

SONOGRAPHIC ASSESSMENT OF SPLEEN SIZE IN SAUDI PATIENTS WITH SICKLE CELL DISEASE

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Background: In patients with SCD, the spleen commonly enlarges during the first two decades of life but then undergoes autosplenectomy due to repeated attacks of vaso-occlusion and infarction. This, however, is not the case in Saudi patients with SCD, where splenomegaly sometimes persists into adult life.

Patients and Methods: Ultrasonography was used to evaluate spleen size in 363 Saudi patients with SCD (340 SCD and 23 sickle β -thalassemia). A total of 363 patients were evaluated. Their ages ranged from 1-60 years (mean 16 years).

Results: Only 24 (6.6%) of our patients had autosplenectomy. The splenic index increased with age until about 40 years of age and then gradually decreased, indicating persistence of splenomegaly in our patients into an older age group. Forty-three patients (11.8%) had marked-massive splenomegaly (splenic index >120 cm²) and these had higher HbF levels (mean HbF=22.2%) when compared with those who had autosplenectomy (mean HbF=14.6). This is significant (P -value=0.0169) and confirms the effect of HbF on persistence of splenomegaly in SCD patients.

Conclusions: Ultrasonography is a simple, safe and accurate method of assessing splenic size in patients with sickle cell disease. Patients with persistent splenomegaly should be followed closely for development of complications which may necessitate splenectomy.

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Key words: Spleen size, sickle cell disease, ultrasound, autosplenectomy.

The spleen enlarges in a variety of clinical conditions, however, determination of splenic size, especially of unpalpable spleen based on percussion, is not always accurate.¹ As a result of the recent advances in ultrasonography assessment of splenic size (either palpable or unpalpable) became feasible and both reliable and accurate.¹ In a recent article based on sonographic measurements, guidelines for normal splenic size in infants and children were established.²

The spleen, which is normally enlarged during the first two decades of life in patients with sickle cell disease (SCD), undergoes progressive atrophy due to repeated attacks of vaso-occlusion and infarction, leading to autosplenectomy. This, however, is not always the case and reports have suggested persistent splenomegaly in Saudi patients with SCD into an older age group, or sometimes into adult life.³⁻⁶ The purpose of this report is to evaluate

splenic size in Saudi patients with SCD in various age groups, determine the frequency of autosplenectomy, study the effect of HbF on persistence of splenomegaly, and discuss the sequelae of persistent splenomegaly in these patients.

Patients and Methods

This is a prospective study on randomly selected Saudi patients with SCD. Ultrasonographic studies were done using a real-time gray-scale ultrasound (GE RT 3000) and 3½ and 5 Mega Hertz transducer. The spleen size was measured during deep inspiration to minimize masking by the lung. Transverse and vertical diameters of the spleen were measured and the spleen index (SI) was obtained by the following formula: SI (cm²) = a (cm) x b (cm), where a is the transverse diameter and b is the ventricular diameter of the maximum cross-sectional image of the spleen.¹ The splenic index was arbitrarily classified into seven grades: grade 0, not visualized; grade I, 1-30 cm²; Grade II, 31-60 cm²; Grade III, 61-90 cm²; Grade IV, 91-120 cm²; Grade V, 121-150 cm²; Grade VI, more than 150 cm². The splenic index was also classified according to the different age groups as well as the level of HbF.

The patients studied were 363 Saudi SCD patients in

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chronic status, with ages ranging from 1-60 years. There were 340 sickle cell disease patients and 23 sickle β -thalassemia patients. The diagnosis of SCD was made by a positive sickling test and Hb electrophoresis (Helena Laboratories, Super Z electrophoresis kit). All ultrasound tests were performed without sedation and by one radiologist, to exclude observer variation. None of the patients studied had had splenectomy in the past.

Results

Three hundred and sixty-three patients were evaluated, comprising 205 males and 158 females. Their ages ranged from 1-60 years (mean 16 years). The grading of SI in relation to the number of patients is shown in Table 1. Only 24 of our patients (6.6%) had autosplenectomy as determined by non-visualization of the spleen during ultrasonographic examination. Only eight of them were below 20 years of age. Forty-three (11.8%) had splenic index of more than 120 cm^2 , which is defined as marked massive splenomegaly. The mean splenic index in relation to age is shown in Figure 1. The splenic index increased with the age of the patients until about 40 years of age, and then gradually decreased, with a large number of our patients over 20 years having persistent splenomegaly. Our patients tended to have high levels of HbF. The overall mean HbF level was 19.9% (range 3.2-47). The mean HbF level is shown with the splenic index in relation to various age groups in Figure 2. The mean HbF level of those with non-visualized spleen was 14.6% (range 3.2-38), while that of those with marked to massive splenomegaly (i.e., $\text{SI} > 120 \text{ cm}^2$) was 22.2% (range 5.9-40.2) which is significantly higher (P -value = 0.0169 using Student's t -test).

Discussion

Sickle cell disease (SCD), which is due to homozygous inheritance of the hemoglobin S variant, results from a single amino acid substitution of valine for glutamic acid in the sixth position among the 146 amino acids of the hemoglobin B-chain. It is one of the commonly inherited hemoglobinopathies in the Eastern Province of Saudi Arabia, with a sickle cell trait frequency of nearly 20% in some areas.^{3,7} In this region SCD is reported to be more benign than in other parts of the world. This has been attributed to high levels of HbF and the frequently associated α -thalassemia.^{3,8}

One of the main organs to be affected in SCD is the spleen. The spleen commonly enlarges during the first decade of life but then undergoes progressive atrophy due to repeated attacks of vaso-occlusion and infarction leading to autosplenectomy; however, sometimes splenomegaly persists beyond the first decade of life, and in some even into adult life.³⁻⁶ The reason for the failure of these individuals to undergo autosplenectomy is unknown. This study clearly shows persistence of splenomegaly in Saudi

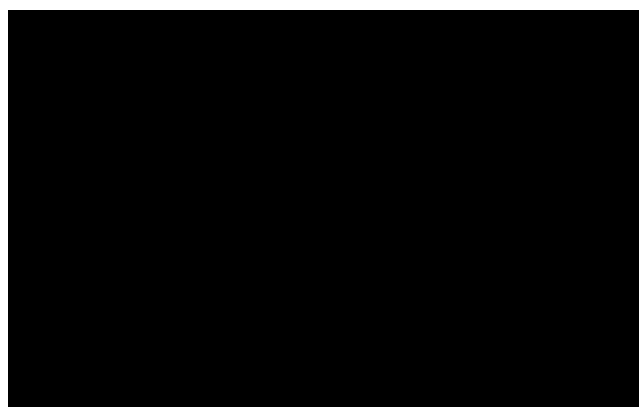


FIGURE 1. Mean splenic index in relation to age.

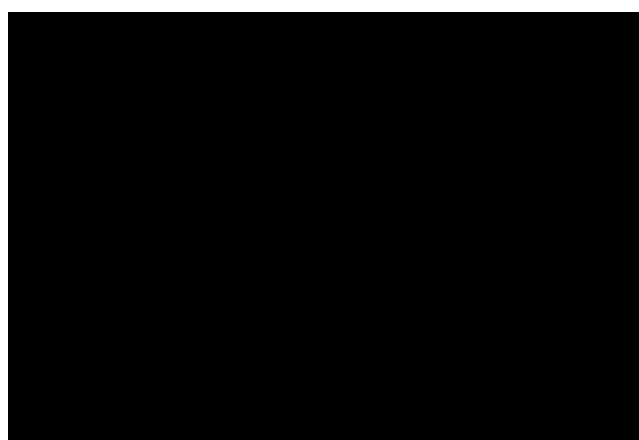


FIGURE 2. Mean HbF level and mean splenic index in relation to age.

patients with SCD into older age groups and even into adult life, a fact previously noted by other studies.³⁻⁶ A normal value of SI obtained from 204 healthy adults was reported as $19.8 \pm 12.3 \text{ cm}^2$. The majority of our patients had an SI greater than this at various age groups (Figure 1), and only 6.6% of our patients had non-visualized spleens on ultrasonography (autosplenectomy). This is in contrast to studies from Jamaica and the US, where autosplenectomy is found in most adult patients with SCD.⁹⁻¹¹ There is a correlation of persistent splenomegaly and elevated HbF level, which was demonstrated in our study. Patients who had persistent marked to massive splenomegaly had higher HbF levels when compared with those who had autosplenectomy. It has been suggested that HbF exhibits its favorable influence through inhibition of HbS polymerization and thus survival of HbF containing cells and less sickling.^{12,13}

The mere presence of splenomegaly in these patients does not imply function. Previously, 65% of Saudis from the Eastern Province with SCD were shown to have a functioning spleen and in some the spleen continued to function normally into adult life.^{5,8,14} This is in contrast to patients with SCD in the Western hemisphere, where

between five months and five years of age virtually all patients became functionally hyposplenic.¹⁵⁻¹⁷ A strong correlation between normal splenic function and high hemoglobin F levels was made.^{5,18} Functional hyposplenia was originally defined as the lack of uptake of ^{99m}Tc sulfur colloid by the clinically enlarged spleens of young children with hemoglobin SS disease,¹⁵ but Pearson and his colleagues developed a technique based on calculating the percentage of circulating pocked RBC.¹⁶ The presence of >3.5% circulating pocked RBC has a high correlation with non-visualization of the spleen by radionuclide scanning. It has been found that the majority of Saudi patients had much lower pocked RBC when compared with a similar group of American patients, indicating a better splenic function.⁵ This gives a protective effect to these patients. On the other hand, persistence of splenomegaly in these patients predisposes them to pathological abnormalities which can lead to morbidity and in some to mortality. The first abnormality is chronic hypersplenism, leading to progressive shortening of RBC survival, leukopenia and thrombocytopenia. In these patients, splenectomy is beneficial in decreasing their transfusion requirements and correcting their leukopenia and thrombocytopenia.^{9,20} The second abnormality is acute splenic sequestration crisis, which usually occurs within the first five years of life. Splenic sequestration crisis is a life-threatening event and a major cause of death.²¹ Approximately half of those dying in the first two years of life died as a direct result of acute splenic sequestration crisis. It can effectively be treated with blood transfusions, but has a propensity to recur with several episodes in a short period of time, and surgical splenectomy is frequently required in the long-term management of such patients.^{6,20,22-24} Recurrence of acute splenic sequestration becomes less likely after the age of five years, and the tendency to spontaneous splenic atrophy in SCD has favored a conservative approach. This, however, is not the case in our patients. We have shown that persistence of splenomegaly into an older age group in our patients predisposes them to the risk of acute splenic sequestration crisis.⁶ Although further episodes of ASSC can be prevented by a chronic transfusion program, in an environment like ours with the poor compliance of parents and limitations in blood availability with its attendant risks, chronic transfusion is not a suitable form of therapy in these patients, and splenectomy becomes an important alternative.^{6,20}

The third complication is splenic abscess. Splenic abscess is generally uncommon, but in patients with SCD there is a high incidence of splenic infarction in addition to the opportunity for bacteremia, especially in the presence of functional asplenia which renders these patients prone to developing splenic abscess.^{20,25} This is often due to *Salmonella*.^{20,25} Whereas percutaneous abscess drainage has been effective in treating splenic abscess in children and adults,²⁶⁻²⁸ the presence of functional asplenia in these patients makes them prone to recurrent infections, and

TABLE 1. Grading of splenic index.

Grade	Splenic index (cm ²)	No. of patients	Percentage
0	Not visualized	24	6.6
I	1-30	41	11.3
II	31-60	108	29.7
III	61-90	91	25
IV	91-120	57	15.6
V	121-150	36	9.9
VI	>150	7	1.9

splenectomy together with prophylactic pneumococcal vaccination and antibiotics is the treatment of choice.^{20,25}

In conclusion, ultrasonography is a simple, safe, reliable, accurate, and repeatable method of assessing splenic size in patients with sickle cell disease, and it is devoid of radiation. The presence of splenomegaly in these patients should be correlated with function using either the pocked red cells method or splenic uptake of ^{99m}Tc sulfur colloid. Those patients with persistent splenomegaly should be followed closely for development of complications which may necessitate splenectomy.

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