calcium. Cases of congenital and acquired deficiency of proteins C&S have been identified and due to a decreased blood anticoagulant potential, have a higher risk of developing thrombo-embolism thus producing recurrent thrombotic episodes. Since activated protein C, a serine protease, plays an important regulatory role in blood coagulation through its ability to degrade coagulation factors Va and VIIIa reduced levels of protein C result in thrombo-embolic disorders. Congenital protein C deficiency occurs but at a low frequency and results in fatal neonatal thrombosis characterized by purpura fulminans. In patients who are heterozygous to the congenital defect mild to severe thrombophilia has been reported. In a study on patients with intravascular coagulation, the protein C level was found to be significantly reduced. Cases with acquired protein C deficiency have been reported. They are generally patients on anticoagulant therapy and have a high rate of protein C degradation. Acquired protein C deficiency also occurs in patients with liver diseases (e.g. chronic hepatitis and liver cirrhosis), due to decreased synthesis of protein C, in patients with disseminated intravascular coagulation, due to decreased synthesis and/or increased

clearance of protein C during neonatal period due to decreased production and during post-operative period.

Figure 7.39: Activation of Protein C



A few studies have shown that protein C&S deficiency occurs in patients with Hb SS. In an attempt to study the hypothesis whether the sickle cell crises is a thrombotic events, 24 Hb SS patients were investigated during and between episodes of painful crises using several sensitive tests of haemostatis i.e. fibrinogen, beta thrombo-globulin, fibrino-peptide and protein C estimation. From the results obtained it was concluded that though chronic intravascular coagulation was common in Hb SS, there was no evidence that painful crises is thrombotic event. This study also showed a significantly lower level of protein C in Hb SS patients. In another study, it was shown that protein C&S level were significantly reduced in Hb SS and Hb SC patients, but the protein C activity was normal.

We conducted a study on 65 Hb SS patients (male = 35; female = 30), 18 HbS/β°-thalassaemia (male = 11, female = 7) and 17 Hb AS (male = 10; female = 7) patients and compared the results with 40 Hb AA normal controls (male 25; female 15). All patients and controls were Saudis from the different regions of the country.

The severity index was calculated in each patient and haematological parameters, and protein C & S were estimated. The levels of protein C&S in these patients are presented in Table 7.68. The level of both proteins were lower in the Hb SS patients compared to the control group and the difference in the values was statistically significant. In the Hb S/β°-thalassaemia patients and Hb AS heterozygotes the values were intermediate between those of the normal Hb AA and Hb SS group. Within each group of patients there was a wide variation in the level of protein C&S and several patients had values significantly lower than the normal reference value in the Hb AA group. The prevalence of deficiency of the two proteins was calculated and the results are present in

Table 7.69 (El-Hazmi et al, 1993).

Table 7.68: Level of protein C&S in Saudi homozygous sickle cell disease patients and controls

Group	Protein C (mg/l)	Protein S (mg/l)
Hb SS	85.6 ± 27.4	82.6 ± 14.5
Hb AS	88.8 ± 8.5	90.2 ± 18.3
Hb S/β°-Thal	94.3 ± 68.3	91.0 ± 50.0
Control	110.0 ± 49.0	116.8 ± 24.0

Table 7.69: Prevalence of proteins C&S deficiency in Saudi sickle cell disease patients and controls

Group	Prevalence of deficiency (%)	
	Protein C	Protein S
Hb SS (65	24.6 (16)	24.6 (16)
HB S/β°-Thal (18)	38.9 (7)	44.4 (8)
Hb AS (17)	0	23.5 (4)
Controls (40)	10.0 (4)	5.0 (2)

( ) = number

Table 7.70: Level of Protein C&S in Saudi sickle cell disease patients with severe and mild disease

Nature of Disease	Protein C (mg/l)	Protein S (mg/l)
Severe (23)	88.0 ± 27.4	95.0 ± 42.7
Mild (30)	78.5 ± 13.3	87.0 ± 33.0

( ) = Number include Hb SS and Hb S/β°-Thal. cases

The patients with a mild or severe Hb SS were grouped separately and the protein C&S values were calculated separately. No significant difference was encountered in the two groups (Table 7.70). In 10 Hb SS patients the protein C&S values were estimated both during the steady state and during crises and the results are presented in Table 7.71. No significant difference was observed in the level of the proteins. Thus these results showed that protein C&S are lower in Hb SS patients and Table 7.68 this may be due to either a decreased synthesis of the proteins, due to a malfunctioning liver or due to an increased rate of turn-over of these proteins or that both mechanisms co-exist.

7.3.24 Endocrine pattern in Saudi homozygous sickle cell disease

The endocrine functions in Hb SS patients have been investigated in several studies though contradictory and varied results have been documented. This difference in the results in different reports may be due to the different severity of the Hb SS or to other contributory factors such as tissue damage resulting from tissue hypoxia secondary to red cell sickling. In an attempt to study the endocrine pattern we investigated 80 male and 80 female suffering from Hb SS (age range 4-50 years) and 60 healthy controls (male = 30, females = 30). The Hb SS patients were assessed clinically and the severity index of the disease was calculated in order to determine the severity of the Hb SS. The hormones estimated included cortisol, free triiodothyronine (fT3), free thyroxine (fT4), growth hormone (GH), testosterone, luteinizing hormone (LH) and follicle stimulating hormone (FSH). The mean and standard deviation for each hormone in the male and female patients group, compared to the control group are presented in Table 7.72. The distribution of fT3 and fT4, cortisol and hormone are presented in Figures 7.40 to 7.42. The free T3 and T4

levels showed a slight difference though non-significant increase in

Table 7.71: Level of Protein C & S during steady state and crises in 10 Hb SS patients

	Protein C (mg/l)	Protein S (mg/l)
Steady state	85.6 ± 27.4	82.6 ± 14.5
Crises	82.9 ± 25.2	78.9 ± 13.3

Table 7.72: Hormonal levels in the Saudi male and female sickle cell disease patients

	Hb SS patients (Mean ± SD)		Controls	
	Male (46)	Female (34)	Male (30)	Female (30)
Testosterone (nmol/l)	8.8 ± 7.5*	0.39 ± 0.32*	13.8 ± 3.5	1.16 ± 0.63 1.17
LH (U/l)	2.8 ± 3.0*	5.83 ± 6.3*	9.9 ± 7.8	13.0 ± 9.7
FSH (U/l)	3.2 ± 2.8	3.1 ± 2.0	4.5 ± 3.3	5.7 ± 3.0
Cortisol (nmol/l)	9.3 ± 4.6*	9.7 ± 3.6*	14.1 ± 8.2	14.9 ± 8.1
Free T3 (nmol/l)	5.9 ± 0.59	5.85 ± 1.0	6.1 ± 1.0	5.5 ± 0.7
Free T4 (nmol/l)	20.7 ± 4.4	18.7 ± 4.1	18.5 ± 2.9	18.4 ± 2.7
GH	2.8 ± 3.1	3.0 ± 3.6	1.9 ± 1.8	1.5 ± 1.5

The difference in the mean value compared to the control group is statistically significant (P <0.05)

our Hb SS patients. Other studies have shown a significant increase in the basal metabolic rate. Since the physiologically active form is the free hormone, the slight elevation encountered in our patients may account for the slight increase in the basal metabolic rate.

The cortisol level was significantly lower in both male and female Hb SS patients. This may result from low level of cholesterol, precursor of cortisol, in the Hb SS patients, or may be due to hypofunction of the adrenal cortex. In addition, hypothalamus or/and anterior pituitary hypofunction cannot be ruled out. We have encountered low cholesterol levels in the Hb SS patients (El-Hazmi and Warsy, 1993). This may be yet another factor with a role in the development of growth derangement of Hb SS patients. It was noted that the level of growth hormone was generally within the normal range and even higher in a few patients, though the mean in the patients group, compared to the normal controls was not significantly different. Low levels of GH have been reported in some earlier studies and have been implicated as one of the factors for delayed growth in these patients. On the other hand, other studies have reported normal or even slightly elevated GH levels and the growth delay has been shown to have a positive correlation with the degree of anaemia and with deficiency of certain nutritional factors rather than endocrine abnormalities.

The level of LH, FSH and testosterone in the Hb SS patients and normal controls are presented in Figure 7.43 to 7.45. Significant differences were encountered in the testosterone was correlated with LH and the results showed a statitically significant positive correlation (Figure 7.46).

In an attempt to investigate whether there were any differences in the hormone levels growth in patient with a mild or severe disease, the patients were grouped according

to the severity index (SI) into those with a SI < 6 (mild Hb SS) and SI ≤ 6

Figure 7.40: Distribution of free T3 and T4 in homozygous sickle cell disease patient compared to controls

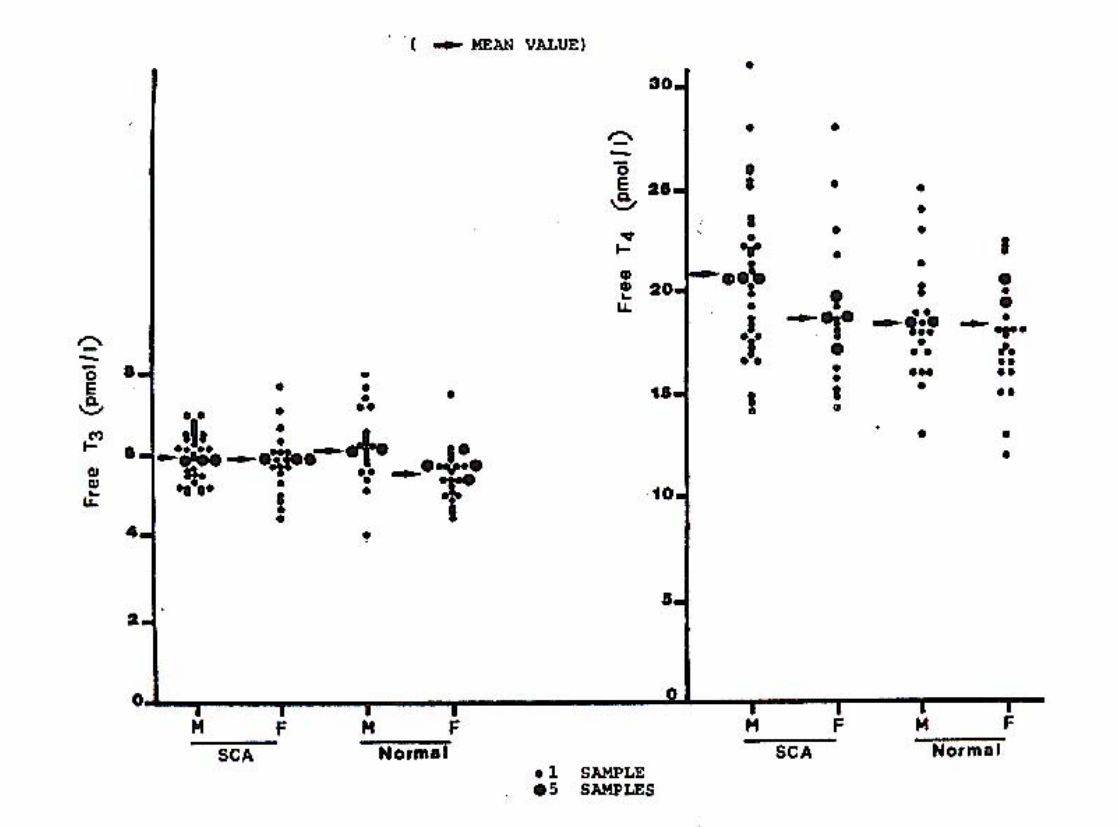


Figure 7.41: Distribution of growth hormone in homozygous sickle cell disease patients compared to controls

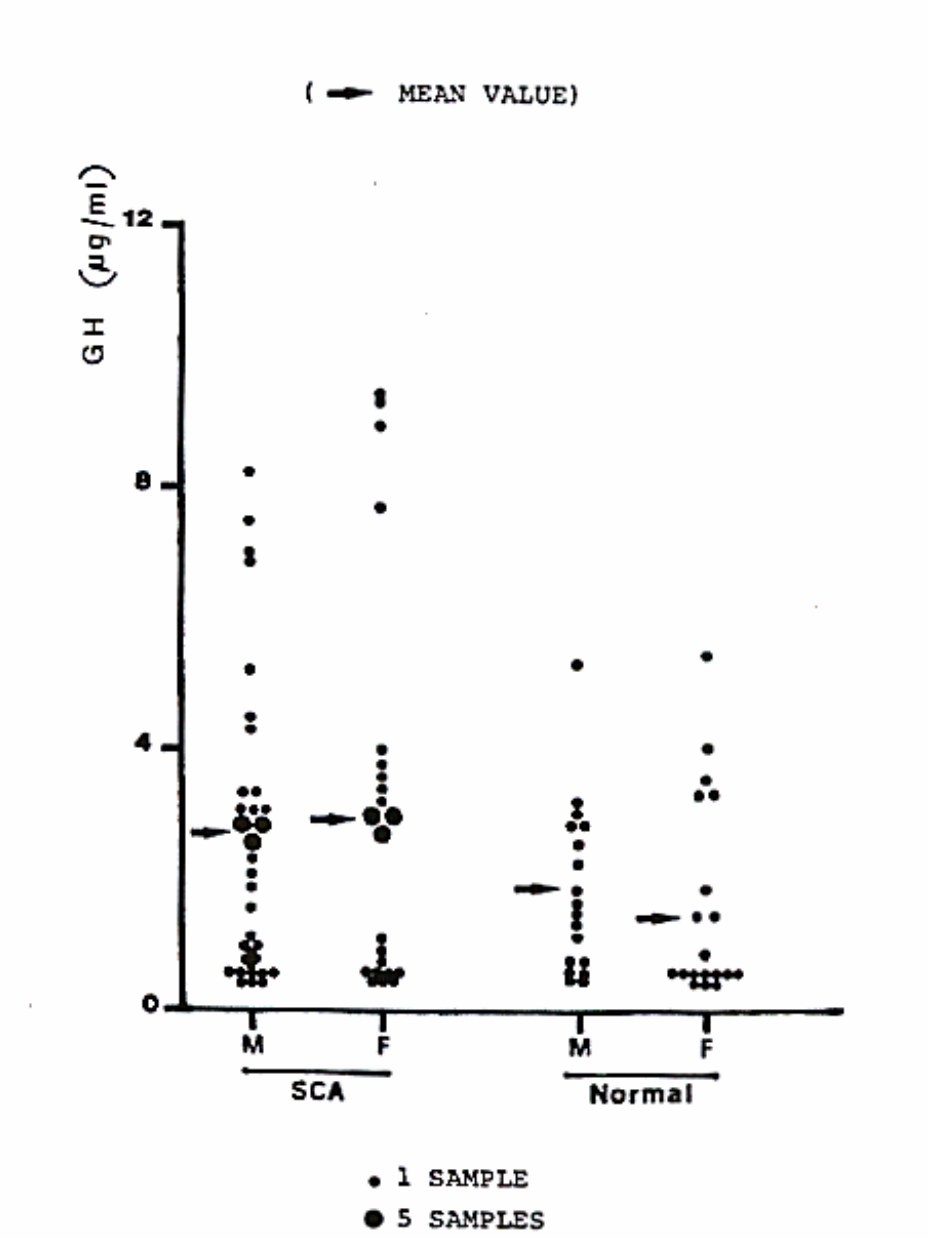


Figure 7.42: Distribution of cortisol in homozygous sickle cell disease patients compared to controls

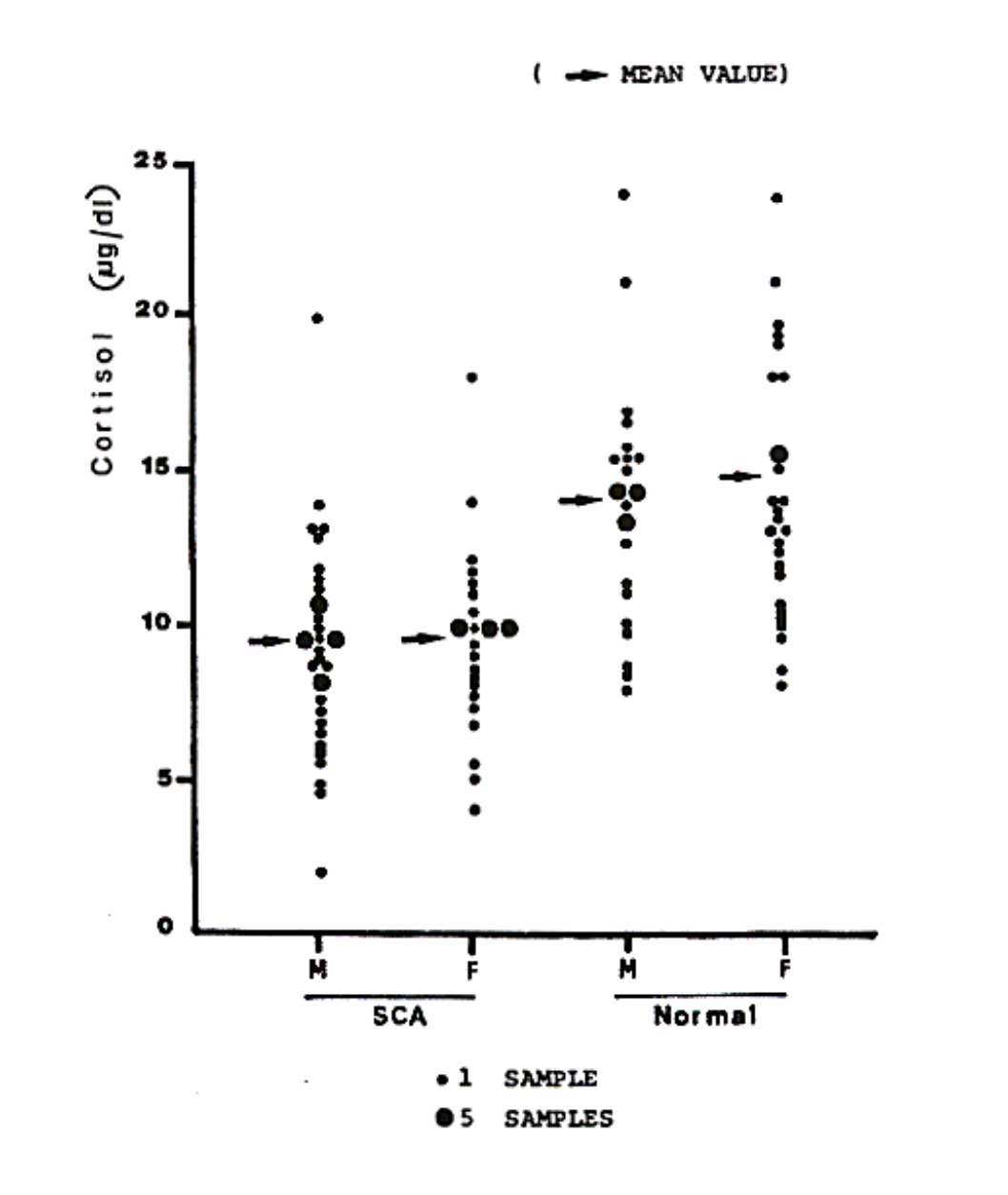


Figure 7.43: Distribution of testosterone in sickle cell disease patients and normal controls

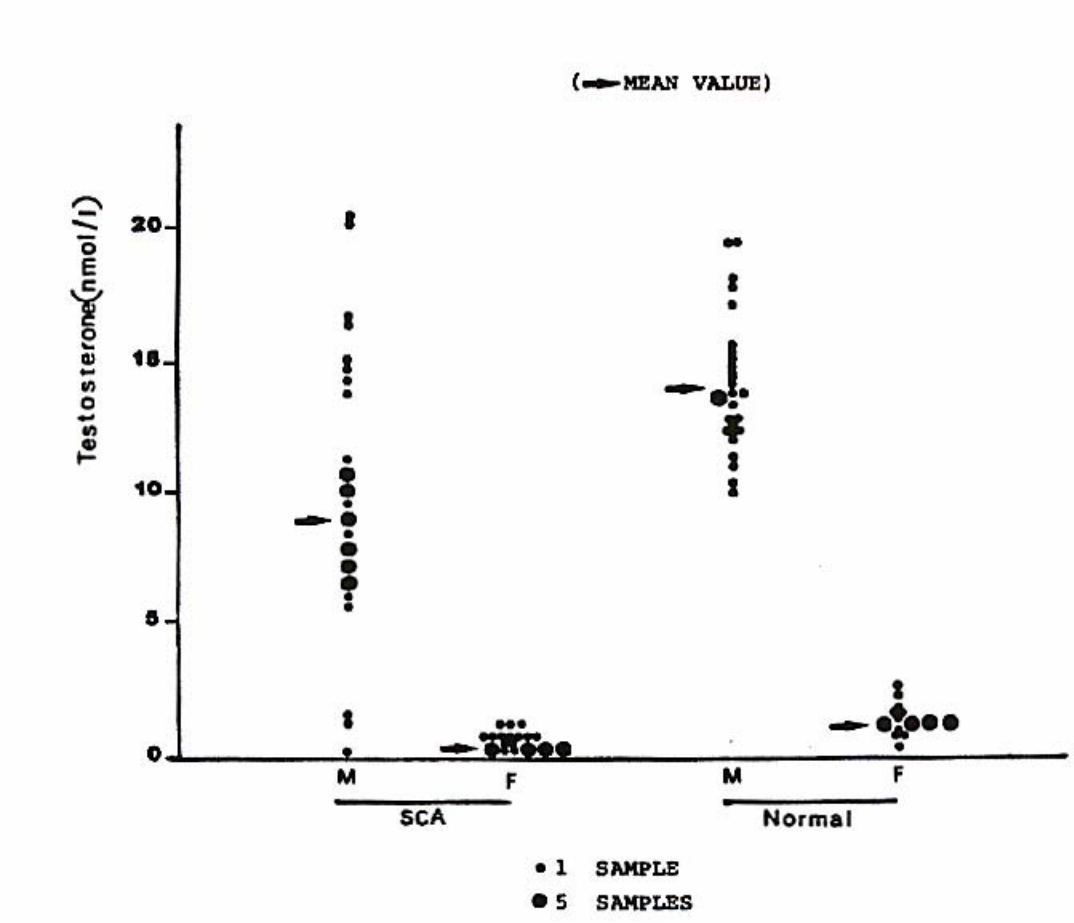


Figure 7.44: Distribution of FSH and sickle cell disease patients and normal controls

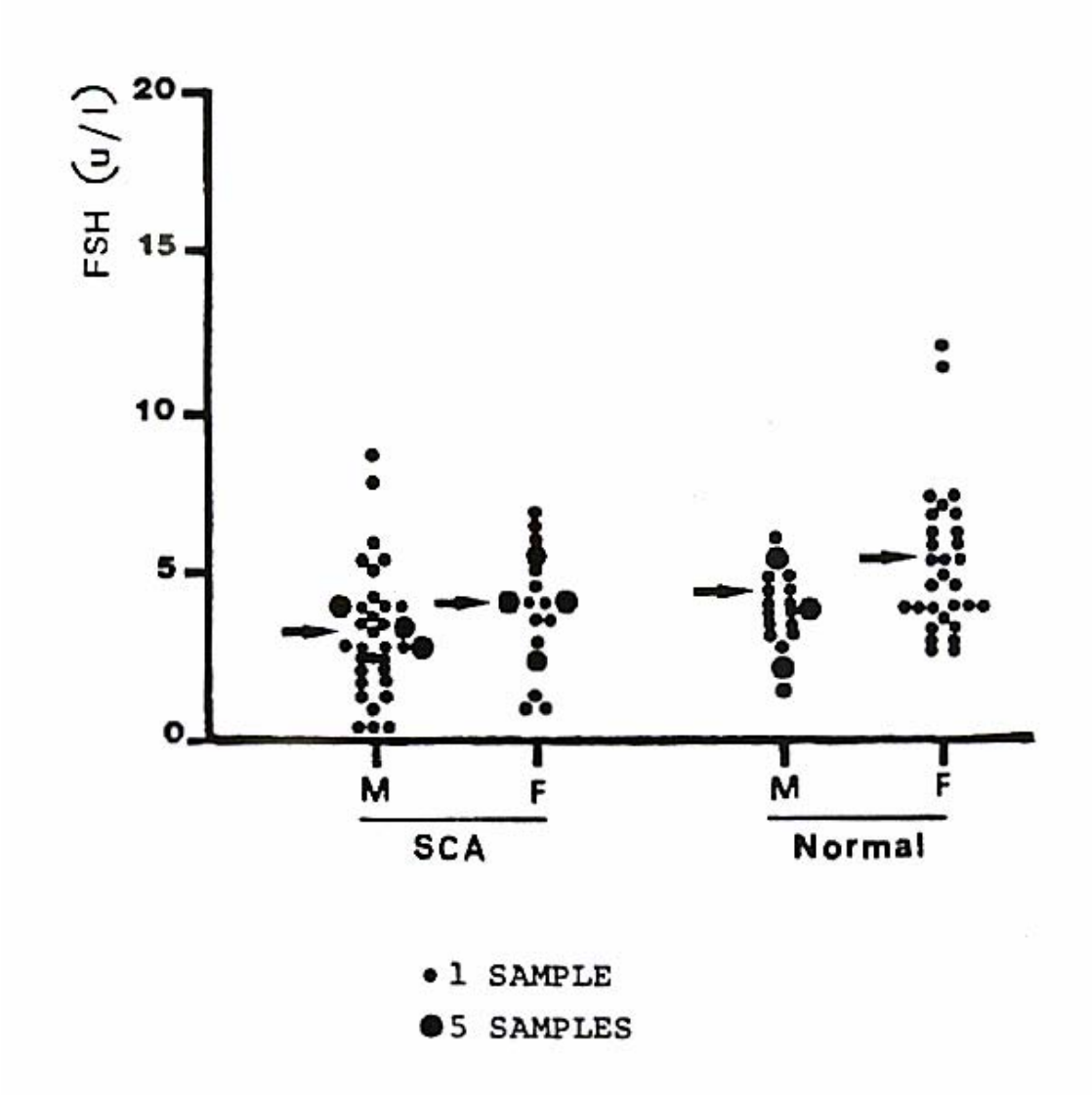


Figure 7.45: Distribution of LH in sickle cell disease patients and normal controls

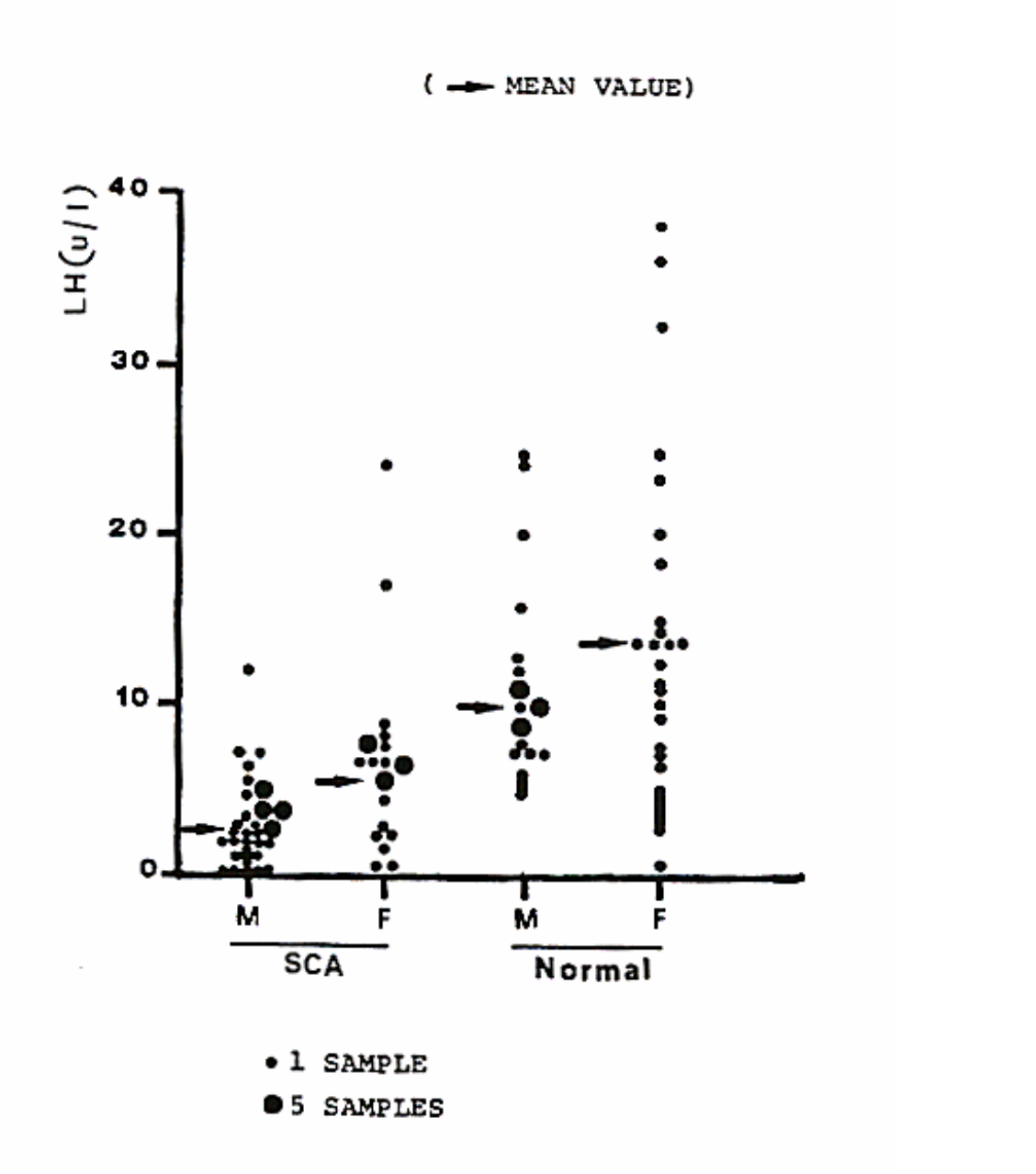


Figure 7.46: Correlation between testosterone and LH level in sickle cell disease patients

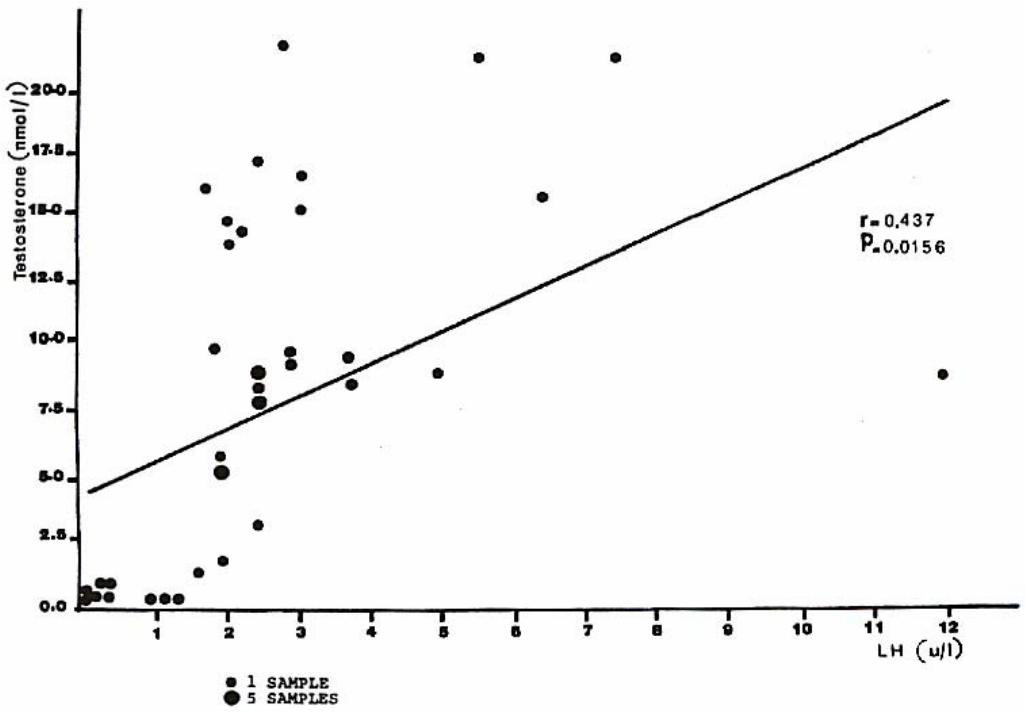


Table 7.73: Hormone levels in Hb SS patients with severe or mild disease (grouped on the basis of Severity Index)

Parameter	Male Hb SS		Female Hb SS	
	SI ≤ 6	SI < 6	SI ≥ 6	SI < 6
Cortisol (nmol/l)	8.77 ± 7.78	12.2 ± 7.6	9.66 ± 4.08	9.3 ± 2.6
T3 (nmol/l)	6.05 ± 0.6	6.7 ± 0.8	5.60 ± 0.84*	6.7 ± 0.9*
T4 (nmol/l)	20.52 ± 4.32	22.6 ± 3.0	17.07 ± 2.44*	22.7 ±4.2*
GH (nmol/l)	2.80 ± 3.47	3.4 ± 2.8	2.86 ± 3.65	3.7 ± 4.4

- Statistically significant P <0.05