Sudan University of Science and Technology

College of Graduate Studies

Evaluation of Abdominal Organs in Patients with Sickle Cell Anemia using Ultrasonography

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A Thesis Submitted for Partial Fulfillment of Requirement of Msc Degree in Medical Diagnostic Ultrasound

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الآية

قال تعالى:

بسم الله الرحمن الرحيم

(فَتَبَسَّمَ ضَاحِكًا مِّن قَوْلِهَا وَقَالَ رَبِّ أَوْزِعْنِي أَنْ أَشْكُرَ نِعْمَتَكَ الَّتِي أَنْعَمْتَ عَلَيَّ وَعَلَىٰ وَالِدَيَّ وَأَنْ أَعْمَلَ صَالِحًا تَرْضَاهُ وَأَدْخِلْنِي بِرَحْمَتِكَ فِي عِبَادِكَ الصَّالِحِينَ)

صدق الله العظيم

(سورة النمل الآية رقم ١٩)

Dedication

To My kind mother (Aesha Ahmed Ballah)

To my brothers and sisters

To my wife (Nedal Omar)

And to my kids (Ramzi and Ali)

Acknowledgement

I am deeply grateful to God for gave me patience and power to complete this study; then to my supervisor Prof. Caroline Edward Ayad for her great support and valuable guidance.

Best wishes for whole staff of Jafar Ibn Ouf Pediatrics Hospital for their unlimited support and valuable advices and comments. Thanks Dr. Sara Isameldin Hammad and Dr.Madena Ali Mohamed Mustafa for their great help.

Thanks to my colleagues.

Finally I would like to thank everybody who helped me to prepare and finish this study.

Abstract

The study was descriptive study among a sample consists of 100 SCD patients with different gender and age it was carried out in JafarIbnOuf Pediatrics Hospital, in period from September 2018 to February 2019. The aim of this study was to evaluate abdominal organs (liver, gallbladder, spleen and kidneys) as texture, echogenicity, size and intraluminal contents in Sudanese patients with sickle cell anemia (SCA) by using ultrasonography. The data collected using data collecting sheet which contains patient's ages, gander, tribe, spleen length, echotexture, liver length, echotexture, gallbladder wall thickness, kidneys length, C/M differentiation and other findings. The results analysis carried out by Excel and Statistical Package for Social Sciences (SPSS) software for the collected variables which revealed that, the incidence of SCA among the selected sample was (62%) males and (38%) female with mean age of 8.5 years, most of patient descended from messeryia tribe in western Sudan. The study revealed that increased liver echogenicity was found in 7% of SCA patients all of them were males, 96% homogenous texture and 4% heterogeneous texture with equally distribution in gender, hepatomegaly was detected in 28% and the result of this study revealed that liver size had direct proportion to age in years. In the spleen the study found 93% were homogenous texture and 7% were heterogeneous texture all of them were males, also found 39% SCA patients with normal spleen size, 22% splenomegaly, 6% shrunken spleen 33% autosplenectomy. The study found there was linear relationship of the SCA patients' spleen size and age, as the age increased significantly at p= (0.000) the spleen size decreased by0.47 cm starting from 10cm. . Gall bladder in addition to wall thickness the study found intraluminal deposits like stone and sludge; the study reported a progressive age-related increase in the prevalence of gallstones. The study found 87% SCA patients

with normal kidneys, 10% enlarged kidneys, 3% shrunken kidneys, also showed 88% of good C/M differentiation and 12% poor C/M differentiation. From this study the spleen size will be predicted for SCA patients with known age by a new predictive equation.

$$\text{Spleen size} = 11.59x - 0.47x \text{ participant age}$$

The study revealed varied remarkable changes in abdominal organs sizes, echotexture, intraluminal deposits and wall thickness among the studied patients.

The study recommend for further studies with large sample size well be correlate with Doppler studies (resistive index RI) and laboratory investigations in the most affected tribe.

مستخلص الدراسة

كانت دراسة وصفية لعينة تتكون من 100 مريض مصابين بفقر الدم المنجلي مع اختلاف الجنس والأعمار. أجريت الدراسة في مستشفى جعفر بن عوف لطب الأطفال ، في الفترة من سبتمبر 2018 إلى فبراير 2019. كان الهدف من هذه الدراسة هو تقييم أعضاء البطن (الكبد والمرارة والطحال والكلى) كملمس ، صدى طبيعي ، حجم والترسبات الداخلية في المرضى السودانيين المصابين بفقر الدم المنجلي باستخدام الموجات فوق الصوتية. جمعت البيانات باستخدام ورقة جمع البيانات التي تحتوي على أعمار المرضى ، جنسهم ، القبيلة ، طول الطحال ، ملمسه ، طول الكبد ، ملمسه ، سمك جدار المرارة ، طول الكلى ، التمايز النخاعي القشري وغيرها من النتائج.

حللت المتغيرات التي تم جمعها بواسطة برنامج الحزم الاحصائية للعلوم الأجتماعية واكسل والتي كشفت أن نسبة الإصابة بمرض فقر الدم المنجلي بين العينة المختارة كانت 62٪ من الذكور و 38٪ من الإناث بمتوسط عمر 8.5 سنوات ، ينحدر معظم المرضى من قبيلة المسيرية في غرب السودان. كشفت الدراسة أنه تم العثور على زيادة الصدى الراجع من الكبد في 7 ٪ من مرضى فقر الدم المنجلي وجميعهم من الذكور ، وأن 96 ٪ منهم من ذوي النسيج الكبدي المتجانس و 4 ٪ منهم يعانون من عدم تجانس نسيج الكبد بنسب متساوية بين الجنسين ، تم الكشف عن ضخامة الكبد في 28 ٪ من المرضى. كما كشفت هذه الدراسة أن حجم الكبد يزيد بزيادة عمر المرضى. اما بالنسبة للطحال ، وجدت الدراسة أن 93 ٪ من المرضى كان لديهم نسيج متجانس و 7 ٪ منهم يعانون من عدم تجانس النسيج في الطحال وجميعهم من الذكور ، كما وجدت ان 39 ٪ من مرضى فقر الدم المنجلي لديهم طحال بحجم طبيعي ، 22 ٪ يعانون من تضخم في الطحال، 6% يعانون من انكماش حجم الطحال 33 ٪ يعانون من الاستئصال الذاتي للطحال. أوضحت الدراسة أن هناك علاقة خطية بين حجم الطحال وعمر مرضى فقر الدم المنجلي ، حيث كلما زاد العمر بشكل ملحوظ عند (p = 0.000) ينقص حجم الطحال بمقدار 0.47 سم بدءًا من 10 سم. اما المرارة بالإضافة إلى سمك الجدار وجدت الدراسة رواسب بداخلها مثل الحجر والحمأة ، وأفادت الدراسة ان زيادة تدريجية ذات صلة بالعمر في انتشار حصى المرارة. ووجدت الدراسة أن 87 ٪ من مرضى فقر الدم المنجلي لهم كليتين بحجم طبيعي و 10 ٪ منهم بكلى متضخمة و 3 ٪ يعانون من انكماش في حجم الكلى ، كما أظهرت الدراسة ان 88 ٪ من مرضى فقر الدم المنجلي لديهم كلى ذات تمايزنخاعي قشري جيد و 12 ٪ منهم يعانون من سوء التمايز النخاعي القشري للكلى.

من خلال هذه الدراسة سيتم التنبؤ بحجم الطحال لمرضى فقر الدم المنجلي مع العمر المعروف من خلال المعادلة التنبؤية الجديدة.

$$\text{حجم الطحال} = 11.59 \times (-0.47) \times (\text{عمر المريض})$$

كشفت الدراسة عن تغيرات ملحوظة متنوعة في أحجام أعضاء البطن ، وسمك جدارالمرارة بين المرضى الذين شملتهم الدراسة.

توصي الدراسة بإجراء المزيد من الدراسات مع زيادة حجم العينة وأن تكون مرتبطة بدراسات الدوبلر (مؤشر المقاومة) ونتائج المختبر في القبيلة الأكثر تضرراً.

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List of Abbreviations

BMI	Body Mass Index
Cm	Centimeter
CT	Computerized Tomography
FNH	Focal Nodular Hyperplasia
GFR	Glomerular Filtration Rate
Hb	Hemoglobin
HBA	Alfa Hemoglobin
HbA	Adult Hemoglobin
HBB	Beta Hemoglobin
HbF	Fetal Hemoglobin
HbS	Sickle Cell Hemoglobin
HbSC	Sickle Cell Hemoglobin C
HbSS	Sickle Cell Hemoglobin S
MHz	Mega Hertz
MRI	Magnetic Resonance Imaging
RBCs	Red Blood Cells
SCA	Sickle Cell Anemia
SCD	Sickle Cell Disease
SCT	Sickle Cell Trait
SPSS	Statistical Package for Social Sciences
US	Ultrasound

Chapter One

Chapter one

1.1. Introduction

Sickle cell disease refers to a group of inherited hematological disorders that affect different races across the geographical areas worldwide. It is an autosomal recessive disorder of the beta (β) hemoglobin chain. In normal adults, there are two alpha (α) and two ß globin chains in hemoglobin A; however, in patients with SCD, a mutations in the ß globin leads to sickle cell hemoglobin (HbS). This mutation was first discovered by Linus Pauling 1949. He proved that this abnormal hemoglobin molecule causes detrimental pathology. Normally, there are three different types of hemoglobin A, A2, and F. HbS in patient with SCD contains an abnormal ß globin chain encoded by a substation in chromosome II genes that result in valine instead of glutamic acid (Galloway et al 2011).

There are many theories about how the deformed red blood cells (RBC) containing HbS cause the clinical manifestations of SCD. Traditionally, it has been considered that the distortion of the diseased RBC causes sickling crises. This distortion is precipitated by status of low oxygen tension including dehydration, surgery, trauma, physiological stresses and temperature extremes. Because of RBC deformity blood viscosity increases leading to disruption of blood flow, consequent vascular obstruction, and even necrosis of the end organs. Such affected organs can cause numerous systemic complication including body pain syndrome, neurological, pulmonary, ophthalmological, hepato-biliary, renal, genitourinary, musculoskeletal and many other complications including splenic diseased (Al-Salem 2003).

New evidence shows that the pathogenesis of SCD is more complicated and is not limited to a simple distortion of the RBC and vascular occlusion. Such

factures are related to the other hemoglobin variants along with HbS, which reduce polymerization potential and response to oxygen stress; moreover, they alter membrane lipids and adhesion molecules (Ibrahim 1991).

The spleen is one of the most commonly affected organs. A wide spectrum of disease can affect the spleen secondary to SCD, with new evidence surrounding their management, both medical and surgical (Barrett 2009).

1.2. Statement of the problem:

In Sudan and other part of Africa, sickle cell anemia is common and constitutes a major challenge in ultra-sonographic examinations.

Sickle cell anemia manifests in a variety of abdominal problems, including hepatomegaly, splenomegaly, autosplenectomy, biliary tract and renal abnormalities.

Despite high prevalence of sickle cell anemia in our country, no study has been carried out to determine the prevalence of abdominal ultra-sonographic pathologies in sicklers in Sudan.

Questions to be answered are

1. What are abdominal findings in patients with SCA?
2. Can age and gender have role in such findings?
3. Can ultrasound be able to detect findings in abdominal organs in patients with SCA?

1.3. Objectives of the Study:

1.3.1. General Objective:

To evaluate the sonographic findings in abdominal organs in Sudanese patients with sickle cell anemia.

1.3.2. Specific Objectives:

1. To identify sonography findings of the (liver, gallbladder spleen and kidneys) in patients with sickle cell anemia.
2. To correlate this findings in (spleen, liver, gallbladder and kidneys) with the age and gender.
3. To study most common affected tribes with SCA in Sudan.
4. To established an equation for prediction of spleen size in SCA patients.

1.4. Significance of the Study

This study highlighted the significance of U/S to be utilized as an early diagnosis and predictor for the complications of SCD impact in liver, gallbladder, spleen and kidneys in Sudanese population.

1.5. Overview of the Study

This study divided into five chapters, chapter one is an introduction which is include the problem of the study, objective, significance of the study and overview. While chapter two contains literature reviews and previous studies, chapter three include the material used to collect the data and method of data collection. Chapter four include the results and finally chapter five which present discussion, conclusion and recommendations**.**

Chapter two

Literature Reviews and Previous Studies

Chapter two

Literature Reviews and Previous Studies

2.1. Literature Reviews

2.1.1. Sickle Cell Anemia (SCA)

Sickle cell anemia is an inherited disease in which the body produces abnormally shaped red blood cells that have a crescent or sickle shape. These cells do not last as long as normal, round, red blood cells, which lead to anemia (low number of red blood cells). This condition is caused by mutations in the HBB gene and is inherited in an autosomal recessive pattern. The sickle cells also get stuck in blood vessels, blocking blood flow (figure 1) (Gersten 2016).

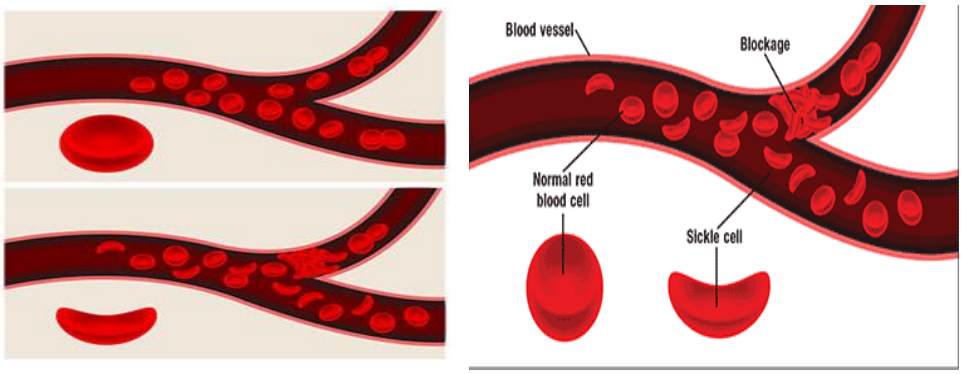


Figure 2.1. Illustration of vaso-occlusion event (www.naturalrugs.store).

Signs and symptoms of sickle cell disease usually begin in early childhood and may include anemia. Repeated vas-occlusion accounts for majority of the clinical manifestations of the disease. The most common abdominal manifestations include abdominal pain (mesenteric crisis), hepatomegaly, splenomegaly, autosplenectomy, cholelithiasis, renal enlargement, and increased renal echogenicity (Lonergon et al 2001).

Treatment typically focuses on controlling symptoms and may include pain medicines during crises; hydroxyurea to reduce the number of pain episode, antibiotics and vaccines to prevent bacterial infections and blood transfusions (Stephans & Scott 1980).

SCD is a multisystem disorder affecting almost every tissue of the body, Dysfunction of the liver and biliary tract is a common complication of sickle cell anemia (SCA). Hepatobiliary complications of the sickling disorders can be separated into broad categories of disorders related to hemolysis, the problems of anemia and transfusion management, the consequences of sickling and vascular-occlusion, and diseases unrelated to sickle hemoglobin (HbS) (Bunn1999**)**.

2.1.2. Pathophysiology of SCA

The normal human hemoglobin molecule consists of four globin chains: two α chains and two β chains. When α and β chains are normal, this is abbreviated Hb A. Abnormal hemoglobin is designated by the type of abnormality in the globin chain. For example, the presence of one sickle cell (S) β chain and one C β chain is abbreviated Hb SC. Homozygous sickle cell disease is designated Hb SS. Abnormal hemoglobin, such as Hb SS, is usually the result of an abnormality in the β (not α) chains (Bookchin, Lew 1996).

The β globin chain is coded on the short arm of chromosome 11. Sickle cell hemoglobin (Hb S) is formed when the amino acid valine is substituted for glutamic acid at the sixth position of the β chain; this is the result of a point mutation in the gene coding for β globin synthesis. This single amino acid substitution has far-reaching effects on hemoglobin interactions, RBC morphology, and hemodynamic. The Hb S β chain, with valine at the sixth position, has an

unusual propensity to bind with other Hb S chains (contained in other hemoglobin molecules within the RBC) when deoxygenated (Ballas 1998).

The basic structural unit that results is a twisted, ropelike structure composed primarily of two complete hemoglobin molecule strands, with binding between the β chains. This process is referred to as polymerization. The result is a strand of relatively rigid, polymerized hemoglobin molecules. Onto this basic polymer, other hemoglobin molecules may also polymerize, leading to large polymer strands. These rigid strands distort the RBC into a variety of elongated shapes and decrease its deformability. This sets the stage for vascular obstruction and hemolysis (Bunn1999).

Deformability of individual RBCs is necessary for normal RBC passage through the smallest of vascular channels. Cellular dehydration leads to increased viscosity of the RBCs, with resultant decreased deformability of Hb S cells, even when oxygenated. The membrane of Hb SS RBCs is also abnormal in a variety of ways, contributing to abnormal deformability. Finally, deoxygenation profoundly alters deformability through its induction of polymerization. These features make negotiation of the microvasculature difficult, if not impossible, for many Hb SS RBCs (Ballas1996).

RBCs in SCA also appear to have an increased binding affinity for vascular endothelium. The degree of affinity correlates strongly with the severity of clinical disease. Several molecular interactions are likely to contribute to this endothelial affinity. One is a surface complex on reticulocytes that binds to endothelium. Another mechanism is a complex present on both reticulocytes and endothelium that binds thrombospondin (secreted by activated platelets). Several other plasma proteins, perhaps increased in times of stress, promote adhesion of Hb SS RBCs to

vascular endothelium, which worsens vaso-occlusion. It has also been shown that adherent sickled RBCs inhibit vasorelaxation (Mosseri etal1993).

Finally, it has long been known that the microvasculature of patients with SCA may develop intimal hyperplasia. This creates irregular areas of endoluminal narrowing, which likely worsen vaso-occlusion by promoting thrombosis. (Hebbel &Vercelotti 1997).

2.1.3. Clinical Presentation of SCA

Acute, painful vaso-occlusive crises are the most common, and earliest, clinical manifestations of SCA. Half of all patients with SCA experience a painful crisis by 4 to 9 years of age. The pain is usually described as bone pain, although crises may involve virtually any organ. They are presumed to be caused by micro vascular occlusion with subsequent tissue ischemia. In young children, vaso-occlusive crises most commonly manifest as dactylitis, a painful swelling of the hands, fingers, feet, and toes. Other problems in SCA include osteomyelitis, osteonecrosis, splenic infarct, splenic sequestration, acute chest syndrome, stroke, papillary necrosis, and renal insufficiency (Yaster et al 2000).

2.1.4. Liver Complications

The liver is a largest solid organ that located on the right upper quadrant just below the diaphragm a portion of the liver goes into the left upper abdomen as well.

The hepatic complications attributed to vascular occlusion encompass a variety of clinical syndromes. In many patients, the liver is generally enlarged throughout life, especially when its measurement is adjusted for body size. Hepatic infarction is seen as a characteristic wedge shaped, peripherally located hypo

intense lesion on computed tomography (CT) scan. Single or multiple abscesses have been described with an irregular shape on CT scan. Focal nodular hyperplasia (FNH) of the liver has been seen angiographically with a characteristic a vascular mass (Davies, Brozovic 1987).

Hepatomegaly was the most predominant findings in the liver of SCD patients in this study. The liver is generally affected by a number of complications due to the SCD and its treatment, in addition to the vascular complications from the sickling process, multiple transfusions often place SCD patients at the risk of viral infections such as hepatitis B and C, iron overload, and combined with the effects of chronic hemolysis, all of which may contribute to the development of liver disease. Infiltrative and granulomatous diseases, infections, malignancy, and other hematologic diseases may also cause hepatomegaly (Ballas 1996).

Acute hepatic sequestration, a rarely recognized complication of vascular-occlusion, is characterized by a rapidly enlarging liver accompanied by a decrease in hemoglobin/hematocrit and a rise in reticulocyte count. The liver is smooth and variably tender. Sonography demonstrate only diffuse hepatomegaly.

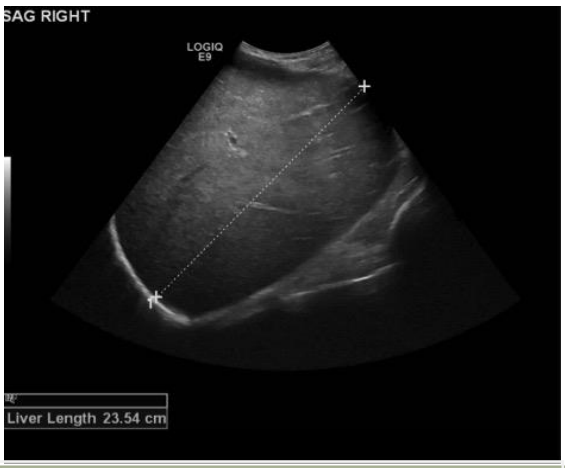


Figure 2.2.Ultrasound image shows hepatomegaly(23.54 cm) in patient 19 yrs with SCA (www.event scribe.com).

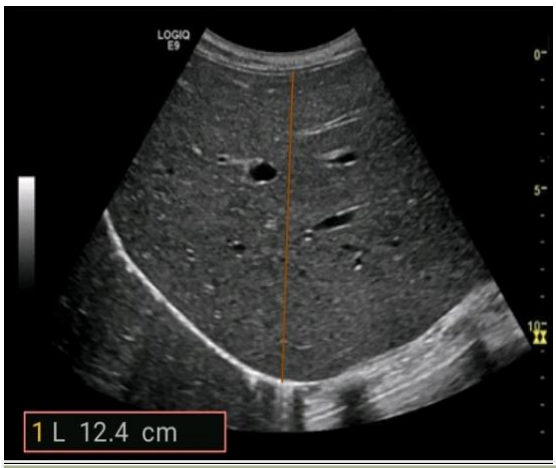


Figure 2.3. Ultrasound image shows normal liver measured (12.4 cm) in patient 19 yrs with SCA (www.GE Healthcare.com)

Intrahepatic cholestasis with bile plugs in canaliculi may be seen. Hepatocyte necrosis is unusual. Acute hepatic failure has been reported in several cases where massive hepatic necrosis was seen in the absence of markers for viral hepatitis (Johnson et al 1985).

There are many causes for liver disease development in sickle cell disease (SCD). Diagnosis and treatment are difficult based on clinical features and laboratory findings. Ten percent of autopsy cases had associated SCD and otherwise unexplained liver cirrhosis. Abnormalities in liver function tests are also frequent in a symptomatic patient. These findings are described as chronic hepatopathy in sickle cell anemia (Ahn H, Li CS, and Wang 2005).

2.1.5. Gallbladder Complication

The occurrence of gallstones is one of the most important manifestations of SCD in the digestive tract. Chronic hemolysis, with its accelerated bilirubin turnover, leads to a high incidence of pigment gallstones (West et al 1992).

However, many SCD patients with marked hemolysis do not develop gallstones. Thus, abnormalities in gallbladder function or bile acid metabolism may contribute to gallstone formation in these patients (Everson et al 1989).

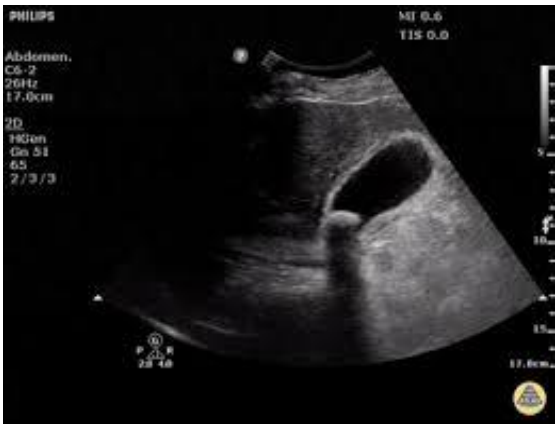


Figure2.4. Sonograph shows solitary gall stone (www.Radiopedia.com).

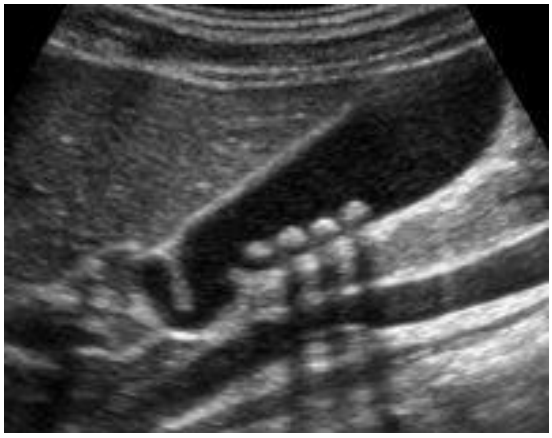


Figure 2.5. Ultrasound image shows multiple gallstones (www.ultacare.com).

Sonographic surveys of patients indicate that the onset of cholelithiasis occurs as early as 2 to 4 years of age and progressively increases in prevalence with age (Walker, Hambleton 2000).

Biliary sludge (figures 6&7) is a viscous material detectable by non acoustic shadowing on sonography and may be a precursor of gallstone development (Lee SP, Maher , Nicholls 1988).

Certain antibiotics such as ceftriaxone seem to promote sludge formation. Studies in patients with SCD indicate that sludge is often found with stones, but sludge alone may or may not progress to stone formation (Al-Salem, Qaisruddin1998).

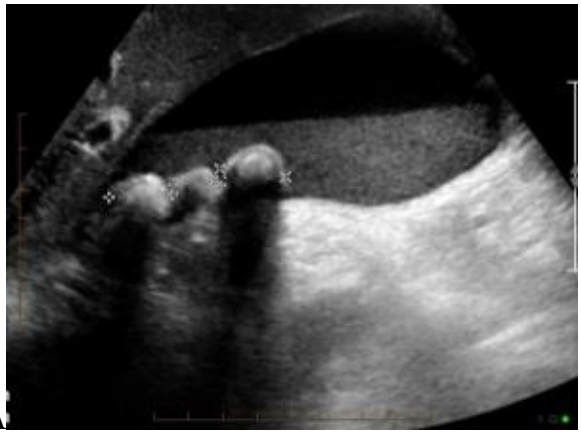
A 

Figure 2.6. Ultrasound image shows sludge and multiple gall stones (www.Radiopedia.com).

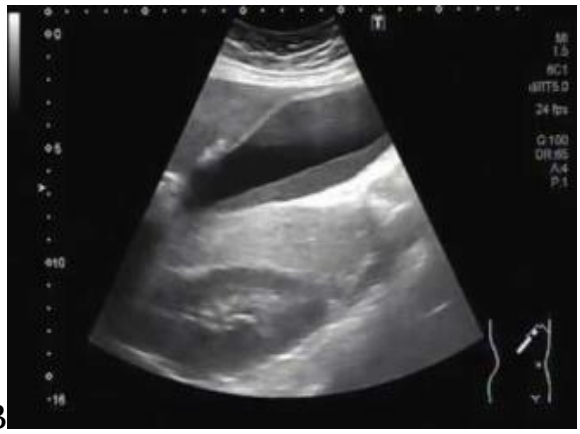
B 

Figure 2.7. Ultrasound image shows sludge only (www.wikipidia.com).

Sonographic appearance of gallstones includes echogenic foci that typically cast a strong shadow (Figures 2.4, 2.5 and 2.6). Shadowing may not be demonstrated if the stone is imaged off-axis or when the diameter of the stone is smaller than the width of the beam. With careful scanning using focused high-frequency (5-MHz) probes, shadowing will be visualized with stone sizes as small as a millimeter. Stones are usually found in the dependent part of the gallbladder but can float in concentrated bile and may layer within it. Changes of posture usually cause them to move, but if they become immobile they may adhere to the gallbladder mucosa. Unlike cholesterol deposits or polyps, stones have posterior shadowing, whereas cholesterol and polyps do not usually cast an acoustic shadow. The accuracy of sonography in the diagnosis of gallstones is very high (around 98%) when the classic findings of an echogenic lesion with acoustic shadowing and postural movement are present. When these features cannot be demonstrated, the accuracy falls accordingly. Problems of interpretation may arise at the neck of the gallbladder and cystic duct as the valves of Heister normally return strong echoes and cast a shadow. Cholecystitis produces thickening of the gallbladder

wall above the normal 2 to 3 mm (measured in the normally filled gallbladder) ((Billa et al 1991).

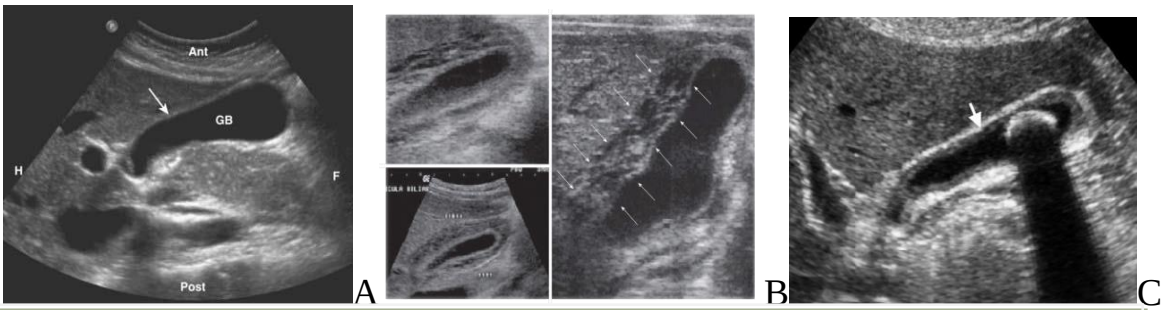


Figure 2.8. Ultrasound images show normal gallbladder wall thickness (A), thickened gallbladder wall (B) and thick bladder wall with stone(C) (www.Researchgate.net)

In acute cholecystitis, a circumferential lucent zone may be seen in the gallbladder wall (Cosgrove, McCready 1980).

In addition, a "striated" appearance of the gallbladder wall has been described, consisting of alternating, irregular, discontinuous, and lucent and echogenic bands. In chronic cholecystitis, the fibrosis leads to high-level echoes, and the gallbladder is usually small (Barnet1985).

2.1.6. Splenic Complications

The spleen normally lies in the left upper quadrant, with its long axis aligned along the left tenth rib. Spleen size can vary normally with patient height, age, gender and race. The spleen has homogeneous echo texture on ultrasound

Spleen is the most affected organ in SCD, because it receives the insults of the associated clinical conditions of this pathology earlier than the other vulnerable body organs such as the liver, gallbladder, kidneys and bone marrow (De Montalembert2008).

This is due to its peculiar anatomy and physiology - it has narrow blood vessels and filters the systemic blood. Early monitoring and detection are enhanced by ultrasonography of the spleen because the spleen responds to different pathologic states such as fever and sickle cell disease by dimensional and parenchyma changes (Curry, Tempkin 1995).

Regional variations in size and parenchyma echo-texture of the spleen among sickle cell disease (SCD) patients have been documented in various publications(Awotua et al 2004).

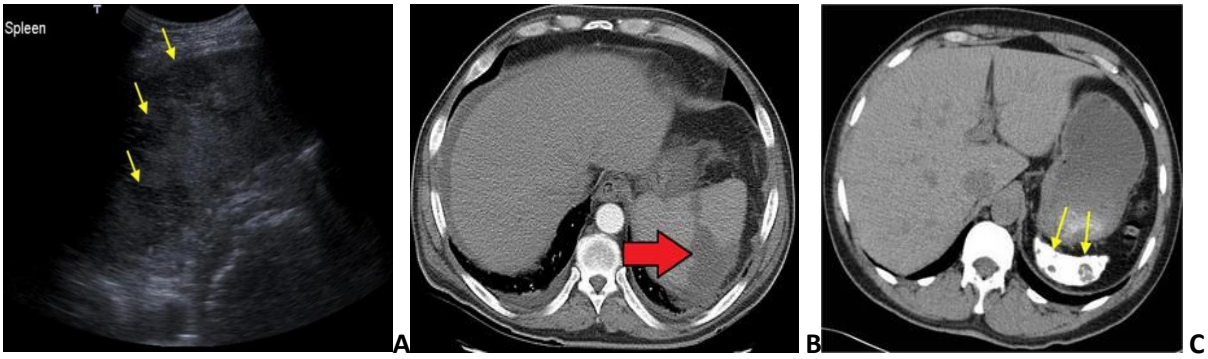


Figure 2.9.Ultrasound demonstrating peripheral hypo echoic lesions consistent with infarcts in a patient with sickle cell disease 3 yellow arrows (A).Splenic infarct seen on CT red arrow (B)CT demonstrating densely calcified spleen (yellow arrows) in a patient with sickle cell disease (C). (www.Wikipedia.com)

Splenomegaly appears in the first year of life and should be suspected in children if the spleen is more than 1.25 times longer than the adjacent normal kidney (Hasan et al 1996).

Pathologically, the end stage spleen is small and fibrotic with marked deposition of hemosiderin and calcium (Loftus& Metreweli 1998).

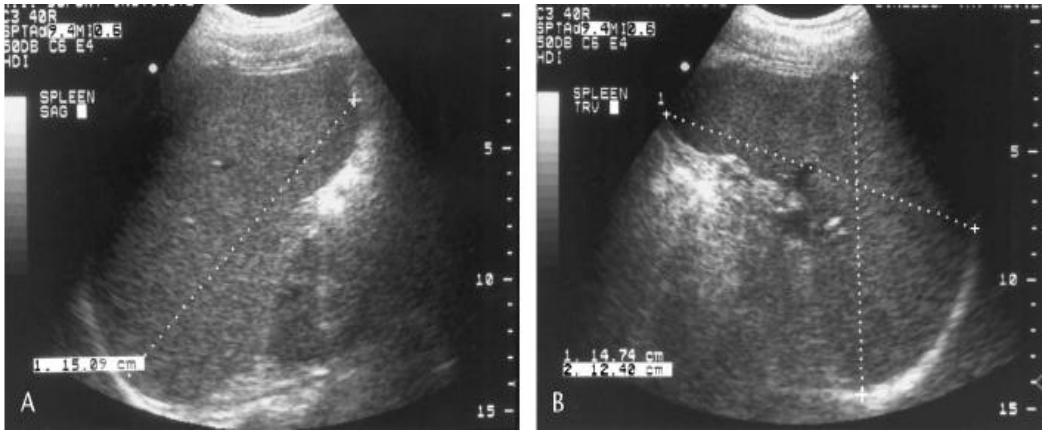


Figure 2.10.Sonographs show (A) Splenomegaly (15.09 cm) in length (B) enlarged spleen measured (14.74X12.42 cm) (www.Ultrasound cases.info)

In patients with SCD, intrasplenic benign nodules corresponding to normal splenic tissue may be identified on imaging studies (Fischer, Shapiro and Treves 1977).

Vascular occlusions and repetitive local splenic infarction (is a condition in which oxygen supply to the spleen is interrupted), leading to partial or complete infarction(tissue death due to oxygen shortage) tend to cause the so-called autosplenectomy of the spleen in homozygous disease, with splenic function being lost by advanced age. Over time with infarction the spleen becomes small, dense, and calcified. This calcification may be visible at radiography and CT (Fig 2.9-C). The infracted, fibrotic spleen has low signal intensity, regardless of MRI pulse sequence, secondary to ferrocalcinosis. Rarely, splenomegaly may persist in homozygous patients, but such spleens are also nonfunctional, densely fibrotic, and calcified. Moreover, clinical disappearance of the spleen does not imply atrophy since splenomegaly may recur years later in some patients during undercurrent illness (Loftus& Metreweli 1998).

Infarcts usually appear as wedge-shaped or rounded hypo echoic areas on ultrasonography (Lonergan, Cline 2001).

Another splenic complication of SCA is known as sequestration syndrome. It is characterized by rapid pooling of blood within a solid organ (almost always the spleen, although it has been reported in the liver), with resulting intravascular volume depletion and dropping hematocrit values (a drop of >2 g/dL is considered significant).Sequestration syndrome may be quite severe, however, and severely affected children present with a rapidly enlarging spleen, abdominal fullness, thirst, lethargy, pallor, tachycardia, and tachypnea. The condition may progress rapidly (within hours) to cardiovascular collapse and death. The diagnosis of sequestration syndrome must be considered in a child with any of the above symptoms and signs (Levin et al 1996).

2.1.7. Kidneys Complications

SCD is associated with many structural and functional abnormalities of the kidneys, which may progress to chronic renal failure and end-stage renal disease (Ataga, Orringer 2000).

The kidney in SCA has increased renal plasma flow and increased glomerular filtration rate (GFR). These changes are thought to arise from compensatory hypersecretion of prostaglandins with vasodilatory effects. The glomerulus is large and hyperfiltrating and as a result develops glomerulosclerosis. By adolescence, the GFR is normal and by age 40 it is reduced (Schmitt et al1994).

Clinical and pathologic data indicate that intravascular sickling occurs more readily in the kidney than in any other organ (Raj et al 2002).

A series of progressive and random pathologic events involving the kidney begins early in the first decade of life in a patient with SCD and continues throughout life. The combination of hypoxia, hyper tonicity, and acidosis in the renal medulla leads to stasis in the vasa recta and to ischemia of the renal medulla and papillary tip, distortion of regional blood flow, focal interstitial nephritis and fibrosis, tubular dysfunction atrophy, and papillary necrosis (Pearson1984).

Uric acid nephropathy is a rare condition; it is recurrent and may lead to a radiolucent uric acid stone formation, which can be detected by sonography (ALK, Jennette 1994).

Several studies have reported a medullary or diffuse increase in reflectivity on renal sonography in patients with SCD (Fixler, Styles 2002).

Figure 2.11.Ultrasound images show **{**A. Diffuse increased renal echogenicity with small size (end stage). B. Diffuse decreased renal echogenicity with increased in size. (Poor C/M differentiation)**}.** C. Normal renal echogenicity (good C/M differentiation) (www.Wikipedia.com).

2.2. Previous Studies

(Geofery and Charles 2015).reported that participants within the age range of 10–15 years had the highest frequency with 88 (34.9%), followed by those within the age group of 17–23 years with 86 (34.1%), and the least were those within the age group of 30 years and above with 8 (3.2%). Hepatomegaly was found in 53 (75.7%), and increased echogenicity of the liver was found in 50 (94.3%) of the SCD patients. Gallstones were found in 45 (17.9%), gallbladder sludge was found in 51 (21.4%) and thickened gallbladder wall was found in 84 (33.3%) of the SCD patients. Autosplenectomy was found in 45 (17.9%), splenomegaly in 63 (24.9%), and calcified spleen in 18 (8.7%) of the SCD patients. Enlarged kidneys in SCD patients were found in 61 (98.4%) and 63 (98.4%) on the right and left kidneys, respectively. Shrunken kidneys were found in 5 (2.0%) and 4 (1.6%) of the SCD patients on the right and left kidneys, respectively.

(Balci et al 2008) found hepatomegaly was the most predominant findings in the liver of SCD patients in this study it was found in 66 (26%), increased echogenicity of the liver was found in 53 (21%) of SCD patients, gallstones were found in 45 (17.9%), gallbladder sludge was found in 51 (94.4%), thickened gallbladder wall in 84 (33.3%), 18 (9.8%) patients with normal spleen, splenomegaly was found in 63 (24.9%), autosplenectomy was found in 45 (17.9%),increased renal echogenicity was found in 56 (22.2%) and 60 (32.4%) and 59 (32.1%) SCD patients with normal right and left kidneys.

(Diagn 2008) reported that the most frequent US findings (expressed as percentages of all patients) were hepatomegaly (71.6%) bright liver was identified in 6 patients (5.9%). cholelithiasis (30.4%) and splenomegaly (17.4%), autosplenectomy (33.3%), renal enlargement (30.4%) and Medullary or diffusely

increased renal echogenicity was observed in 16 patients (15.7%). Sonographic findings typical of renal papillary necrosis were observed in one patient. Periportal lymphadenopathy was detected in 10 (11.9%) of 84 patients and 2 (11.1%) of 18 patients.

(Traina et al2007). Reported that 96% patients had some liver abnormality; these included abnormal liver function tests, viral hepatitis, liver sonographic changes, or cholelithiasis. The sickling process was the only explanation for the abnormal liver function tests or liver sonographic changes in 24% of these patients.

(Mohanty et al 2004) found increased echogenicity of the liver was found in 53 (21%) of SCD patients. Several features of liver histology in patients with SCD may contribute to brightening liver echo like hemosiderin pigment, periportal fibrosis, and distention of the sinusoid with sickle cell.

(Bauer,Moor GWand Hutchins 1980) reported the sonographic appearance of the liver in SCD and thalassemiaintermedia was described in 105 patients. Hepatomegaly was demonstrated in 70.5% and bright liver in 3.8% of these patients.

(Attalla 2010) Reported Gallstones were found in 45 (17.9%) of SCD patients in this study gallbladder sludge was found in 51 (94.4%) sickle cell disease patients in this study. Most of the patients with biliary sludge may eventually develop gallstones, however not in all cases. Also found thickened gallbladder wall in 84 (33.3%) SCD patients. This may be due to the condition of the GB at the time of the scan, as normally filled GB will best demonstrate thickened GB wall.

(Eze CU et al 2013). Found in their study the spleen of SCD patients generally had undulating variations in size increasing rapidly from 2 years of age

to the childhood/adulthood transitional age of 18 years. Beyond 18 years, there was a mixture of sharp reduction and increase in spleen size in an undulating form up to the age of 58 years. Maximum numbers of shrunken spleen and autosplenectomy were recorded between 18 years and 33 years age in this study. This implies that, in our locality, the spleen of patients with SCD increases rapidly in size from early age and peaks at 18 years, and generally declines sharply to either a shrunken state or autosplenectomy. The mean spleen sizes of SCD patients were generally larger than those of the controls ($P < 0.05$), specifically in children (age range 2 – 17 years). This could be due to low body immunity in this age range with resultant high susceptibility of SCD patients to the acute complications of sickle cell condition.

(Walker and Serjeant1995) Reported increased medullary echogenicity in 5 of 179 patients (2.8%). In the same study, diffusely increased renal echogenicity was reported in 15 of 179 patients (8.4%). Renal enlargement has been reported in up to 50% of patients with SCD. The etiology of renal enlargement in SCD is unknown. One patient in the study had typical sonographic findings of renal papillary necrosis, as well as multiple round or triangular cystic spaces communicating with the collecting system in the medullary region without a dilated renal pelvis.

(Eltahir 2017).found the average measurement of the right kidney length (cm) and volume (cm3) for SCD patients was 8.78±1.04 & 59.41±2.21 respectively, while the left kidney measures 8.93±5.22/cm (length) & 98.38±21.38/ cm3 (volume), the control group shows 9.14±1.04/cm and 97.85±29.53/ cm3 for right kidney length and volume respectively, as well as the left kidney length = 9.5±1.04/cm, while the volume =100.2±22.73/ cm3 so that the left kidney size & volume greater than the right kidney.

(Majdi & Hanan 2014). Found some findings of a study conducted in Elobied hospital in north Kordofan state, showed that sickle cell trait in relatives of patients suffering from sickle cell disease (SCD) who were referred to this Hospital, was 54% of target samples, which concentrated mainly in two tribes, Bederia and Fulani. Sickle cell disease in Messeryia of Darfur and Messeryia Hummer of Kordofan showed a prevalence of 30.4% and 18% respectively. It is estimated that one in every 123 children born in Messeryia tribe is at risk of having SCD.

Chapter Three

Materials and Methods

Chapter Three

Materials and Methods

3.1. Materials

3.1.1 Patients:

The study was descriptive cross-sectional study carried out in Khartoum state at JafarIbnOuf Pediatrics Hospital. The study started in September 2018 and finished in February 2019 in which a group of (100) patients with sickle cell disease with different age and gender were drown for abdominal US examination.

3.1.2 Machine

A real-time ultrasound machine General Electric; LOGIQ F 6- Malaysia; model number: 5415172, (Figure12) was used for the study

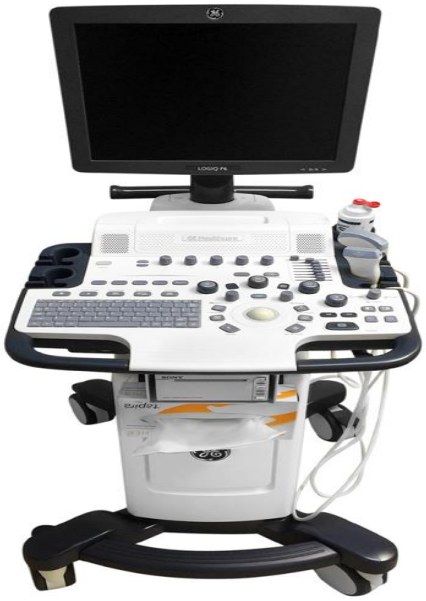


Figure 3.1.LOGIQ F 6-Genaral Electric Malaysia; model number:

3.2. Methods

3.2.1 Technique

All the patients fasted over night or at least for 6 h before being scanned. The examinations were performed with the patients in the supine position for comfort and to obtain optimal views. Curvilinear probe with multi-frequencies ranging from 4–9 MHz was used to evaluate the abdominal organs. The choice of the frequencies was to give adequate penetration and resolution of intraperitoneal and retroperitoneal abdominal organs in both pediatrics and adult patients. An US gel was used and it was put at the top of the transducer to avoid reflection of ultrasound and to maintain a good transmission of US beam inside the body. Right and left decubitus positions were used as alternate positions if the organs were not clearly visualized in the supine position. The liver span was measured in the right lobe with the longitudinal center of the right kidney in the plane of imaging. Liver parenchyma was assessed for echotexture and focal abnormalities. Hepatomegaly was defined if the long axis of the liver was more than the reverence values of the hospital. The gallbladder, its wall thickness, and content were also assessed.

The long axis of the spleen was measured at the level of the hilum Splenomegaly and shrunken spleen was defined in adults when the long axis of the spleen was more or less than reverence values. Autosplenectomy was defined as the spleen is not visualized in its position. The spleen was also assessed for parenchymal echotexture changes and focal abnormalities.

The length of the kidneys was obtained by measuring the bipolar length (long axis) of the kidneys. The kidneys were considered abnormally echogenic if the renal cortex was more echogenic than adjacent spleen or liver. Renal corticomedullary differentiation was considered abnormal when the cortex was

difficult to visually distinguish from the medulla. Kidneys were also assessed for the presence of renal calculi, cysts, or other focal parenchymal abnormalities. All ultrasound images were presented and diagnosd confirmed with Dr Sara Isam Eldin Hammad and Dr Madena Ali Mohamed Mustafa (MD Radiologists).

3.2.2 Data Collection

The data collected using data collecting sheet which contains patient's ages, gander, tribe, spleen length, echotexture, liver length, echotexture, gallbladder wall thickness, kidneys length, C/M differentiation and other findings

3.2.3 Statistic analysis

Excel 2010 and Statistical Package for Social Sciences (SPSS) software were used to analyze the data to find the significant difference between variables of patients with sickle cell disease and reference values.

3.2.4 Ethical consideration

An ethical approval from hospital in which the study was carried out to collect the data from the patient for the research and verbal consent from the patient and their relatives was taken.

Chapter Four
Results

Chapter Four
Results

Table 4:1 Descriptive statistics of the Sickle cell participants' demographic data (mean and standard deviation, maximum and minimum values

Variables	N	Minimum	Maximum	Mean	Std. Deviation
Age/years	100	2.00	23.00	8.50	5.88
liver size/cm	100	7.80	18.00	11.55	2.84
spleen size/cm	100	.00	16.00	6.59	5.20
GB wall thickness/mm	100	2.10	5.00	2.90	0.67
Right Kidney length/cm	100	6.20	13.80	8.74	1.87
Left kidney length/cm	100	6.20	13.90	8.88	1.90

Table 4:2 Descriptive statistics of the Sickle cell participants' demographic data (mean and standard deviation, maximum and minimum values and p value classified according to age

Variables	***Range of age***	***N***	***Mean***	***Std. Deviation***	***Minimum***	***Maximum***	***P-value***
liver size	2-5 years	43	10.08	2.06	7.80	15.90	0.000
	6-10 years	21	11.01	1.96	9.00	16.50	
	11-15 years	21	12.24	2.48	9.30	16.80	
	16-23 years	15	15.52	2.35	10.70	18.00	
	Total	100	11.55	2.84	7.80	18.00	
spleen size	2-5 years	43	8.64	4.05	.00	14.90	0.000
	6-10 years	21	7.30	4.22	.00	14.30	
	11-15 years	21	3.66	5.57	.00	15.30	
	16-23 years	15	3.80	6.15	.00	16.00	
	Total	100	6.59	5.20	.00	16.00	
GB wall thickness	2-5 years	43	2.70	.44	2.20	4.70	0.035
	6-10 years	21	3.04	.82	2.10	5.00	
	11-15 years	21	3.19	.89	2.30	4.90	
	16-23 years	15	2.90	.51	2.40	4.10	
	Total	100	2.90	.67	2.10	5.00	
Right kidney length	2-5 years	43	7.34	1.04	6.20	11.40	0.000
	6-10 years	21	9.14	.92	7.80	11.50	
	11-15 years	21	10.61	1.68	8.70	13.80	
	16-23 years	15	9.58	2.02	6.30	11.60	
	Total	100	8.74	1.87	6.20	13.80	
Left kidney length	2-5 years	43	7.44	1.02	6.20	11.20	0.000
	6-10 years	21	9.26	.90	8.00	11.30	
	11-15 years	21	10.88	1.64	9.00	13.90	
	16-23 years	15	9.66	2.07	6.20	12.20	
	Total	100	8.88	1.90	6.20	13.90	

Table 4:3 Descriptive statistics of the Sickle cell participants' demographic data Classified according to gender

Variables	*Gander*	*N*	*Mean*	*Std. Deviation*	*Minimum*	*Maximum*	*P-value*
Liver Size	Male	62	11.52	2.75	7.80	17.00	0.914
	Female	38	11.58	3.02	8.30	18.00	
	Total	***100***	***11.55***	***2.84***	***7.80***	***18.00***	
Spleen Size	Male	62	7.40	4.964	.00	16.00	0.047
	Female	38	5.27	5.39	.00	15.30	
	Total	***100***	***6.59***	***5.20***	***.00***	***16.00***	
GB Wall Thickness	Male	62	2.94	0.72	2.10	5.00	0.501
	Female	38	2.84	0.60	2.30	4.70	
	Total	***100***	***2.90***	***0.67***	***2.10***	***5.00***	
Right Kidney Length	Male	62	8.72	1.83	6.20	13.30	0.897
	Female	38	8.77	1.96	6.30	13.80	
	Total	***100***	***8.74***	***1.87***	***6.20***	***13.80***	
Left Kidney Length	Male	62	8.83	1.83	6.20	13.50	0.738
	Female	38	8.96	2.03	6.20	13.90	
	Total	***100***	***8.88***	***1.90***	***6.20***	***13.90***	

Table 4:4. Cross tabulation of the Sickle cell participants' liver texture in both genders

P-value=0.614			**Sex**		**Total**
			Male	***Female***	
liver texture	Homogenous	Count	60	36	96
		% of Total	***60.0%***	***36.0%***	***96.0%***
	Heterogeneous	Count	2	2	4
		% of Total	2.0%	2.0%	4.0%
Total		Count	62	38	100
		% of Total	***62.0%***	***38.0%***	***100.0%***

Table 4:5Cross tabulation of the Sickle cell participants' liver texture Classified according theirages

P-value=0.000			***Age***				***Total***
			2-5 years	***6-10 years***	***11-15 years***	***16-23 years***	
liver texture	homogenous	Count	43	21	21	11	96
		% of Total	***43.0%***	***21.0%***	***21.0%***	***11.0%***	***96.0%***
	heterogeneous	Count	0	0	0	4	4
		% of Total	.0%	.0%	.0%	4.0%	4.0%
Total		Count	43	21	21	15	100
		% of Total	***43.0%***	***21.0%***	***21.0%***	***15.0%***	***100.0%***

Table 4:6Cross tabulation of the Sickle cell participants' liver echogenicity Classified according to gender

P-value=0.032			***Sex***		Total
			Male	***Female***	
Liver echogenicity	Normal	Count	55	38	93
		% of Total	***55.0%***	***38.0%***	***93.0%***
	Hyper	Count	7	0	7
		% of Total	7.0%	.0%	7.0%
Total		Count	62	38	100
		% of Total	***62.0%***	***38.0%***	***100.0%***

Table 4:7Cross tabulation of the Sickle cell participants' liver echogenicity Classified according to age

P-value=0.855			***Age***				***Total***
			2-5 years	***6-10 years***	***11-15 years***	***16-23 years***	
Liver echogenicity	Normal	Count	41	19	19	14	93
		% of Total	***41.0%***	***19.0%***	***19.0%***	***14.0%***	***93.0%***
	Hyper	Count	2	2	2	1	7
		% of Total	2.0%	2.0%	2.0%	1.0%	7.0%
Total		Count	43	21	21	15	100
		% of Total	***43.0%***	***21.0%***	***21.0%***	***15.0%***	***100.0%***

Table 4:8Cross tabulation of the Sickle cell participants' Spleen texture Classified according gender

P-value=0.032			***Sex***		***Total***
			Male	***Female***	
spleen texture	Normal	Count	55	38	93
		% of Total	***55.0%***	***38.0%***	***93.0%***
	Heterogeneous	Count	7	0	7
		% of Total	7.0%	.0%	7.0%
Total		Count	62	38	100
		% of Total	***62.0%***	***38.0%***	***100.0%***

Table 4:9Cross tabulation of the Sickle cell participants' Spleen texture Classified according age

P-value=0.339			***Age***				***Total***
			2-5 years	***6-10 years***	***11-15 years***	***16-23 years***	
spleen texture	Normal	Count	42	18	19	14	93
		% of Total	42.0%	18.0%	19.0%	14.0%	93.0%
	heterogeneous	Count	1	3	2	1	7
		% of Total	1.0%	3.0%	2.0%	1.0%	7.0%
Total		Count	43	21	21	15	100
		% of Total	***43.0%***	***21.0%***	***21.0%***	***15.0%***	***100.0 %***

Table 4:10 the Sickle cell participants' Spleen size compared to their reference values

Spleen size	***N***	***Mean***	***Std. Deviation***	***Minimum***	***Maximum***	***P-value***
Normal	39	8.84	1.05	7.10	11.30	0.000
Splenomegaly	22	13.12	1.38	11.10	16.00	
Autosplenectomy	33	.00	.00	.00	.00	
Shrunken	6	4.26	.33	3.60	4.50	
Total	100	6.59	5.20	.00	16.00	

Table 4:11 the Sickle cell participants' Spleen size compared to their reference values using Post Hoc Tests of the Multiple Comparisons(Dependent Variable: spleen size with the reference)

(I) RV	*(J) RV*	*Mean Difference (I-J)*	*Std.Error*	*Sig.*	*95%Confid Interval*	
Normal	Splenomegaly	-4.28368(*)	.24747	.000	-4.7749	-3.7925
	Autosplenectomy	8.84359(*)	.21952	.000	8.4078	9.2793
	Shrunken	4.57692(*)	.40700	.000	3.7690	5.3848

* The ***mean difference is significant at the .05 level.***

Table 4:12 Descriptive table of the Sickle cell Gall bladder participants' findings

Descriptive					
GB findings	***N***	***Mean***	***Std. Deviation***	***Minimum***	***Maximum***
Stone	18	4.65	5.42	0.00	15.00
Sludge	1	8.60	0.0	8.60	8.60
Total	***19***	***4.86***	***5.34***	***0.00***	***15.00***

Table 4:13 the Sickle cell participants' kidneys size compared to their reference values

Kidneys size	*male*	*female*	*Total%*
Normal	54	33	87
	54%	33%	87%
Large	6	4	10
	6%	4%	10%
small	2	1	3
	2%	1%	3%
	62%	38%	100%

Table 4:14Cross tabulation of the Sickle cell participants' kidney cortico medullary differentiation (C/M)Classified according gender

P-value=0.780			***Sex***		***Total***
			Male	***Female***	
C/M Differentiation	Good	Count	55	33	88
		% of Total	***55.0%***	***33.0%***	***88.0%***
	Poor	Count	7	5	12
		% of Total	7.0%	5.0%	12.0%
Total		Count	62	38	100
		% of Total	***62.0%***	***38.0%***	***100.0%***

Table 4:15Cross tabulation of the Sickle cell participants' kidneys cortico medullary differentiation (C/M) Classified according age

P-value=0.241			***Age***				***Total***
			2-5 years	***6-10 years***	***11-15 years***	***16-23 years***	
C/M Differentiation	Good	Count	41	18	17	12	88
		% of Total	41.0%	18.0%	17.0%	12.0%	88.0%
	Poor	Count	2	3	4	3	12
		% of Total	2.0%	3.0%	4.0%	3.0%	12.0%
Total		Count	43	21	21	15	100
		% of Total	***43.0%***	***21.0%***	***21.0%***	***15.0%***	***100.0%***

Table 4:16Cross tabulation of the Sickle cell participants' tribes Classified according gender

P-value=0.466			***Sex***		***Total***
			Male	***Female***	
TRIBE	Masalit	Count	1	2	3
		% of Total	1.0%	2.0%	3.0%
	Hawsa	Count	4	2	6
		% of Total	4.0%	2.0%	6.0%
	Rezaigat	Count	7	4	11
		% of Total	7.0%	4.0%	11.0%
	Kawahla	Count	3	1	4
		% of Total	3.0%	1.0%	4.0%
	Goraan	Count	2	0	2
		% of Total	2.0%	.0%	2.0%
	Barno	Count	5	4	9
		% of Total	5.0%	4.0%	9.0%
	Messeryia	Count	10	7	17
		% of Total	10.0%	7.0%	17.0%
	Bargo	Count	2	1	3
		% of Total	2.0%	1.0%	3.0%
	Falata	Count	11	1	12
		% of Total	11.0%	1.0%	12.0%
	Rofaa	Count	0	2	2
		% of Total	.0%	2.0%	2.0%
	Banihalba	Count	4	2	6
		% of Total	4.0%	2.0%	6.0%
	Taisha	Count	3	4	7
		% of Total	3.0%	4.0%	7.0%
	Tama	Count	2	3	5
		% of Total	2.0%	3.0%	5.0%
	Ahamda	Count	2	1	3
		% of Total	2.0%	1.0%	3.0%
	Hamar	Count	2	3	5
		% of Total	2.0%	3.0%	5.0%
	Gawamaa	Count	3	0	3
		% of Total	3.0%	.0%	3.0%
	Kenana	Count	1	1	2
		% of Total	1.0%	1.0%	2.0%
Total		***Count***	***62***	***38***	***100***
		% of Total	***62.0%***	***38.0%***	***100.0%***

Table 4:17 Cross tabulation of the Sickle cell participants' tribes Classified according to age

P-value=0.090			*Age*				*Total*
			2-5 years	*6-10 years*	*11-15 years*	*16-23 years*	
TRIBE	Masalit	Count	2	1	0	0	3
		% of Total	2.0%	1.0%	.0%	.0%	3.0%
	Hawsa	Count	0	3	3	0	6
		% of Total	.0%	3.0%	3.0%	.0%	6.0%
	Rezaigat	Count	5	3	1	2	11
		% of Total	5.0%	3.0%	1.0%	2.0%	11.0%
	Kawahla	Count	1	2	0	1	4
		% of Total	1.0%	2.0%	.0%	1.0%	4.0%
	Goraan	Count	1	0	1	0	2
		% of Total	1.0%	.0%	1.0%	.0%	2.0%
	Barno	Count	3	1	3	2	9
		% of Total	3.0%	1.0%	3.0%	2.0%	9.0%
	Messeryia	Count	3	3	8	3	17
		% of Total	3.0%	3.0%	8.0%	3.0%	17.0%
	Bargo	Count	1	1	0	1	3
		% of Total	1.0%	1.0%	.0%	1.0%	3.0%
	Falata	Count	8	3	0	1	12
		% of Total	8.0%	3.0%	.0%	1.0%	12.0%
	Rofaa	Count	0	0	1	1	2
		% of Total	.0%	.0%	1.0%	1.0%	2.0%
	Banihalba	Count	1	2	1	2	6
		% of Total	1.0%	2.0%	1.0%	2.0%	6.0%
	Taisha	Count	5	2	0	0	7
		% of Total	5.0%	2.0%	.0%	.0%	7.0%
	Tama	Count	1	0	2	2	5
		% of Total	1.0%	.0%	2.0%	2.0%	5.0%
	Ahamda	Count	3	0	0	0	3
		% of Total	3.0%	.0%	.0%	.0%	3.0%
	Hamar	Count	5	0	0	0	5
		% of Total	5.0%	.0%	.0%	.0%	5.0%
	Gawamaa	Count	2	0	1	0	3
		% of Total	2.0%	.0%	1.0%	.0%	3.0%
	Kenana	Count	2	0	0	0	2
		% of Total	2.0%	.0%	.0%	.0%	2.0%
Total		***Count***	***43***	***21***	***21***	***15***	***100***
		% of Total	***43.0%***	***21.0%***	***21.0%***	***15.0%***	***100.0%***

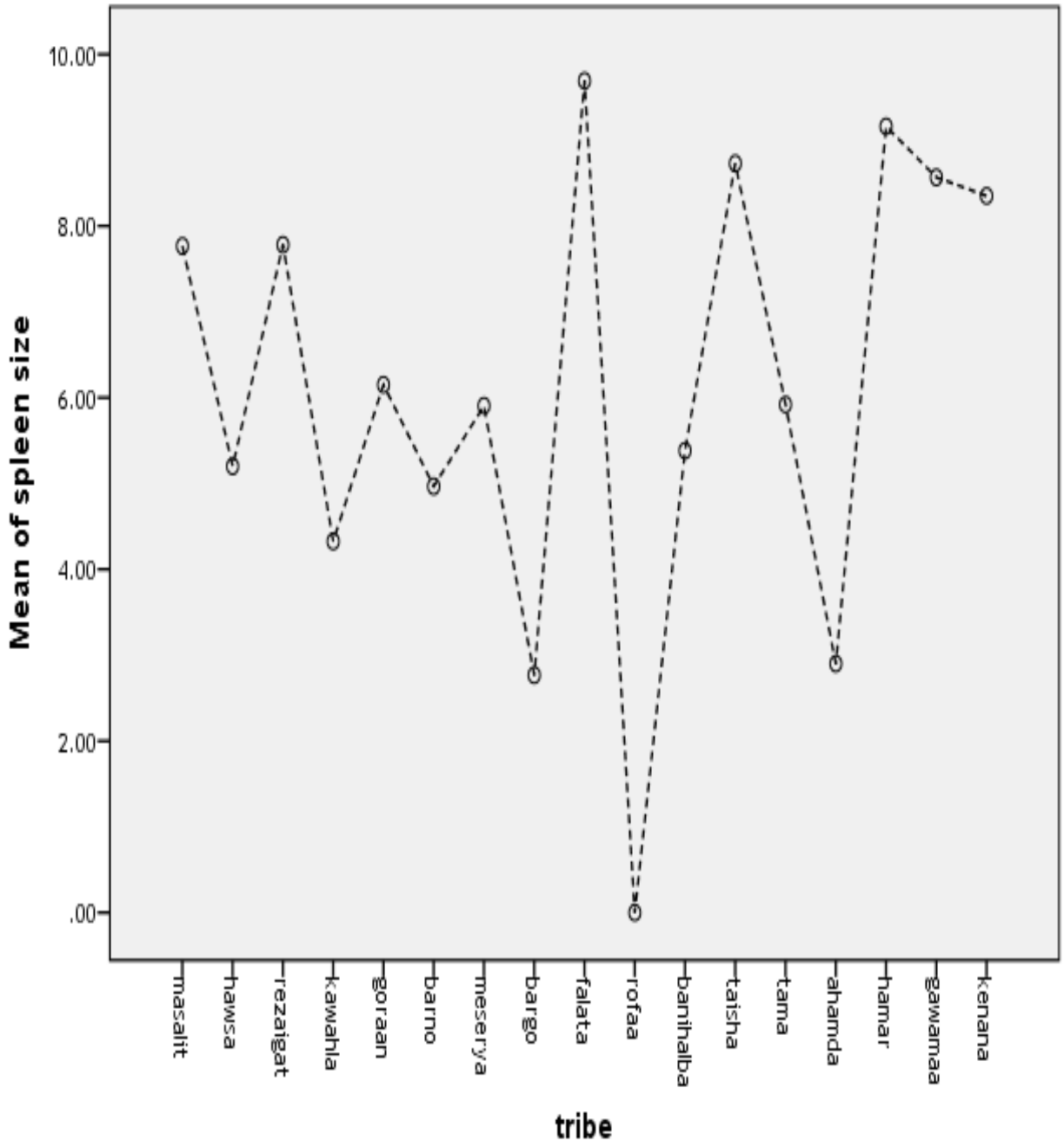


Figure 4:1 Showed the distribution of the Sickle cell participants' spleen size Classified according tribes

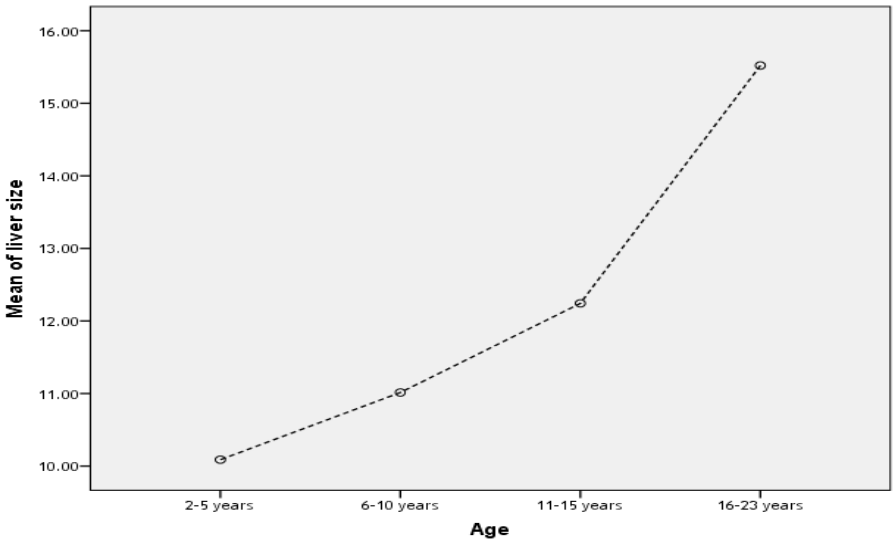


Figure 4:2 Mean Plot of the Sickle cell participants' liver size distributed according to age

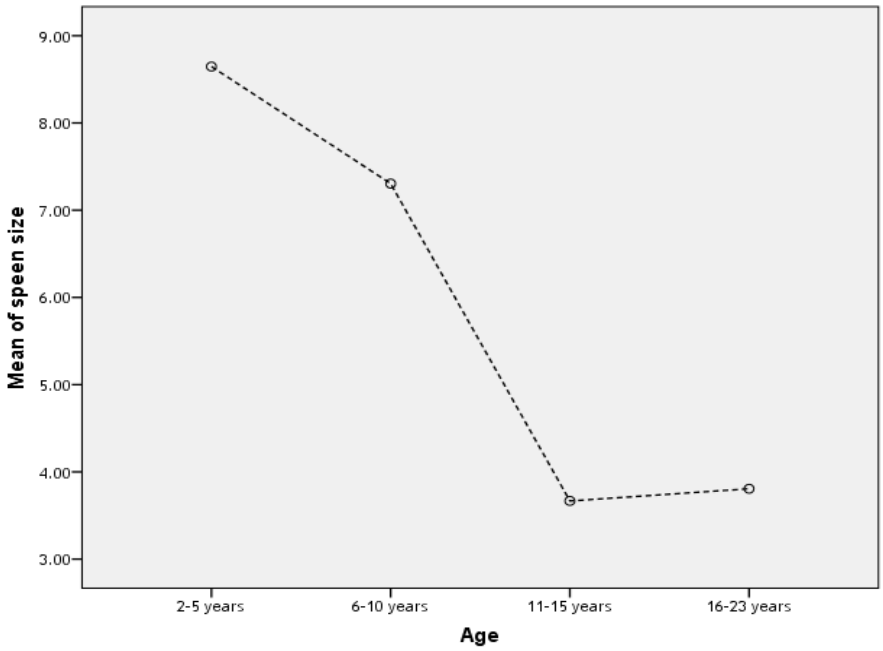


Figure 4:3 Mean Plot of the Sickle cell participants' Spleen size distributed according to age

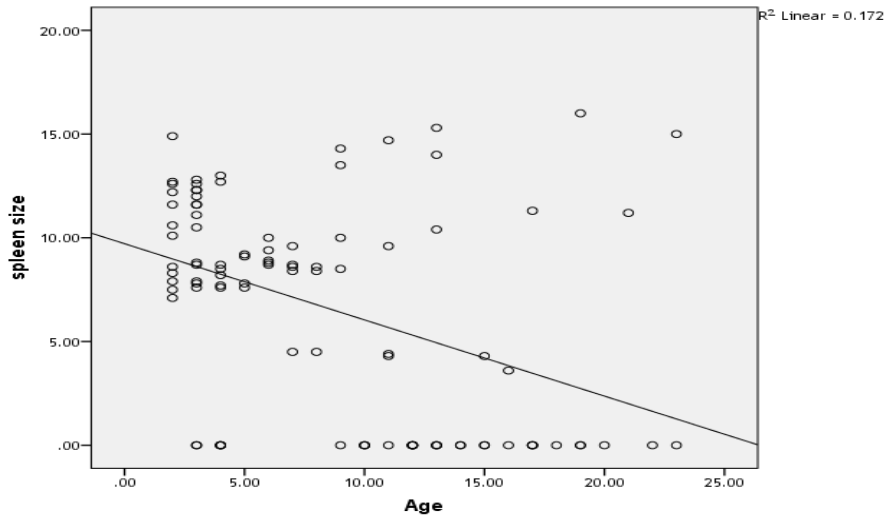


Figure 4.4 Linear relationship of the Sickle cell participants' Spleen size and age, as the age increased significantly at p= (0.000)the spleen size decreased by0.47 cm starting from 10cm

Table 4:18 Coefficient of the Sickle cell spleen size for the known participants' age (Predictive Equation)

Coefficients						
Model		***Unstandardized Coefficients***		***Standardized Coefficients***	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	11.591	.871		13.310	.000
	spleen size	-.469	.104	-.415	-4.515	.000
a. Dependent Variable: Age						

The New predictive Equation =Spleen size =11.59x-0.47x participant age

Chapter five
Discussion, Conclusion and Recommendations

Chapter five

Discussion, conclusion and recommendations

5. 1 Discussion

This study was conducted to detect the changes in abdominal organs (liver, gallbladder, spleen and kidneys) in patients with sickle cell disease in Sudan using ultrasonography.

100 SCA patients were participate in this study, participants in this study with age range of 2–23 years with mean age of 8.5, most of participants ranged in 2-5 years, there were (62) male (62%) and 38 female (38%) this explain the high incidence of SCA among male, no significant justification for this result reported, most of patient descended from messeryia tribe in western Sudan 17% table 17 this results agree with (Majdi & Hanan 2014).

The mean age (8.5 years) of patients with SCA and means measurements of liver size, spleen size, gallbladder wall thickness, right kidney length and left kidney length (11.55 cm, 16.59, 2.9 mm, 8.74 cm and 8.88 cm) respectively as shown Table (4.1).

The study correlated measurements of organs with age and gender of participants, found that there was significant relationship between measurements and age p.v=0.00. all measurements had not significant relations with gender except the spleen size 0.047<p.v, this may be due to in nature, the organ size proportion with body mass index (BMI), as we know BMI is greater in males than females (although BMI not taken in this study) (Tables 4.2&4.3).

This study evaluated the liver as (texture, echogenicity and size) as shown in tables (4.4, 4.5, 4.6, 4.7 and figure 4.2), and showed 96 homogenous and 4 heterogeneous with equally distribution in gender. Liver texture had significant relation with age of patients < pv. Increased echogenicity of the liver was found in 7 (7%) of SCA patients all of them are males. Increased liver echogenicity findings are less than findings from previous studies (Geofery 2015), (Diagn 2008) and (Mohanty 2004). These differences may be due to the socioeconomic status of the patient, lifestyle, and diet as these may also affect the echogenicity of the liver.

The liver size compared to reference value (BHAVNA et al 2010) shown in appendix (II.A), the study found that liver size increased with age of patients as shown in figure (4.2). Hepatomegaly was detected in 28% in this study; previous study (Balci 2008) had reported similar findings.

The study evaluated the spleen texture and size correlated with age and gender, and found 93 were homogenous and 7 were heterogeneous all of them were males, heterogeneity of spleen in males in SCA patients is unknown. (tables 4.8, 4.9, 4.10 and figure 4.3).

The spleen size compared to reference value (BHAVNA et al 2010) shown in appendix (II.A), the study found 39 (39%) SCA patients with normal spleen. It should be noted that sonographic normal findings on the spleen among the sickle cell patients do not rule out the presence of other complications, and other complications may not be sonographically visible at the time of scan, and the technique is also operator dependent.

Splenomegaly in this study was found in 22 (22%) of the patients with SCA. Several studies have reported splenomegaly as a common abdominal manifestation among SCA patients. This is due to sequestration syndrome which means rapid

pooling of blood within the spleen; the blood pooling may be larger than expected for a child or adult with sickle cell anemia, resulting in intravascular volume which leads to splenomegaly.

Autosplenectomy in this study was found in 33 (33%) of the SCA patients. Previous studies (diagn 2008) have reported similar findings. These findings could be due to the tortuous vasculature of the spleen and repeated multiple splenic infarctions.

Ultrasound had accuracy to detect spleen size changes (normal, splenomegaly, shrunken spleen and autosplenectomy). There was linear relationship of the Sickle cell participants' Spleen size and age, as the age increased significantly at p= (0.000) the spleen size decreased by0.47 cm starting from 10cm, as shown in(table 4.11).

Gall bladder in addition to wall thickness the study found intraluminal contents like stone and sludge table 4.12, gallstones were found in 18 (18%) of SCA patients in this study. Previous study (Geofery 2015) had similar finding, the study reported a progressive age-related increase in the prevalence of gallstones.

Gallbladder sludge was found in 1 (1%) sickle cell anemia patients in this study. findings were less than those reported by previous researchers (Geofery 2015) and (Balci 2008), this may be due to small sample size.

The kidneys size compared to reference value (Utah pediatric radiology 2010) shown in appendix (II.B), the study found 87 (87%) SCA patients with normal kidneys, this result are more than previous studies (Balci 2008). It should be noted that sonographic normal findings of the kidneys among the SCA patients do not rule out the presence of other complications like intravascular sickling which may not be sonographically visible and it is also highly operator dependent.

Enlarged kidneys were found in 10 (10%) SCA patients, this result are less than previous studies, (Diagn 2008) (Balci 2008). The etiology of renal enlargement in sickle cell patients is unknown. However, enlargement of sickle cell kidneys has been attributed to vascular dilatation, engorgement of vessels interstitial edema.

Decreased kidneys size in this were found in study about 3 (3%) SCA patients, this result are less than previous studies; this could be due to sickle cell nephropathy, (chronic condition) that may progress to end-stage renal disease as part of renal complications in SCA.

The study found there were 88% had good C/M differentiation and 12% poor C/M differentiation this are feature of renal diseases (Tables 4.13&4.14).

From this study the spleen size will be predicted for SCA patients with known age by new predictive equation.

Spleen size =11.59x-0.47x participant age

5.2. Conclusion

After the scoring of the thesis objectives, the most important points to be implied in the conclusion would be as following:

The incidence of SCA among the selected sample was greater in male than female and the most of patients were children.

Most affected tribe was messeryia tribe in western Sudan.

Assessment of abdominal organs such as the liver, gallbladder, spleen, and kidneys by ultrasound among SCA patients in this study has revealed varied remarkable changes in these organ sizes, echotexture, intraluminal deposits and wall thickness among the studied patients.

Although small sample size were included in this study, the results were helpful in establishing abnormalities that may occur in abdominal organs of SCA patients. Abdominal sonography is an easy, affordable, readily available, accurate, and non-invasive diagnostic modality for early detection of organ changes for further management and follow-up of SCA patients.

5.3. Recommendations

The main recommended points after successful finishing of the thesis study could summarize in the following: -

1. Early investigations for children in affected tribes must be encouraged.
2. Encouraging the population for marriage from non relative one
3. Community education and awareness about the morbidities of the SCD.
4. Further studies with large sample size well are including Doppler studies resistive index (RI) and laboratory investigation are recommended to confirm the result of this study.

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Appendices

Appendix 1 Data collection sheet

Sudan University of Science and Technology

College of Graduate Studies

Evaluation of Abdominal Organs in Patients with Sickle Cell Anemia using Ultrasonography

Personal information

Patient code..... patient age ……..years/months

Gender Male ☐ Female ☐

Tribe.....

Ultrasound Findings

1-Spleen:-

Length..... cm

Echo texture:-

Homogenous ☐ heterogeneous ☐ autosplenectomy ☐

2- Liver:-

Liver span..... cm

Echo texture:-

Homogenous ☐ Heterogeneous ☐ others ……..

3- Gall bladder:-

Stone ☐ Sludge Wall thickness …….. mm

4- Kidneys size:-

RT kidney Length .....cm Lt Kidney Length .....cm

C/M differentiation:-

Good ☐ Poor ☐

Others……

Appendix II – A

TABLE II LIVER AND SPLEEN LENGTH BY ULTRASONOGRAPHY IN HEALTHY CHILDREN (*N*=597)[#]

Age and Sex	No.	Liver length (cm)			Spleen length (cm)		
		Mean (SD)	3rd centile	97th centile	Mean (SD)	3rd centile	97th centile
1-<3 mo							
M	10	6.5 (1.23)	4.8	8.9	4.9 (1.44)	3.7	8.7
F	11	6.2 (0.66)	4.9	7.2	4.5 (0.53)	3.2	5.2
3-<6mo							
M	26	7.1 (0.77)	5.9	8.9	5.4 (0.61)	4.4	6.6
F	09	7.2 (0.94)	5.3	8.0	5.5 (0.51)	4.7	6.5
6-<12 mo							
M	28	7.5 (0.88)	6.1	9.5	6.0 (0.86)	4.4	8.3
F	23	7.9 (0.92)	6.3	9.6	5.6 (0.61)	4.7	7.2
1-<2y							
M	44	8.6 (0.85)	7.1	10.2	6.4 (1.01)	4.7	9.8
F	33	8.5 (1.51)	6.3	11.1	6.1 (0.74)	4.5	7.6
2-<4y							
M	79	9.0 (1.34)	7.2	11.9	6.9 (1.01)	4.1	9.3
F	53	8.9 (0.97)	6.9	11.3	6.7(0.74)	5.3	8.3
4-<6y							
M	62	10.3 (1.27)	7.3	14.7	7.4 (0.99)	5.0	10.9
F	53	9.8 (1.24)	6.5	13.3	7.1 (0.90)	5.2	9.3
6-<8y							
M	31	10.8 (0.94)	09	12.3	7.9 (0.94)	6.3	9.7
F	20	10.9 (1.29)	8.2	13.3	7.6 (0.99)	5.5	9.5
8-<10y							
M	35	11.9 (1.08)	10	14.1	8.2 (1.02)	6.8	10.9
F	27	11.7 (1.11)	9.4	14.0	8.2 (1.02)	6.5	9.8
10-<12y							
M	32	12.6 (1.20)	11	15.5	8.7 (1.84)	6.3	11.7
F	21	12.3 (1.39)	9.7	15.2	8.7 (1.20)	6.7	11.3

[#] *M-MALES, F-FEMALE, No difference between sexes either in the spleen size (P=0.11) or the liver size (P=0.57).*

Appendix II – B

SONOGRAPHY OF KIDNEYS IN CHILDEN

0 mo	= 3-9 cm – 6.0 cm
1 mo	= 4.0 cm – 6.1 cm
2 mo	= 4.2 cm – 6.3 cm
3 mo	= 4.4 cm – 6.4 cm
4 mo	= 4.5 cm – 6.6 cm
5 mo	= 4.7 cm – 6.7 cm
6 mo	= 4.8 cm – 6.9 cm
7 mo	= 4.9 cm – 7.1 cm
8 mo	= 5.1 cm – 7.3 cm
9 mo	= 5.2 cm – 7.4 cm
10 mo	= 5.4 cm – 7.5 cm
11 mo	= 5.5 cm – 7.7 cm
1 yr	= 5.6 cm – 8.0 cm
2 yr	= 5.7 cm – 8.4 cm
3 yr	= 5.8 cm – 8.6 cm
4 yr	= 6.1 cm – 8.9 cm
5 yr	= 6.4 cm – 9.1 cm
6 yr	= 6.6 cm – 9.4 cm
7 yr	= 6.9 cm – 9.7 cm
8 yr	= 7.2 cm – 9.9 cm
9 yr	= 7.5 cm – 10.2 cm
10 yr	= 7.7 cm – 10.4 cm
11 yr	= 7.9 cm – 10.7 cm
12 yr	= 8.4 cm – 11.3 cm
13 yr	= 8.6 cm – 11.6 cm
14 yr	= 8.8 cm – 11.9 cm
15 yr	= 9.0 cm – 12.1 cm

Appendix III Ultrasound images

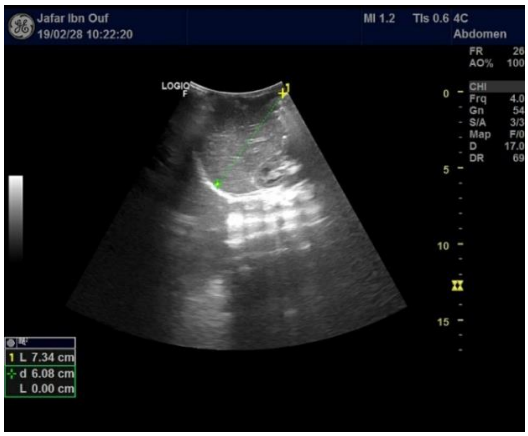

Image1:- 6 years old female shows normal liver size (7.34 cm) and echotexture

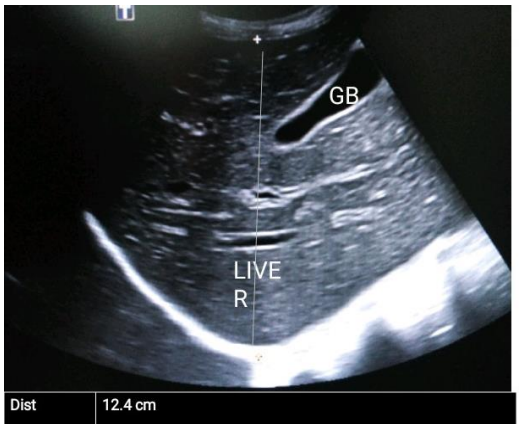

Image2:- Normal liver size (12.4 cm) and texture in 13 years old male patient with SCA

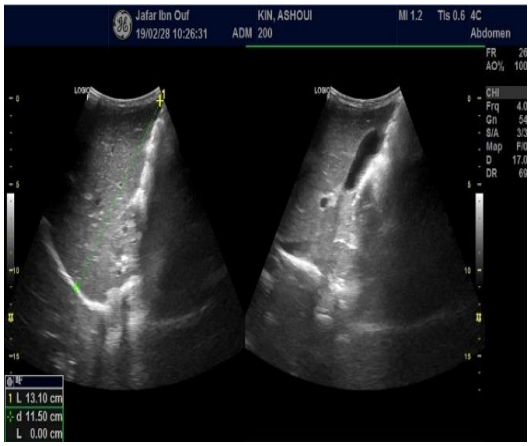

Image 3:-Hepatomegaly (13.10) in 3 years old patient SCA

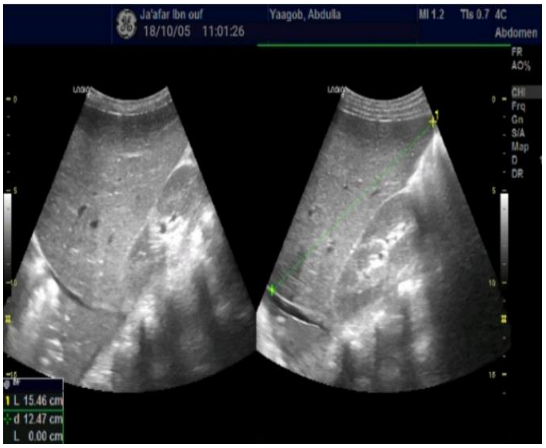

Image4:-Sonograph for 16 years old male patient with SCA shows hepatomegaly (15.46) with bright liver.

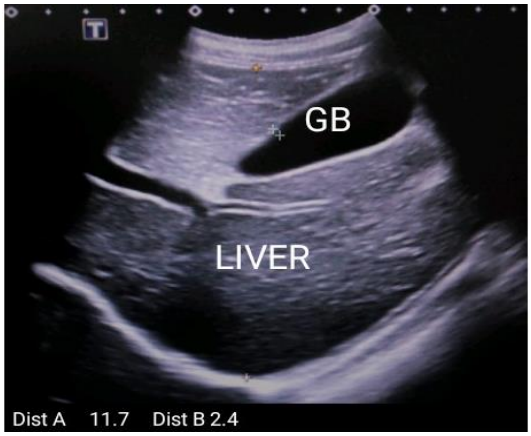

Image5 :-Normal gall bladder wall thickness (2.4 mm) in 9 years old male patient with SCA

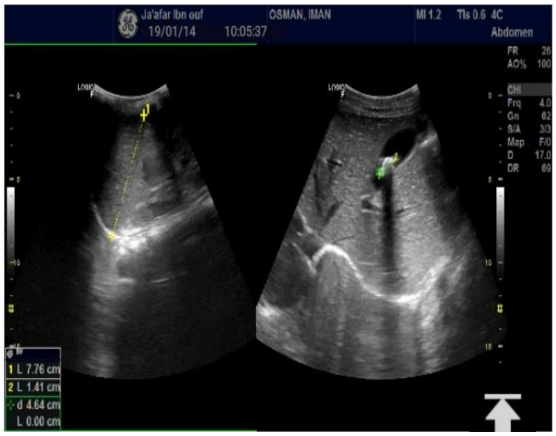

Image6:-Ultrasound image for 7 years old female shows normal liver size (7.76cm) and solitary gall stone measured (1.41 cm) with normal gall bladder wall thickness

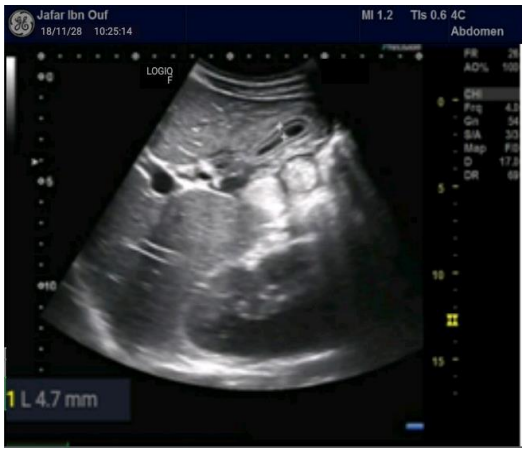

Image7:-Ultrasound image for 12 years old patient with SCA shows thick layered bladder wall (4.7 mm)

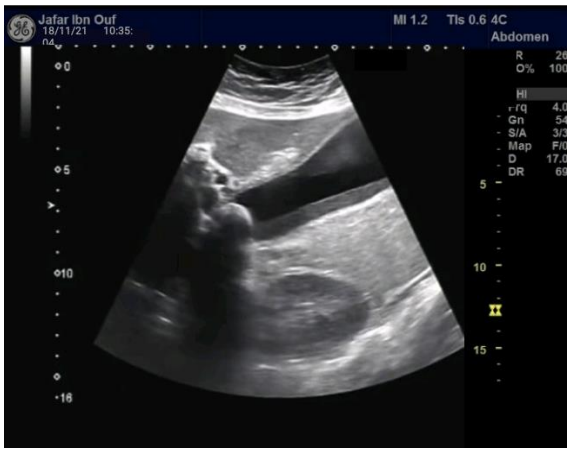

Image8:-Sludge and gall bladder neck stone in 15 years old male patient with SCA

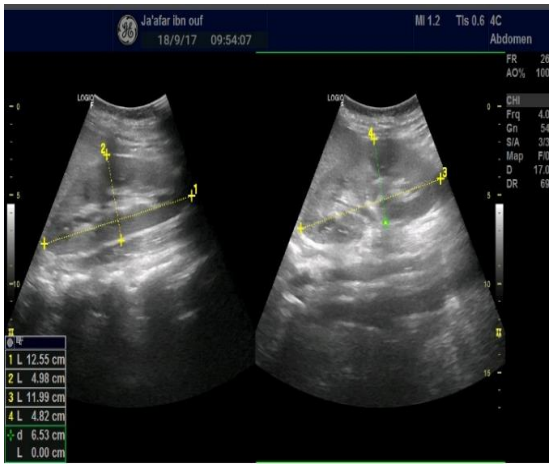

Image9:-13 years old male patient with sickle cell disease shows normal size and echogenicity of both kidneys.

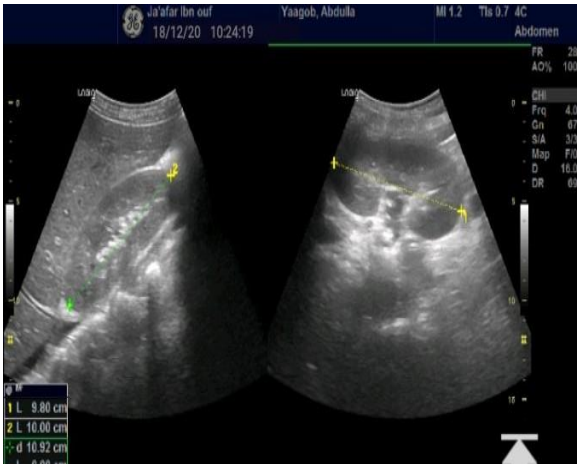

Image10:-Normal size and echogenicity of both kidneys in 11 years old male patient with sickle cell disease

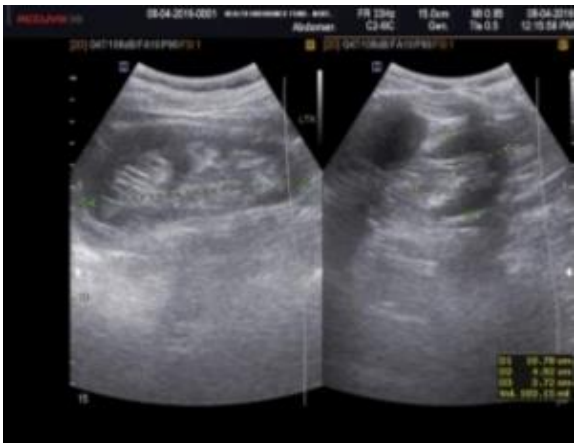

Image11:-8 years old male patient with SCA show enlarged left kidney with increased echogenicity

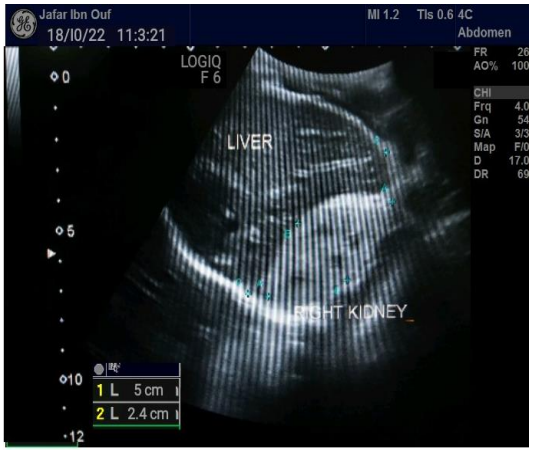

Image12:-Ultrasound image for patient with SCA 10 years old male shows small right kidney with increased echogenicity

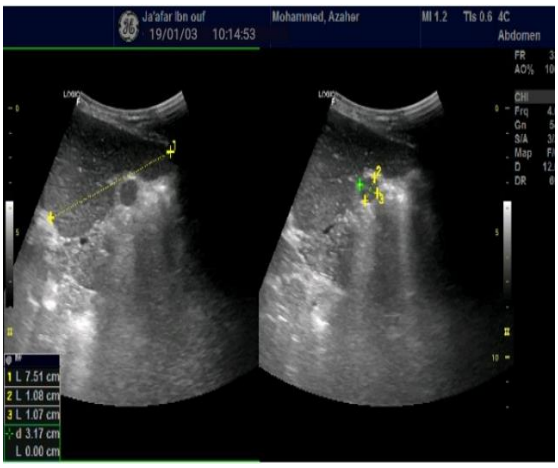

Image13:-Normal size (7.51 cm) and echogenicity of the spleen with splenule in 11 years old male patient with sickle cell disease

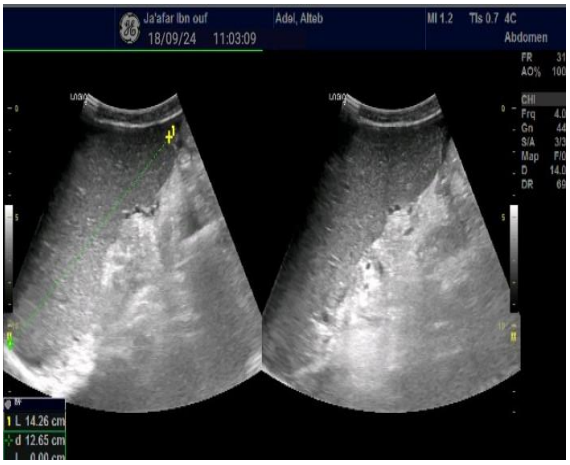

Image14:-16 years old male patient with SCA show enlarged spleen (14.26 cm) with normal echotexture

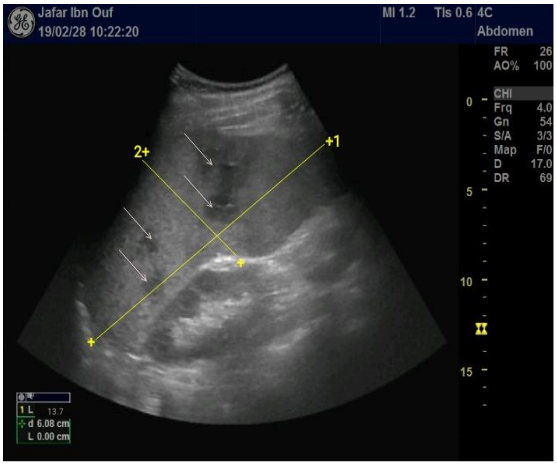

Image 15:-12 years old female patient with SCA shows splenomegaly (13.7X6.08 cm) with multiple splenic infarctions

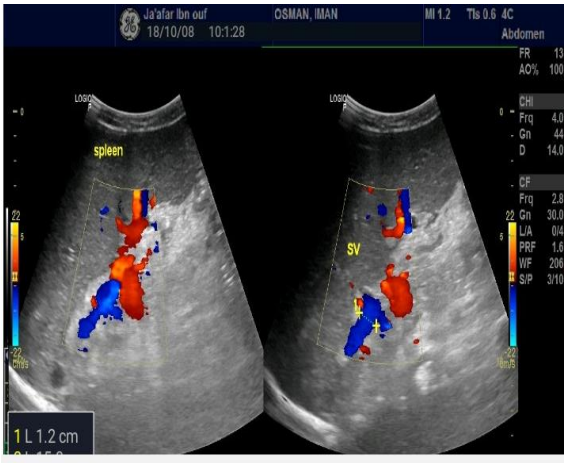

Image 16:-14 years old male with SCA shows enlarged spleen (15.3 cm) with mild dilated splenic vein