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Computerized Tomography Findings in Abdomen and Chest of Patients with Sickle Cell Disease

نتائج التصوير المقطعي المحوسبه للبطن والصدر لدي مرضي الأنيميا المنجليه

Thesis submitted in fulfillment of the requirements for the PhD degree in Diagnostic Radiologic Technology

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Abstract

The study aimed to characterize the spleen in patients with SCD using computerized tomography scan in all enhancement phases. The spleen locations, shape, size, CT number and vascular findings were also been evaluated. As well full depiction of the associated lesions characteristics were studied at all types of SCD including hemoglobin SS, hemoglobin SC, hemoglobin SB+ (Beta) thalassemia and Beta-Zero thalassemia. And the complications occur in abdominal organs and chest were correlated according to patient's age and SCD types.

A total of 67 Saudi SCD patients were evaluated with CT in Ballasmar general hospital and King Fahad central hospital during the period spanned from 2014-2017.

The Study characterized the spleen in SCD patients ,it was found to be extended until the lower third of the left kidney when it is enlarged by percentage of 38%, and it can be oval, irregular, blurred out line with loss of its normal medial concavity. The features of spleen size was variants to be enlarged or shrunken present in 31 and 24 cases respectively. This changes in spleen size was significantly correlated with the reduction of HU CT number of the spleen at $p \leq 0.004$.

Study also found that there was a significant relation between the spleenic vein dilatation and splenomegaly and those of enlarged lymph nodes at $p \leq 0.00$ and $p \leq 0.00$.

CT scan contrast enhancement showed well characteristics of spleen lesions occurred as complications from SCD (cysts, abscess and infarctions) and well differentiation between them depending on the timing of intravenous bolus administration of contrast material. Spleen abscess in all of the enhancement phase in patients affected with sickle cell disease is well defined in both venus and delay phase in 15 and 19 cases respectively, and 58.3% are peripherally

enhanced with hypodensity in the center of lesion, where most of the abscess are ill defined in the arterial phase. Cysts are well enhanced in the arterial phase which occurred in 7 patients, and most of them characterized by full regular circle enhancement by percentage of 62.5%, while spleen infarction showed well defined wedge-shaped based area of hypo attenuation which was mostly peripheral without pressure effect on adjacent structures in the delay phase which present in 66.6% of cases. On non-enhanced CT and arterial enhancement, infarcts are poorly visualized.

The study also showed a significant relation between the character of the lesions and degree of enhancement with the scanning technique used (pre contrast, venous and delay phase) in different SCD types at $p \leq 0.05$.

The common SCD type was found to be hemoglobin SS where there are significant relation between the type of the SCD and the character of the lesion in the venous and delay phase at $p \leq 0.037$ and 0.055 in respectively.

Study found that the hepatic complications were, hepatic focal necrosis, hepatomegaly, hepatic abscess, cyst and infarctions occurred in 8,19,12,10 and 10 patients respectively, while pancreatic and biliary complications were acute pancreatitis and cholelithiasis present in 5 and 22 patients respectively. The renal changes include renal papillary necrosis, renal abscess, stones with hydronephrosis, renal vein thrombosis, renal failure and renal infarction found in 15,7,11,4,7 and 11 patients respectively, as well the lung complications was pleural effusion, pneumonia, atelectasis, ground glass nodules, consolidation, fibrosis and lung abscess occurred in 16,6,4,5,8,10 and 7 patients respectively. Study considering patients age and SCD types in all those previous abdominal organs and chest complications.

The study concluded that, the findings of SCD complications can identified by using MDCT at different CT scan phases.

الخلاصة

هدفت الدراسة إلى توصيف الطحال لدى المرضى الذين يعانون من مرض الأنيميا المنجليه باستخدام المسح المقطعي المحوسب في جميع أطوار سريان وسيط التباين .كما تم تقييم موقع الطحال وشكله وحجمه، و وحدة التركيب (الهاونسفيلد) فيه، والمتغيرات الموجودة في أوعيته الدموية, كما تم عمل وصف كامل لجميع الآفات التي تصيب الطحال في جميع أنواع الأنيميا المنجليه التي تتضمن فقر الدم المنجلي متوافق الأمشاج، فقر الدم المنجلي متخالف الأمشاج ،بيتا الثلاسيميا الموجبة وبيتا صفر ثلاسيميا . بالإضافة لدراسة المضاعفات تحدث في أعضاء البطن والصدر ,وعلاقتها بعمر المريض وأنواع الأنيميا المنجليه.

تم تقييم ما مجموعه 67 مريضا من مرضى الأنيميا المنجليه في مستشفى بللسمر العام ومستشفى الملك فهد المركزي خلال الفترة الممتدة من 2014-2017.

وصفت الدراسة الطحال في مرضى الأنيميا المنجليه ، ووجدت الدراسة أن الطحال قد يمتد حتى الثلث السفلي من الكلى اليسرى عندما يتضخم وحدث ذلك بنسبة 38%، ويمكن أن يكون بيضاوي، غير منتظم, عدم وضوح حوافه مع فقدان تقعره الجانبي الطبيعي .وكانت ملامح حجم الطحال متغيره ما بين التضخم والانكماش وجدت في 31 و24 حاله علي التوالي. وقد ارتبطت هذه التغييرات في حجم الطحال بشكل كبير مع النقصان في وحدة التركيب (الهاوندسفيلد) الخاصة بالطحال بقيمه احتماليه اقل من أو تساوي 0.04. ووجدت الدراسة أيضا أن هناك علاقة كبيرة بين توسع الوريد الطحالى وتضخم الطحال وتضخم الغدد الليمفاوية فيه بقيمه احتماليه بلغت اقل من أو تساوي 0.00 و 0.00.

أظهر الفحص المقطعي باستخدام وسيط التباين خصائص جيدة لآفات الطحال التي تحدث كمضاعفات لمرض الأنيميا المنجليه (التكيسات، الخراجات،والاحتشاءات) والتفريق بينهما يعتمد على توقيت بدء سريان وسيط التباين في الوريد.

كانت خراجات الطحال في كل أطوار سريان وسيط التباين للمرضى الذين يعانون من مرض الأنيميا المنجلية أكثر وضوحا في الطور الوريدي والطور المتأخر في 15 و 19 حاله علي التوالي، و 58% منهم أظهر توهين للوسيط في محيط الآفة مع نقص التوهين في مركز الآفة، وكان اغلبهم ضعيف الوضوح في الطور الشرياني لوسيط التباين. فيما أظهرت التكيسات توهينا جيدا للوسيط في الطور الشرياني في عدد 7 مرضي وكان ظهورها بشكل دائري ملئ بالوسيط قد حدث بنسبه بلغت 62.5%, في حين أظهر إحتشاء الطحال وضوحا جيدا (في شكل وتدي ضعيف الامتصاص في أطراف العضو دون تأثير علي الأجزاء المجاورة) في الطور المتأخر

لوسيط التباين حيث وجد ذلك بنسبة 66.6%. فيما كان احتشاء الطحال ضعيف الظهور في طور ما قبل إعطاء وسيط التباين وفي الطور الشرياني له.

وأظهرت الدراسة أيضا وجود علاقة كبيره بين طبيعة الآفات وأطوار سريان وسيط التباين الثلاث(الشريانية, الوريدية و المتأخرة) في الأنواع المختلفة لمرض الأنيميا المنجليه حيث كانت القيمة الاحتمالية اقل من أو تساوي 0.05

وكان أكثر أنواع الأنيميا المنجليه ترددا هو فقر الدم المنجلي متوافق الأمشاج, وكانت هناك علاقة كبيرة بين أنواع الأنيميا المنجليه وطبيعة الآفة في المرحلة الوريدية والوريدية المتأخرة لوسيط التباين عند القيمة الاحتمالية اقل من أو تساوي 0.037 و 0.055 علي التوالي.

ووجدت الدراسة أن المضاعفات الكبدية تمثلت في النخر البؤري الكبدي، تضخم الكبد، الخراج الكبدي، التكيسات والاحتشاءات حيث حدث ذلك في 8, 19, 12, 10 و 10 مرضي علي التوالي. في حين تمثلت مضاعفات البنكرياس و الحويصلة الصفراويه في التهاب البنكرياس الحاد و حصى المرارة في 5 و 22 مريض علي التوالي. واشتملت التغيرات الكلوية علي نخر الحليمات الكلوية، الخراج الكلوي، حصى الكلي مع موه الكلية، تخثر الوريد الكلوي، الفشل الكلوي والاحتشاء الكلوي حيث وجد ذلك في 15, 7, 11, 4, 7 و 11 مريض علي التوالي. وتمثلت مضاعفات الرئة في الانصباب الجنبي، والالتهاب الرئوي، الانخماص، العقيدات الزجاجية الباهتة, التصلد، والتليف وخراج الرئة وحدث ذلك في 16, 6, 4, 5, 8, 10 و 7 مرضي علي التوالي.

وخلصت الدراسة إلي أن مضاعفات مرض الأنيميا المنجليه يمكن الكشف عنها باستخدام الأشعة المقطعية متعددة الكواشف في مختلف أطوار سريان وسيط التباين.

Dedication

To whom he strives to provide comfort and welfare and never stints what he owns to push me in the success way, who taught me to promote life stairs wisely and patiently, to the soul of my dearest father, God bless his soul and forgive him.

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Firstly, I would like to express my sincere gratitude to my advisor Prof. Caroline Edward for the continuous support of my Ph.D study, for her patience, motivation, and immense knowledge. Her guidance helped me in all the time of research and writing of this thesis. I could not have imagined having a better advisor and mentor for my Ph.D study.

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Last but not the least, I would like to express appreciation to my beloved husband who spent sleepless nights and was always a constant source of strength and inspiration.

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List of Abbreviations

ACS	Acute Chest Syndrome
ALARA	As Low As Reasonably Achievable
ASSC	Acute Splenic Sequestration Crisis
CECT	Contrast Enhanced Computerized Tomography
CM	Contrast media
CT	Computerized Tomography
DNA	Deoxyribonucleic Acid,
GIT	Gastrointestinal Tract
Hb	Hemoglobin
HRCT	High Resolution Computerized Tomography
HU	Hounsfield Unit
IMA	Inferior Mesenteric Artery
ILD	Interstitial Lung Disease
IVC	Intravenous Contrast
Kvp	Kilovoltage Peak
mAs	Milli Amperage-seconds
MDCT	Multi-Detector Computed Tomography
MHP	Mid Hepatic Point
MRI	Magnetic Resonance Imaging
MSI	Massive Splenic Infarction
PALS	Periarteriolar Lymphoid Sheaths
PEG	Polyethylene Glycol
SCD or SCA	Sickle Cell Disease or Anemia
SCT	Sickle Cell Trait
SMA	Superior Mesenteric Artery
US	Ultrasonography
WL	Window Level
WW	Window Width

Chapter One

Introduction

1.1 Introduction

Sickle cell disease is a condition was first described in the medical literature by the American physician James B. Herrick in 1910 (Goldberg and Savitt,1989).It is an inherited form of anemia — a condition in which there aren't enough healthy red blood cells to carry adequate oxygen throughout the body(Vichinsky, 2016).

Normally, red blood cells are flexible and round, moving easily through the blood vessels. In sickle cell disease, the red blood cells become rigid and sticky and are shaped like sickles or crescent moons. These irregularly shaped cells can get stuck in small blood vessels, which can slow or block blood flow and oxygen to different body parts(Vichinsky, 2016).

It caused by a mutation in the gene that tells body to make hemoglobin — the red, iron-rich compound that gives blood its red color(Field, 2009). Hemoglobin allows red blood cells to carry oxygen from the lungs to all parts of the body. In sickle cell disease, the abnormal hemoglobin causes red blood cells to become rigid, sticky and misshapen (Field, 2009).

The sickle cell gene is passed from generation to generation in a pattern of inheritance called autosomal recessive inheritance. This means that both the mother and the father must pass on the defective form of the gene for a child to be affected(Field, 2009).

Sickle cell disease is one of the common hemoglobinopathies in the world, specially affects Africans and Middle east(Beldjord et al, 1984). In 2013, it resulted in 176,000 deaths, up from 113,000 deaths in 1990(Siva, 2013). In Saudi Arabia, SCD considered one of the major public health problems specially in

Eastern and Southern province(El-Hazmi, 1992) because it affects 35% of the population and mostly are children and young people, which results in a shortage of working forces in the country and great impact on the economy and different fields of production in the country.

Sickle cell disease can affect any and all major organs system in the body and can lead to many complications(Boateng et al, 2009). The spleen, liver, heart, lungs, kidneys, gallbladder, pancreas, colon, eyes, bones, and joints can suffer damage from the abnormal function of the sickle cells and their inability to flow through the small blood vessels correctly(Boateng et al, 2009).

Sickle cell disease is a life-long illness. The severity of the disease varies widely from person to person. In high-income countries like the United States, the life expectancy of a person with SCD is now about 40–60 years. In 1973, the average lifespan of a person with SCD in the United States was only 14 years. Advances in the diagnosis and care of SCD have made this improvement possible (Gary and Gibbons, 2016). Good treatment, can prevent complications.

Computed tomography (special X-ray tests that produce cross-sectional images of the body using X-rays and a computer (Herman and Gabor, 2009)) represents the most widely applied cross-sectional abdominal imaging technique and is considered the imaging modality of choice for the evaluation and diagnosis of sickle cell disease complications(Ekeh et al, 2008).

The spleen is one of the most common and early organs to be affected in SCD(Al-Salem, 2006). It is commonly enlarged during the first decade of life but then undergoes progressive atrophy and infarcted leading to autosplenectomy (Al-Salem, 2006). Study gives firstly deep description to the spleen complications and how they are appeared and influenced by this disease. It also tries to cover most of the radiological manifestations, in different systems affected by the disease, as organ-based approach in Saudi Arabian patients and some

complications that can occur in some abdominal organs and chest and how they are influenced by the disease including liver, kidneys, gallbladder, pancreas and lungs.

Study show the role of computed tomography scanning to diagnose and discover the complications that can occur from sickle cell disease for all previously mentioned organs.

1.2 Study problem

In Saudi Arabia, sickle cell disease considered one of the major public health problems specially in Eastern and Southern province, because it affects 35% of the population and mostly are children and young people, if patients are starting good treatment, they can prevent complications, and reduce the mortality rate among young people and thus increase the productive force.

No recent studies was done through this disease in the last three years as well most patients are requested only for doing abdominal ultrasound exclusively to evaluate spleen complications and not requesting for abdominal and chest CT scan, even though CT scanning is the noninvasive and proper diagnostic method in addition to possibility of using of contrast media enhancing technique at different CT phases in detecting all the SCD complications.

This research was obtain to study deeper characterization of spleen complications from SCD like splenomegaly, infarctions and autosplenectomy and their appearance in CT image as well to study complications that can occur in certain abdominal organs and chest when they are affected by all types of SCD, by doing both chest and abdominal CT scan, because CT scan considered more sensitive and accurate tool in diagnosis of SCD complications, and so able to manage and treat complications.

1.3 Objectives of the study:

1.3.1 General objective:

To study all impact of sickle cell disease in spleen and to characterize the spleen in the all types of sickle cell disease in the all CT enhancement phases, as well to study the all complications in certain abdominal organs and chest by using multidetector computed tomography.

1.3.2 Specific objectives:

To characterize the spleen in patients affected with sickle cell disease (location, shape, size, and CT number).

To evaluate the vascular findings of the spleen and correlated with the spleen and other lymphnode findings.

To give full depiction for each spleen lesions characterization and their appearance in the all CT scanning phase.

To study the frequencies of sickle cell disease types.

To identify the spleen lesions at all types of sickle cell disease.

To determine the frequencies of the sickle cell disease complications in another abdominal organs and chest.

To correlate the findings of the sickle cell disease complications in certain abdominal organs and chest with the patient's ages and sickle cell disease types.

1.4 Thesis outline:

This thesis concerned Characterization of some abdominal and chest organs in pt with sickle cell disease using multidetector computed tomography, and the thesis divided as following:

Chapter one discussed the problem and objectives of the study.

Chapter two contained literature review of the study, which consists of six parts, part one and two are talked about anatomy and physiology of the concerned

organs in the study, part three explains the SCD as pathology, part four was about CT physics and technique of the abdomen and HRCT scan techniques, part five displayed the normal CT appearance of certain organs, part six showed CT appearance of SCD of the all concerning organs in the study and the literature review finally viewed the previous studies.

Chapter three discussed material and method which used in the study.

Chapter four showed all results that related to the study objectives, and their analysis.

Chapter five contained discussion, Conclusion and recommendations.

Chapter Two

Literature Review

2.1 The anatomy

The abdomen (commonly called the belly) is the body space between the thorax (chest) at the thoracic diaphragm to the pelvis at the pelvic brim.

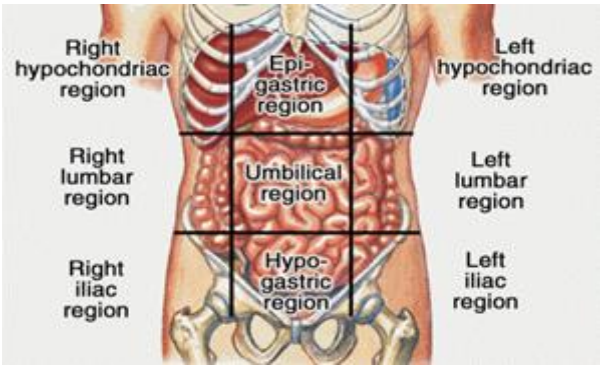
The abdomen contains most digestive organs, including the stomach, small and large intestines, pancreas, liver, and gallbladder. These organs are held together loosely by connecting tissues (mesentery) that allow them to expand and to slide against each other. The abdomen also contains the kidneys and spleen (Elaine, 2015).

Many important blood vessels travel through the abdomen, including the aorta, inferior vena cava, and dozens of their smaller branches. In the front, the abdomen is protected by a thin, tough layer of tissue called fascia. In front of the fascia are the abdominal muscles and skin. In the rear of the abdomen are the back muscles and spine (Elaine, 2015).

The body of the abdomen when viewed from a frontal view is divided into nine imaginary planes, in both vertical and horizontal directions (David, 2013).

2.1.1 Regions of the abdomen

Three horizontal lines and two vertical lines create nine regions of the abdomen. Below is an image of the regions of the abdomen(figure 2.1.1), which are formed within these planes. “Hypo” refers to “below”, “epi” refers to “above”, “chond” refers to the cartilage of the rib and “gast” is in reference to the stomach(Wesley, 1999).



(Figure 2.1.1): 9 Regions of the abdomen (Wesley, 1999)

The above lines intersect and divide the abdomen into 9 regions:

In upper abdomen:

Right hypochondrium / epigastrium / left hypochondrium

In middle abdomen:

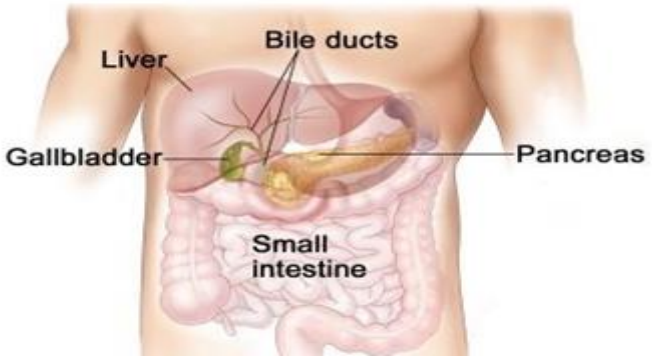
Right lumbar region / umbilicus / left lumbar region

In lower abdomen:

Right iliac region / hypogastrium / left iliac region(Wesley, 1999).

2.1.2 Liver anatomy

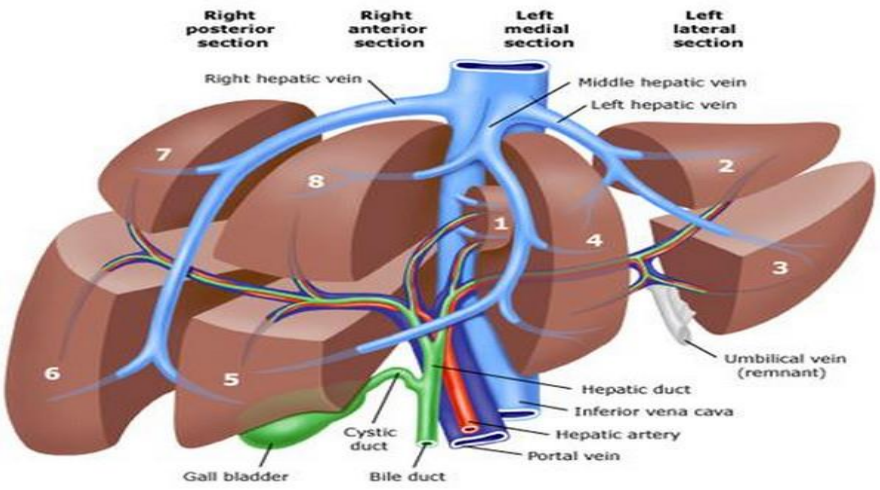
Liver occupies the whole of the right hypchondrium, the greater part of the epigastrium and the left hypochondrium. It rests just below the diaphragm, to the right of the stomach and overlies the gallbladder (figure 2.1.2).



(Figure 2.1.2): Location of liver and its relation with other (main) abdominal organs (Bryan et al, 2008)

It divided into two portions – a right and a left lobe, as viewed from the front (diaphragmatic) surface; but the underside (the visceral surface) shows it to be

divided into four lobes and includes the caudate and quadrate lobes (Bryan et al, 2008).



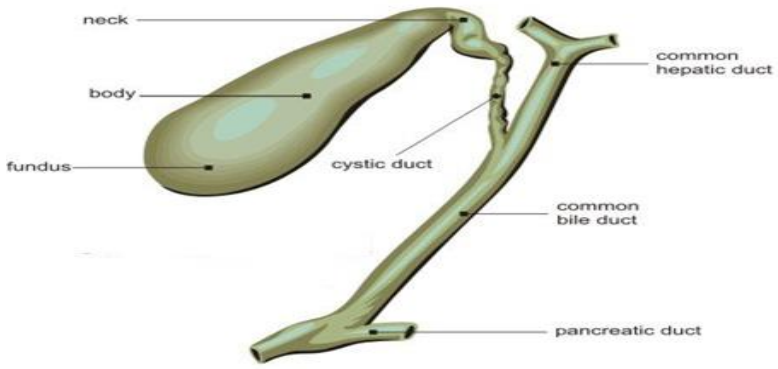
(Figure 2.1.3): Lobes of liver (Misih, 2010).

The liver receives a dual blood supply from the hepatic portal vein and hepatic arteries (Elaine and Katja, 2012).

2.1.3 Gall-bladder anatomy

It is a bile-reservoir and has a pear-shaped structure. It has the capacity of about 30 to 50ml. Gall-bladder is located in the fossa on inferior surface of the right lobe liver (Jon, 1994). It is divided into fundus, body and neck (figures 2.1.4).

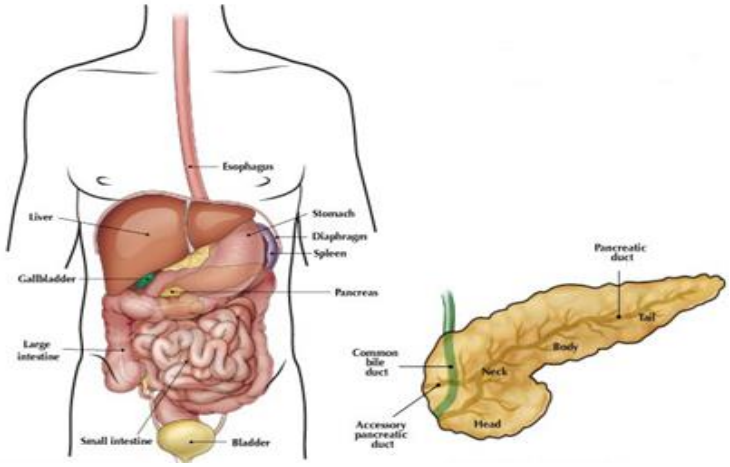
It supplied principally by the cystic artery, which typically branches from the right hepatic artery (Jon, 1994).



(Figure 2.1.4): Shows anatomy of the gallbladder (Jon, 1994)

2.1.4 Anatomy of the pancreas

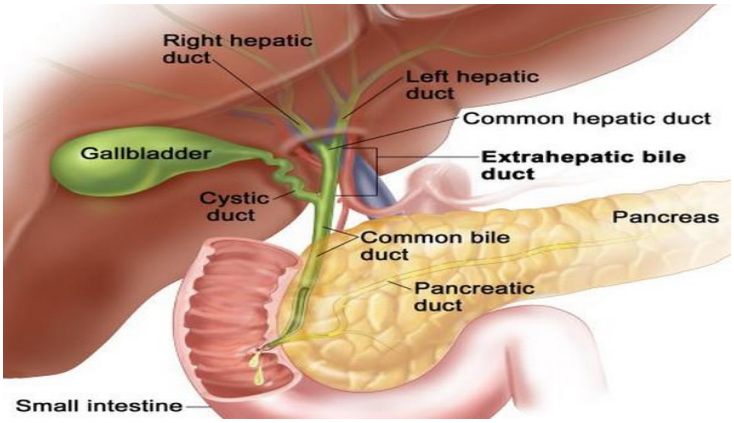
Pancreas lies more or less located transversely over the posterior abdominal wall behind the stomach at the level of lumbar plexus' segments L1 and L2 (figure 2.1.6). It about 15 cm (6 in) long (Adam, 2005). It is divisible into head, neck, body and tail (figure 2.1.5).



(Figure 2.1.5): Anatomy of the pancreas (Adam, 2005)

It has two ducts, main pancreatic duct and accessory pancreatic duct (Barbara and Young, 2006).

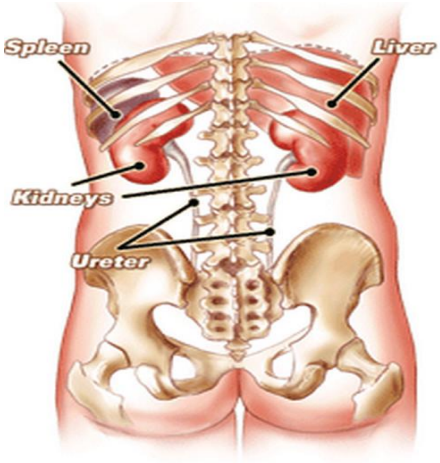
The pancreas receives blood from branches of both the coeliac artery and superior mesenteric artery.



(Figure 2.1.6): Location of the gallbladder and pancreas in addition to biliary tree. (Mortelé et-al, 2006) .

2.1.5 Kidneys anatomy

Kidneys are bean-shaped, brown-colored vital organs that occupy epigastric, hypochondriac, lumbar and umbilical regions. Vertically, they extend from the upper border of vertebrae T12 to the centre of the body of L3(Glodny et al, 2009). The right kidney is located below the diaphragm and posterior to the liver whereas the left kidney is located below the diaphragm and posterior to the spleen(figure 2.1.7). Above both kidneys lie the adrenal glands. The right kidney is slightly smaller than the left kidney(Glodny. et al, 2009).

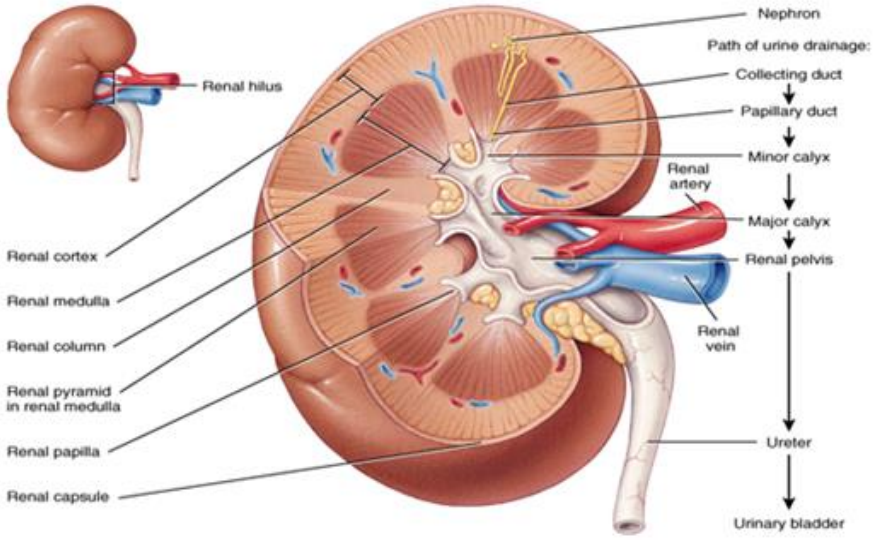


(Figure 2.1.7) :Kidneys location posterior view (Glodny B. et al, 2009*)*.

The indentation on the concave side of the kidney, known as the renal hilus, provides a space for the renal artery, renal vein, and ureter to enter the kidney (Anca and Godfried, 2003).

A thin layer of fibrous connective tissue forms the renal capsule. Deep to the renal capsule is the renal cortex. Seven cone-shaped renal pyramids form the renal medulla deep to the renal cortex (Anca and Godfried, 2003). Each apex connects to a minor calyx, which merge to form 3 larger major calyces, which further merge to form the hollow renal pelvis at the center of the kidney(figure 2.1.8). The renal pelvis exits the kidney at the renal hilus, where urine drains into the ureter (Anca and Godfried, 2003).

The renal arteries branch directly from the abdominal aorta and enter the kidneys through the renal hilus. Inside kidneys, the renal arteries diverge into the smaller afferent arterioles of the kidneys.

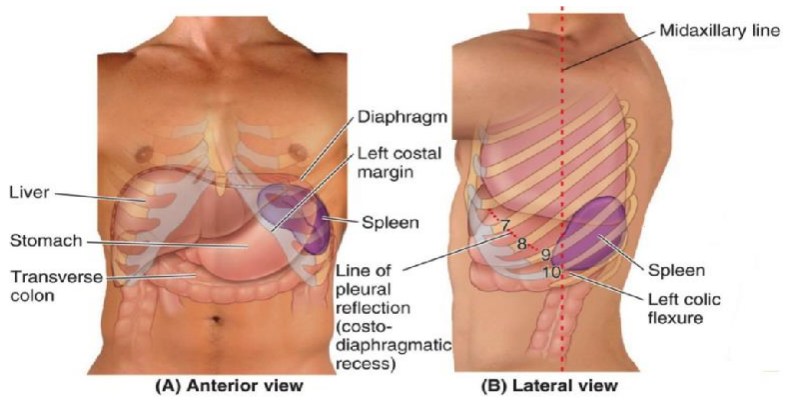


(Figure 2.1.8): Structure of the kidney (Anca and Godfried, 2003).

2.1.6 Spleen anatomy

2.1.6.1 Location

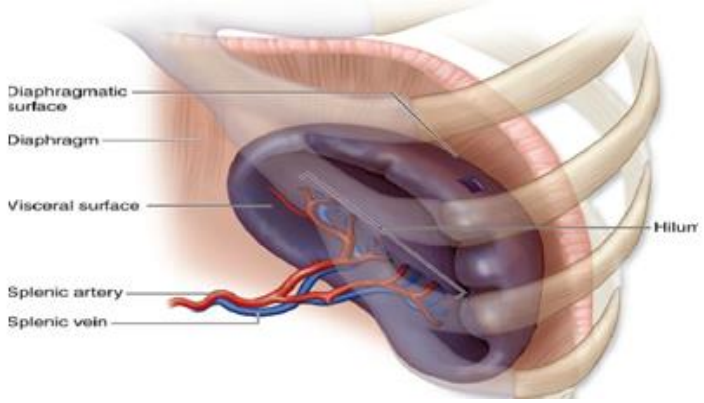
the spleen lies relative to the 9th and 11th ribs and is located in the left hypochondrium and partly in the epigastrium (figure 2.1.9). Thus, the spleen is situated between the fundus of the stomach and the diaphragm (Lichtman et al, 1995). It is the biggest lymphoid organ and very vascular and reddish purple in color; its shape, size and weight vary between people, but it's commonly shoe or fist-shaped, purple, and about 4 inches long in adults. Because the spleen is protected by the rib cage, you can't easily feel it unless it's abnormally enlarged but A healthy spleen is not palpable (Lichtman et al, 1995).



(Figure 2.1.9):Location of spleen (Lichtman et al, 1995)

2.1.6.2 Surfaces

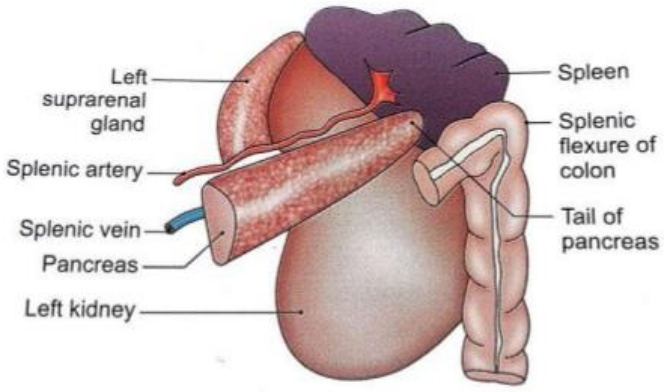
The diaphragmatic surface of the spleen (or phrenic surface) is convex, smooth, and is directed upward, backward, and to the left, except at its upper end, where it is directed slightly to the middle. It is in relation with the under surface of the diaphragm, which separates it from the ninth, tenth, and eleventh ribs of the left side (figure 2.1.10), and the intervening lower border of the left lung and pleura (Lichtman et al, 1995).



(Figure 2.1.10): Spleen surfaces (Lichtman et al, 1995)

The visceral surface of the spleen is divided by a ridge into two regions: an anterior or gastric and a posterior or renal. The gastric surface (faciesgastrica) is directed forward, upward, and toward the middle, is broad and concave (figure 2.1.10), and is in contact with the posterior wall of the stomach. Below this it is in contact with the tail of the pancreas (figure 2.1.11). Near to its mid-border is a long fissure, termed the hilum. This is pierced by several irregular openings, for the entrance and exit of vessels and nerves. The renal surface

(faciesrenalis) is directed medialward and downward. It is somewhat flattened, considerably narrower than the gastric surface, and is in relation with the upper part of the anterior surface of the left kidney and occasionally with the left suprarenal gland (Lichtman et al, 1995) (figure 2.1.11).



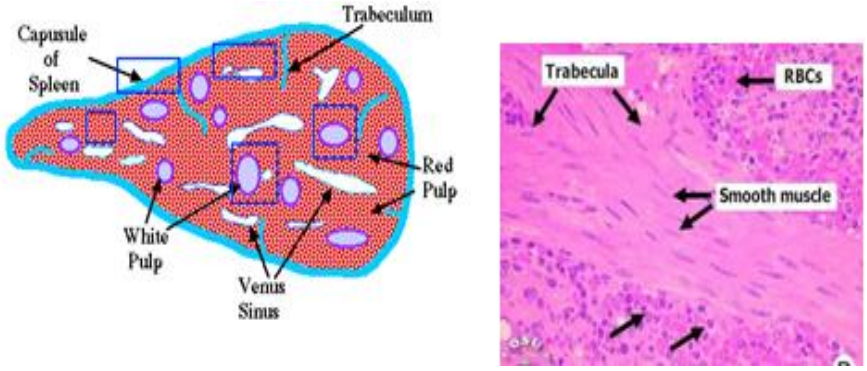
(Figure 2.1.11):Visceral surface of the spleen (Lichtman et al, 1995)

2.1.6.3 Spleen contents

The spleen is surrounded by a capsule composed of dense fibrous tissue, elastic fibers, and smooth muscle. The outermost layer of the splenic capsule is composed of mesothelial cells, which may not be evident on histological section. Irregularly spaced trabeculae of smooth muscle and fibroelastic tissue emanate from the capsule into the splenic parenchyma. These trabeculae also contain blood and lymph vessels and nerves(van Krieken, 1998).

The lining endothelial cells have wide slits between their lateral margins, that act as a filter. The blood cells have to move through these slits, before they can leave the spleen and worn out, or defective blood cells are damaged during this process. The damaged cells are then phagocytosed by the numerous macrophages in the red pulp, that lie just next to the sinusoids(van Krieken, 1998).

The spleen is covered by a dense capsule, and there are connective tissue trabeculae (figure 2.1.12), which provide internal support for the spleen, and carry the blood vessels into the spleen (van Krieken, 1998).



(Figure2.1.12):Spleen histology (van Krieken, 1998)

2.1.6.4 Red Pulp

The red pulp makes up the majority of the spleen(figure 2.1.13) and is composed of a three dimensional meshwork of splenic cords and venous sinuses(figure 2.1.14). The splenic cords are composed of reticular fibers, reticular cells, and associated macrophages (Kraal and Mebius, 2005) (figure 2.1.15). The reticular fibers are composed of collagenous and elastic fibers, microfibrils, reticular cell basal laminae, and unmyelinated adrenergic nerve fibers. Within the spaces between the cords are blood cells, including erythrocytes, granulocytes, and circulating mononuclear cells. Also associated with the splenic cords, are lymphocytes and hematopoietic cells as well as plasma cells and plasmablasts that migrate from the follicles and the outer PALS after antigen specific differentiation (Kraal and Mebius, 2005). The red pulp macrophages are actively phagocytic and remove old and damaged erythrocytes and blood-borne particulate matter. Extra medullary hematopoiesis is common in rodent red pulp, especially in fetal and neonatal. Any combination of erythroid, myeloid, and megakaryocytic cells may be evident(Kraal and Mebius, 2005).

Venous sinuses can be found throughout the red pulp, they are lined by loose network of endothelial cells which sit on a basement membrane that is sandwiched between the endothelial cells and reticular fibers of the red pulp. The penicillar arteries and arteriolar capillaries are also located in the red pulp,

though they are more difficult to identify light microscopically (Kraal and Mebius, 2005).

Various pigments may be present in the spleen. Hemosiderin deposits in the cytoplasm of macrophages in the red pulp, and sometimes in the white pulp as well, are a typical finding. In fact, iron pigments (i.e., hemosiderin and ferritin) are the most common pigments in the macrophages of the red pulp. Iron from the hemoglobin of phagocytized erythrocytes is converted to hemosiderin for storage in the spleen. According to historical control data from the National Toxicology Program (NTP), hemosiderin pigmentation is more prevalent in females than in males. Ceroid and lipofuscin derived from oxidation of lipids is also typically found in the spleen, though they are less abundant than hemosiderin. Melanocytes containing melanin may be present in the spleen, particularly in black mice, usually in the trabeculae or focally in the red pulp(Kraal and Mebius, 2005).

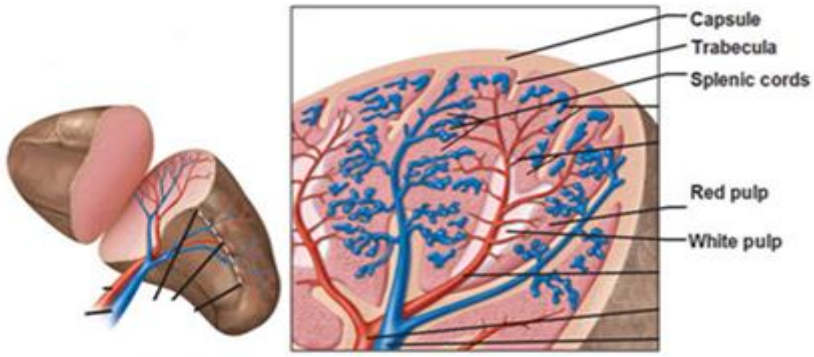
2.1.6.5 White Pulp

White pulp is organized in relation to the splenic arterioles and subdivided into the PALS, the follicles, and the marginal zone (figure 2.1.16). It is composed of lymphocytes, macrophages, dendritic cells, plasma cells, arterioles, and capillaries in a reticular framework similar to that found in the red pulp .As the central arterioles enter the red pulp, they are surrounded by the PALS which are composed of lymphocytes and concentric layers of reticular fibers and flattened reticular cells. The PALS are divided into the inner PALS and the outer PALS. The inner PALS, a T-cell dependent region(figure 2.1.17), may stain slightly more intensely than the outer PALS due to its cellular composition of predominantly small lymphocytes. The difference, however, is not uniformly present and is generally very subtle and difficult to detect by light microscopy. The cells of the inner PALS are largely CD4+ T-cells, though smaller numbers of CD8+ T-cells may also be present, as well as interdigitating dendritic cells, and migrating B-cells(Kraal and

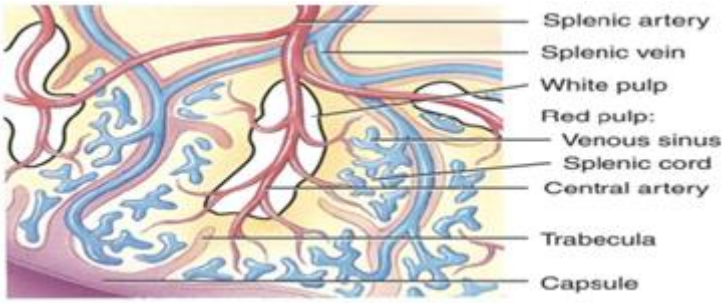
Mebius, 2005) (figure 2.1.17). The outer PALS is populated by small and medium lymphocytes (both B- and T-cells), macrophages, and, upon antigenic stimulation, plasma cells.

2.1.6.6 Marginal Zone

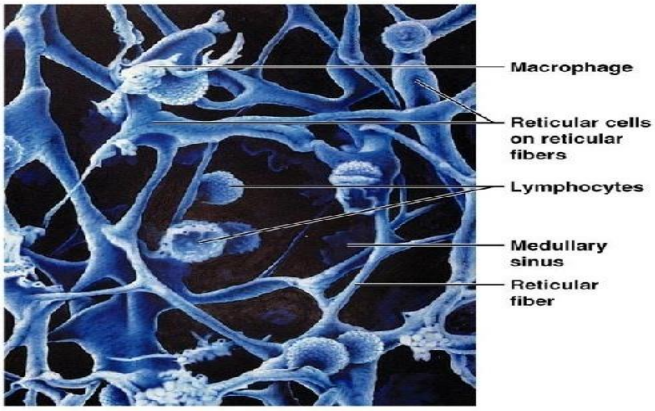
The marginal zone is a unique region of the spleen situated at the interface of the red pulp with the PALS and follicles (figure 2.1.16). Considered by many to be a separate compartment rather than part of the white pulp, it is designed to screen the systemic circulation for antigens and pathogens and plays an important role in antigen processing. A band of macrophages, the marginal zone metallophilic macrophages, and the marginal sinus (Kraal and Mebius, 2005), separate the marginal zone from the PALS and follicles. The marginal zone metallophilic macrophages are a unique subset of macrophages at the inner margin of the marginal zone adjacent to the PALS and follicles.



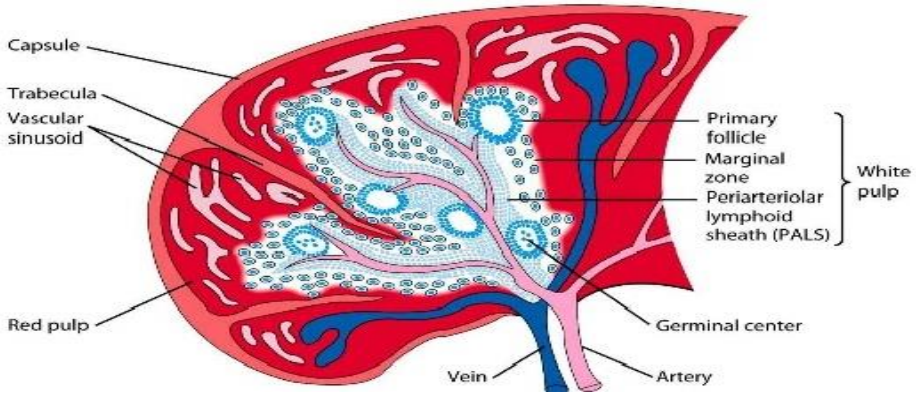
(figure2.1.13):Red and white pulp(Kraal and Mebius,2005)



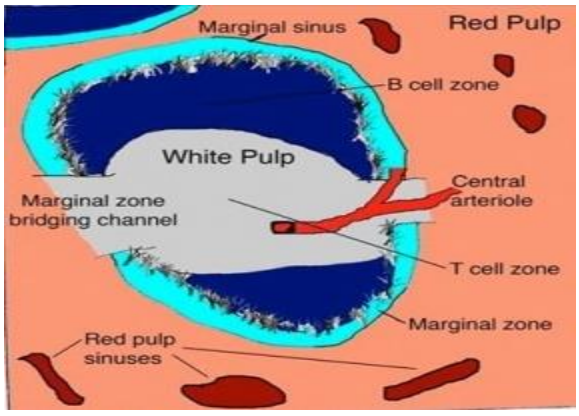
(Figure 2.1.14):Components of the red pulp (Kraal and Mebius, 2005)



(Figure 2.1.15):Components of splenic cord (Kraal and Mebius, 2005)



(Figure 2.1.16):Components of the white pulp (Kraal and Mebius, 2005)

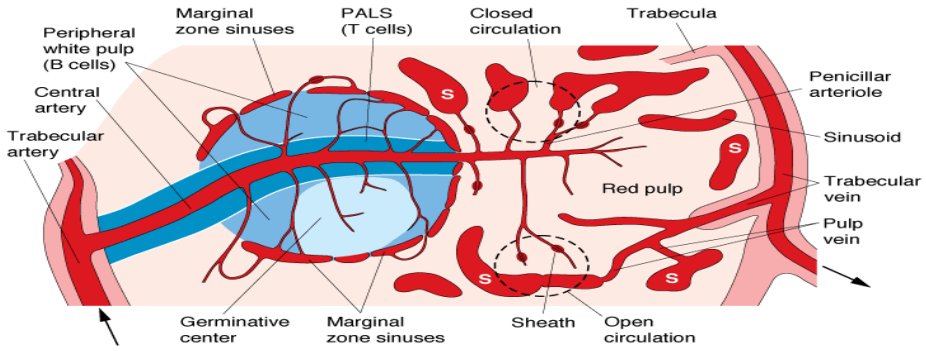


(Figure 2.1.17):White pulp (both B- and T-cells) (Kraal and Mebius, 2005).

2.1.6.7 Blood supply

Blood enters the spleen at the hilus via the splenic artery. The splenic artery divides into trabecular arteries located within the trabeculae entering the splenic parenchyma (Ekberg et al, 2001) (figure 2.1.18). Small arterioles

branch from the trabecular arteries and enter the red pulp where they become central arterioles. Smaller arterioles branch from the central arterioles and feed the white pulp capillary beds. Blood entering the marginal sinus and marginal zone percolates through the marginal zone in the direction of the red pulp. Once through the marginal zone, the blood either flows directly into adjacent venous sinuses whose open ends are continuous with the marginal zone, the so-called "fast pathway," or enters the reticular meshwork of the red pulp, the "slow pathway" (Ekberg et al, 2001). As the central arterioles continue, the white pulp wanes and they become the penicillar arteries surrounded by red pulp (Ekberg et al, 2001). Blood from the red pulp collects in the venous sinuses which enter the trabeculae and merge into the trabecular veins (figure 2.1.18). The trabecular veins then converge at the hilus to form the splenic vein which drains into the hepatic portal system.



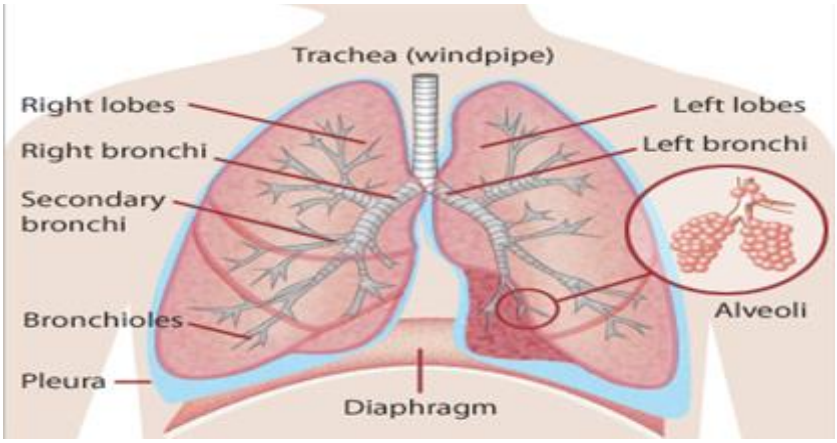
(Figure 2.1.18):Branches of splenic artery and vein (Ekberg et al, 2001)

2.1.7 lungs anatomy:

The right and left lungs are located in the chest on either side of the heart in the rib cage (figure 2.1.19). The left lung shares space with the heart, (Borley and Neil, 2008).The medial surface of the lungs faces towards the centre of the chest, and lies against the heart, great vessels, and the carina where the two main bronchi branch off from the base of the trachea (Borley and Neil 2008). Both lungs have a central recession called the hilum, where the blood vessels and airways pass into the lungs (Richard, 2014).

The lungs are surrounded by the pulmonary pleurae. Between the pleurae is a potential space called the pleural cavity(figure 2.1.19) containing pleural fluid. Each lung is divided into lobes by the invaginations of the pleura as fissures.

The human lung has a dual blood supply *(*Stanton et al, 2008).The tissue of the lungs receive oxygenated blood via the bronchial circulation, the lungs also receive deoxygenated blood from the heart and supply it with oxygen, blood passes through small capillaries next to the alveoli in the lung, receives oxygen, and travels back to the heart. The oxygenated blood is then pumped to the rest of the body *(*Stanton et al, 2008) **.**



(Figure 2.1.19): Lungs structure and location (Richard, 2014)

2.2 Physiology

2.2.1 Liver physiology

It plays a major role in metabolism with numerous functions in the human body, including regulation of glycogen storage, decomposition of red blood cells, plasma protein synthesis, hormone production, and detoxification (Bryan et al, 2008).

2.2.2 Physiology of the gall bladder and biliary flow

The main purpose of the gallbladder is to store bile which is produced by the liver, needed for the digestion of food (Mortelé et-al, 2006*)*. Then flows through the hepatic ducts into the gallbladder. The cystic duct from the gallbladder joins with the common hepatic duct to form the common bile duct(Mortelé et-al, 2006*)* (figure 2.1.6). Bile either drains directly into the

duodenum via the common bile duct, or is temporarily stored in the gallbladder via the cystic duct. The common bile duct and the pancreatic duct enter the second part of the duodenum together at the hepatopancreatic ampulla (Mortelé et-al, 2006).

2.2.3 Physiology of the pancreas

It is an endocrine gland producing several important hormones, including insulin, glucagon, somatostatin, and pancreatic polypeptide which circulate in the blood (Linda and Costanzo, 2006). The pancreas is also a digestive organ, secreting pancreatic juice containing digestive enzymes that assist digestion and absorption of nutrients in the small intestine.

2.2.4 Physiology of the kidneys

The kidneys are the waste filtering and disposal system of the body. Functions of the kidney, including maintenance of acid-base balance; regulation of fluid balance; regulation of sodium, potassium, and other electrolytes; clearance of toxins; absorption of glucose, amino acids, and other small molecules; regulation of blood pressure; production of various hormones, such as erythropoietin; and activation of vitamin D (Andrew et al, 2013).

2.2.5 Physiology of the spleen

The spleen is a major lymphoid and blood filtration organ (Chan et al, 1995). It is responsible for storing and removing erythrocytes from the blood as well as antigen surveillance of the blood and antibody production (Chan et al, 1995).

The spleen has a number of functions:

It filters the blood removing ageing erythrocytes and antigens

It stores erythrocytes and platelets

lymphoid organ

2.2.5.1 Erythrocytes & Platelets

In the fetus the spleen also has a role in haematopoiesis when it becomes the main erythrocyte producing organ during the haematopoietic transitional phase.

In the developed human the red pulp is involved in the removal of aged, damaged or abnormal erythrocytes (along with the liver and bone marrow). As erythrocytes age they become less supple and this causes them to become damaged when they pass through the very narrow capillaries of the spleen, after which they are phagocytised by splenic macrophages. If a splenectomy is performed the number of aged erythrocytes in circulation increases (Chan et al, 1995).

2.2.5.2 Spleen as lymphoid organ

One of the lymphatic system's major jobs is to collect extra lymph fluid from body tissues and return it to the blood. This is crucial because water, proteins, and other substances are always leaking out of tiny blood capillaries into the surrounding body tissues (Mark, 2006). If the lymphatic system didn't drain the excess fluid from the tissues, the lymph fluid would build up in the body's tissues, causing them to swell(Mark, 2006).

The lymphatic system also helps defend the body against germs (viruses, bacteria, and fungi) that can cause illnesses. Those germs are filtered out in the lymph nodes, which are small masses of tissue located along the network of lymph vessels. The nodes house lymphocytes, a type of white blood cell. Some of those lymphocytes make antibodies, special proteins that stop infections from spreading by trapping disease-causing germs and destroying them(Mark, 2006).

The spleen also helps the body fight infection. The spleen contains lymphocytes and another kind of white blood cell (called macrophages) that engulf and destroy bacteria, dead tissue, and foreign matter and remove them from the blood passing through the spleen(Mark, 2006).

But in the same time spleen is not a vital organ – its functions are useful but not essential for life. Red bone marrow, the liver, and lymph nodes can complete the filtration and blood recycling functions of the spleen in its absence. Because it is not a vital organ and is so soft, spongy, and vascular, damage to the spleen is almost always treated by its complete removal. Untreated damage to the spleen can quickly lead to massive internal hemorrhaging and eventual death(Mark, 2006).

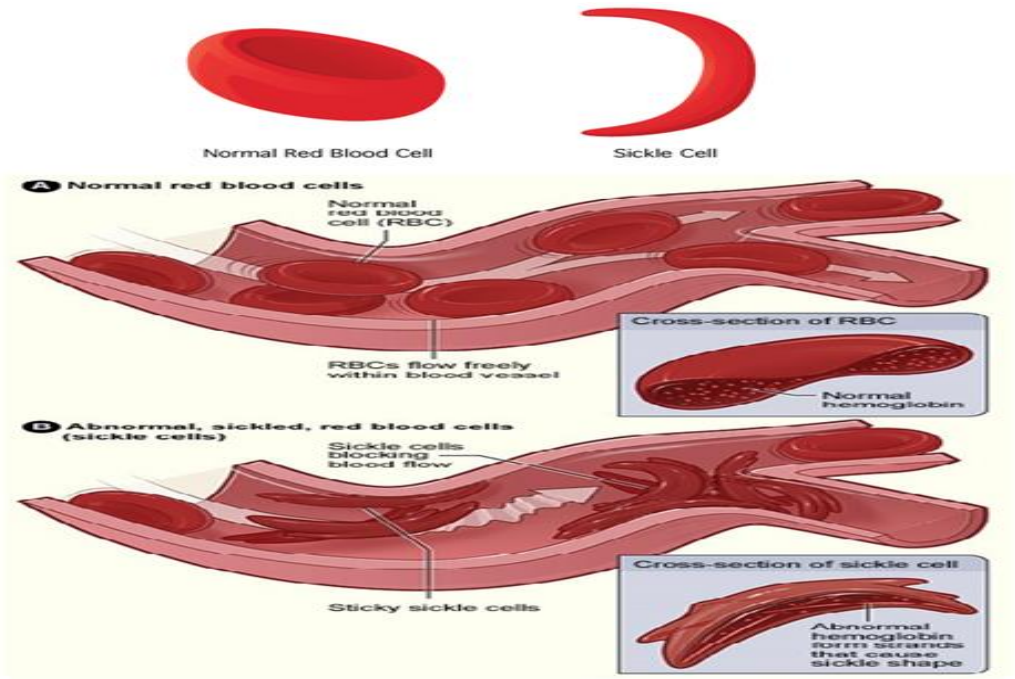
2.2.7 Physiology of the lungs

Their function in the respiratory system is to extract oxygen from the atmosphere and transfer it into the bloodstream, and to release carbon dioxide from the bloodstream into the atmosphere, in a process of gas exchange (Levitzky. and Michael, 2013).

2.3 Pathology

Sickle cell disease (SCD) is a common genetic disorder which represents a major medical problem in certain parts of the world and is the most common inherited haematological disease affecting humans (David et al, 2010).

It's a genetic disease of the red blood cells (RBCs). Normally RBCs are shaped like a disk. This gives them the flexibility to travel through even the smallest blood vessels(figure 2.4.1). However, in people with sickle cell, though, have RBCs that are shaped like sickles, or crescent moons. This makes them sticky and rigid. They can get trapped in small vessels and block blood from reaching different parts of the body. This can cause pain and tissue damage (David et al, 2010) (figure 2.3.1).



(Figure 2.3.1): Shows normal red blood cells flowing freely in a blood vessel. The inset image shows a cross-section of a normal red blood cell with normal hemoglobin. Figure B shows abnormal, sickled red blood cells blocking blood flow in a blood vessel. The inset image shows a cross-section of a sickle cell with abnormal (sickle) hemoglobin forming abnormal stiff rods (David et al, 2010).

2.3.1 Blood hemoglobin

2.3.1.1 Component of hemoglobin

Normal component of hemoglobin (Hardison and Ross, 2012):

Structurally, DNA is made up of nucleotides.

A nucleotide is made up of a sugar, a phosphate and a base.

Nucleotides hook together to make the sugar-phosphate backbone of every strand of DNA.

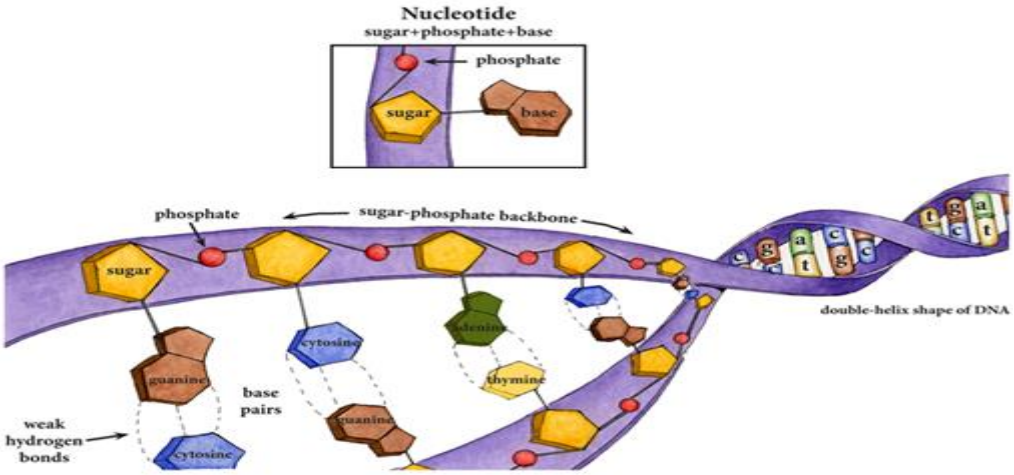
Bases pair up with opposite matching bases on the other strand of DNA.

There are four kinds of base pairs made up of adenine(A), thymine(T), guanine(G), cytosine(C) (figure 2.3.2).

The base (A)always pairs with (T) And (G) always pairs with (C).

The two strands of DNA are linked together by weak hydrogen bonds and stacked like a ladder who's sides spiral around each other into their famous double-helix shape.

Human chromosome spans for about 249 million nucleotide base pairs.



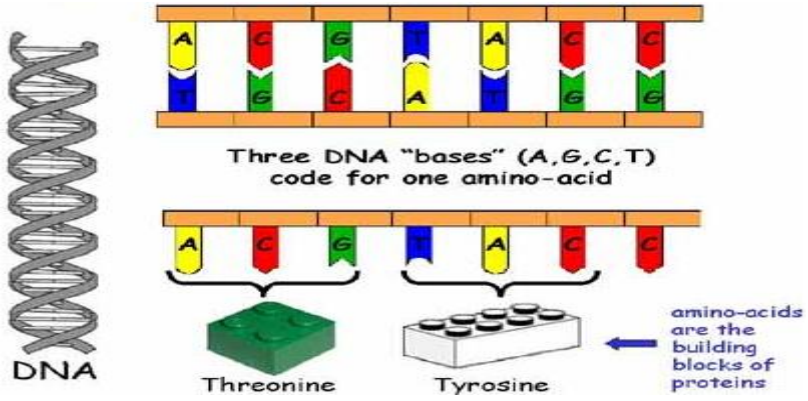
(Figure 2.3.2): Hemoglobin component (Hardison and Ross, 2012)

Each three DNA bases (A,G,C,T) are join together and form code for one amino acid(figure 2.3.3).

There are several amino acids which are coded for by more than one base combination. For example, glycine (Gly) is coded for by GGT, GGC, GGA and GGG. It doesn't matter what the last base is - you would get glycine whatever base followed the initial GG (Hardison. and Ross, 2012).

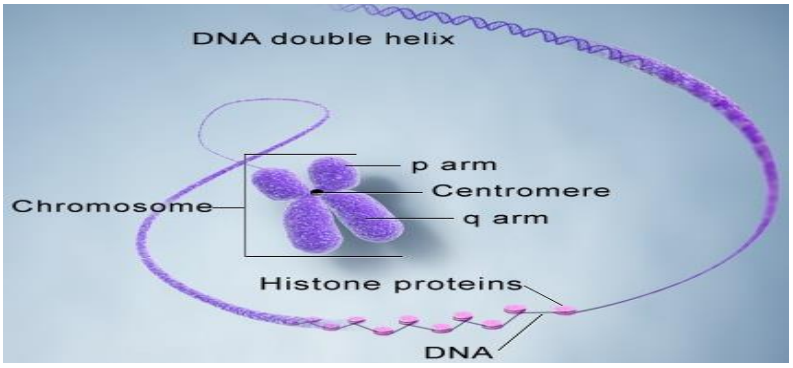
(Table 2.3.1): Examples of some aminoacid's base code (Hardison, 2012):

Amino acid	Abbreviation	Base in code
Alanine	Ala	GCT, GCC, GCA and GCG
Cysteine	Cys	TGT, TGC
Glycine	Gly	GGT,GGC,GGA and GGG
Valine	Val	GTT,GTC,GTA and GTG
Tyrosine	Tyr	TAT,TAC



(Figure 2.3.3): Three DNA codes (A,G,C,T) for one amino-acid (Hardison and Ross, 2012).

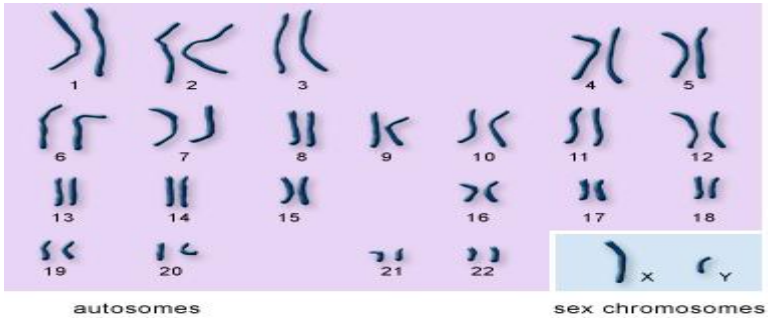
The double-helix shape of DNA makes up chromosomes (figure 2.3.4).



(Figure 2.3.4): Double-helix shape of DNA (Hardison and Ross, 2012).

In humans, each cell normally contains 23 pairs of chromosomes, for a total of 46(figure 2.3.5). Twenty-two of these pairs, called autosomes, look the same in both males and females (Hardison and Ross, 2012).

The 23rd pair, the sex chromosomes, differ between males and females. Females have two copies of the X chromosome, while males have one X and one Y chromosome(Figure 2.3.5).

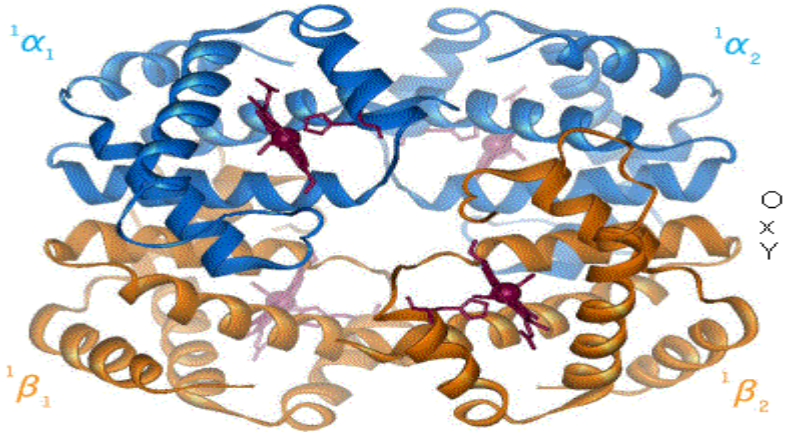


(Figure 2.3.5): 23 Pairs of human chromosomes (Hardison and Ross, 2012).

Dimers of chromosomes are combined together and form globin chains.

Two distinct globin chains combine to form hemoglobin. One of the chains is designated alpha. The second chain is called "non-alpha". With the exception of the very first weeks of embryogenesis, one of the globin chains is always alpha. A number of variables influence the nature of the non-alpha chain in the hemoglobin molecule. The fetus has a distinct non-alpha chain called gamma. After birth, a different non-alpha globin chain, called beta(HbB), pairs with the alpha chain. The combination of two alpha chains and two non-alpha chains produces a complete hemoglobin molecule (a total of four chains per molecule) (Hardison and Ross, 2012).

The combination of two alpha chains and two gamma chains form "fetal" hemoglobin, termed "hemoglobin F". The combination of two alpha chains and two beta chains form "adult" hemoglobin, also called "hemoglobin A".



(Figure 2.3.6): Combination of two alpha chains and two beta chains to form hemoglobin (Hardison and Ross, 2012).

2.3.1.2 Types of hemoglobin

In the fetus:

Hemoglobin F ($\alpha_2\gamma_2$)

After birth:

Hemoglobin A ($\alpha_2\beta_2$) The most common with a normal amount over 95%

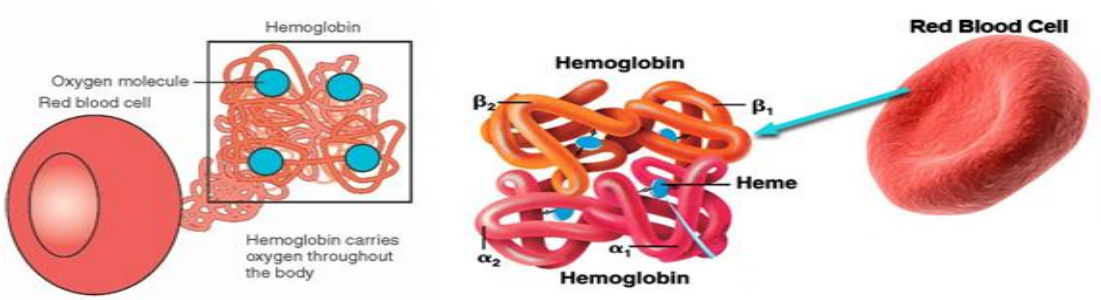
Hemoglobin A_2 ($\alpha_2\delta_2$) – δ chain synthesis begins late in the third trimester and, in adults, it has a normal range of 1.5–3.5%

Hemoglobin F ($\alpha_2\gamma_2$) – In adults Hemoglobin F is restricted to a limited population.

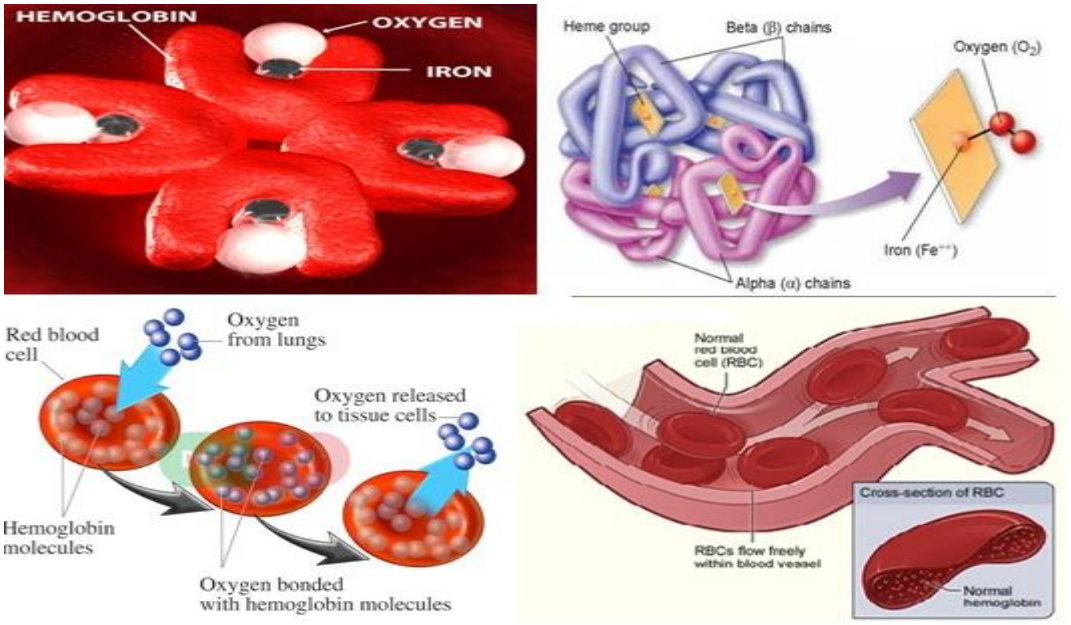
Hemoglobin is the protein molecule in red blood cells that carries oxygen from the lungs to the body's tissues and returns carbon dioxide from the tissues back to the lungs (Huisman, 1996) (figure 2.3.7, 2.3.8).

Hemoglobin also plays an important role in maintaining the shape of the red blood cells. In their natural shape, red blood cells are round with narrow centers resembling a donut without a hole in the middle (Huisman, 1996). Abnormal hemoglobin structure can, therefore, disrupt the shape of red blood cells and impede their function and flow through blood vessels.

Each globulin chain contains an important iron-containing porphyrin compound termed heme. Embedded within the heme compound is an iron atom that is vital in transporting oxygen and carbon dioxide in our blood (Figure 2.3.7). The iron contained in hemoglobin is also responsible for the red color of blood.



(Figure 2.3.7): (a): Hemoglobin carries oxygen molecule, (b): Heme compound within hemoglobin (Huisman, 1996).



(Figure 2.3.8): (a): Iron atom within hemoglobin (b): oxygen and iron atom within hemoglobin(c): exchange of oxygen between lungs and tissue cells (d): normal RBC pass in the blood vessels-(Huisman, 1996).

In adults, hemoglobin normally consists of four protein subunits: two subunits of beta-globin and two subunits of another protein called alpha-globin, which is produced from another gene called HBA. Each of these protein subunits is attached (bound) to an iron-containing molecule called heme; each heme contains an iron molecule in its center that can bind to one oxygen molecule. Hemoglobin within red blood cells binds to oxygen molecules in the lungs. These cells then travel through the bloodstream and deliver oxygen to tissues throughout the body-(Huisman, 1996).

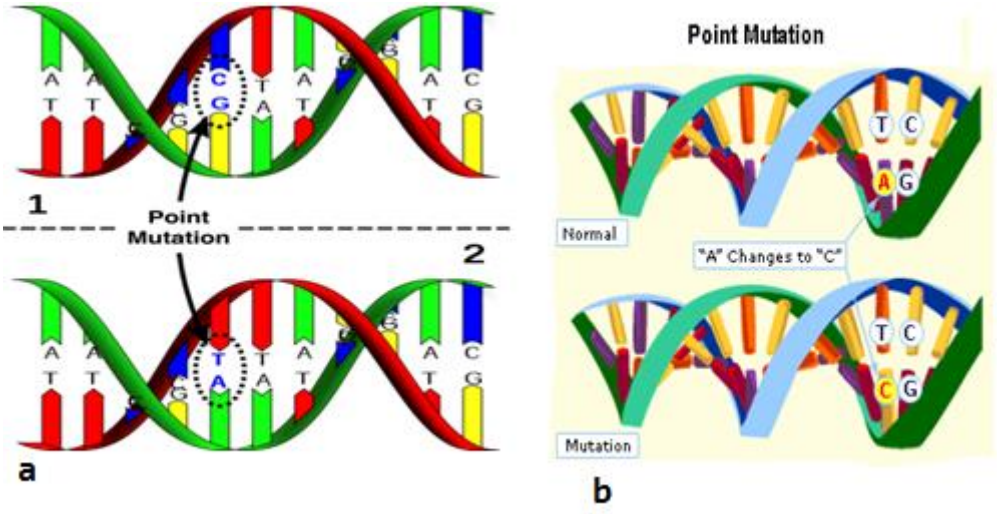
2.3.2 Mutations:

A gene mutation is a permanent alteration in the DNA sequence cause changes or alterations in the amino acid, such that the sequence differs from what is found in most people (Sharma et al, 2015). Mutations range in size; they can affect anywhere from a single DNA building block (base pair) to a large segment of a chromosome that includes multiple genes.

Gene mutations can be classified in two major ways-(Sharma et al, 2015)

Hereditary mutations are inherited from a parent, they are present in the parent's egg or sperm cells

Acquired (or somatic) mutations occur at some time during a person's life and are present only in certain cells, not in every cell in the body.



(Figure 2.3.9): Point mutation of some DNA codes, a. DNA sequence changed from CG to TA and b. sequence changed from A to C (Sharma et al, 2015).

Mutations of hemoglobin:

Genetic changes (mutations) in the globin genes cause alterations in the globin protein, resulting in structurally altered hemoglobin,or a decrease in globin chain production (thalassemia) (Adachi et al, 2011).

Hemoglobin variants are most often inherited characteristics (Adachi et al, 2011).

Autosomal recessive fashion, abnormal beta gene can be inherited. This means that the person who inherits this will have two copies of the altered gene. Both of these genes can be passed to offspring.

Heterozygous fashion, person has one normal beta gene and one abnormal beta gene. This person is considered to be a carrier of whichever hemoglobin variant is inherited. Only the abnormal gene can be passed on to offspring in

this case. Carriers also do not have to deal with having symptoms or any health concerns.

Homozygous fashion, person has two abnormal beta genes. In this case the person produces the associated hemoglobin variant and may have the symptoms and complications that are associated with the specific hemoglobin variant they have. The severity of the conditions mainly depend on the genetic mutation and it may vary from person to person.

List of common hemoglobin variants is lengthy, here are common forms that cause disease (Adachi et al, 2011):

Hemoglobin D-Punjab (α2βD2)

Hemoglobin H (β4)

Hemoglobin Barts (γ4)

Hemoglobin S (α2βS2): variation in the β-chain gene, (a single amino acid substitution 'valine' replacing a 'glutamine' in the 6th position of the beta chain of globin). causing a change in the properties of hemoglobin

Hemoglobin C ($\alpha_2\beta^C_2$): variation in the β-chain gene (substitution of a 'glutamic acid' replacing a 'lysine' at the 6th position of the β-globin chain).

Hemoglobin E ($\alpha_2\beta^E_2$)

Thalassemia: reduces the production of hemoglobin due to reduced or absent of the beta or alpha chains of hemoglobin, so has two main types, alpha thalassemia and beta thalassemia.The severity of alpha and beta thalassemia depends on how many alpha globin or beta globin are missing.

Beta thalassemia:

beta zero thalassemia (ßº thalassemia)(people may have no normal hemoglobin)

beta plus thalassemia(ß+ thalassemia) (reduced amount of normal hemoglobin)

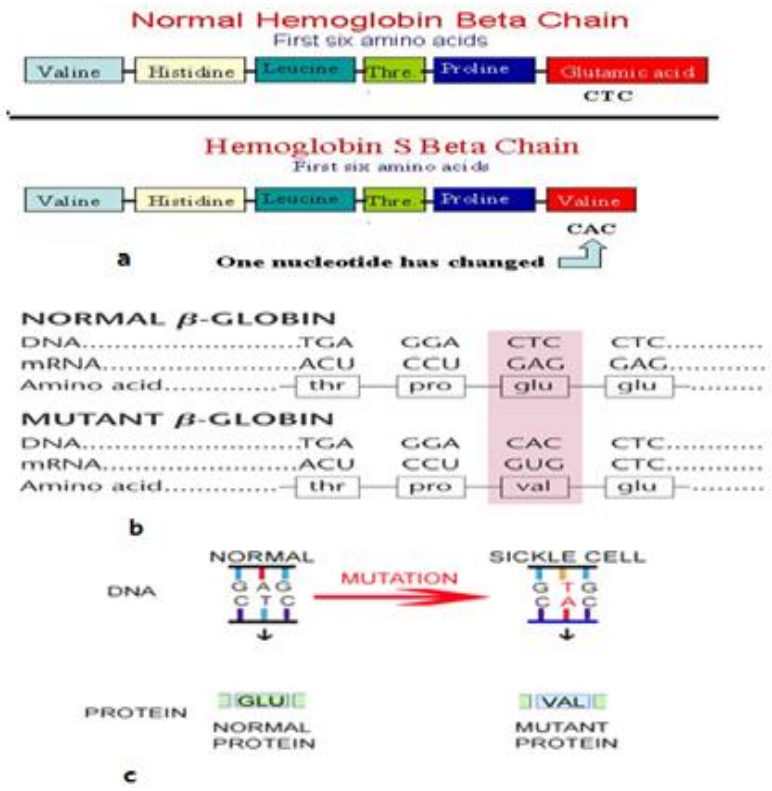
2.3.4 Genetics behind sickle cell disease (Pathophysiology)

Sickle-cell disease occurs when a person inherits two abnormal copies of the haemoglobin gene, one from each parent this occur in the hemoglobin-beta gene found on chromosome 11(Ashley-Koch et al, 2000).

Mutations in the hemoglobin gene is the key factor responsible for causing sickle cell disease.

It caused by a mutation in the HBB gene, The HBB gene provides instructions for making beta-globin, in sickle cell beta-globin subunits in hemoglobin is replaced by hemoglobin S (sickle hemoglobin) (Ashley-Koch et al, 2000).

The point mutation in the β-globin chain of hemoglobin, causes the hydrophilic amino acid glutamic acid to be replaced with the hydrophobic amino acid valine at the sixth position (Ashley-Koch et al, 2000) (figure 2.3.10).



(Figure 2.3.10):a, b and c shows comparison between normal β-globin and point mutation in the β-globin chain of hemoglobin (the glutamic acid replaced with valine) (Ashley-Koch et al, 2000)

Normally, hemoglobin in red blood cells takes up oxygen in the lungs and carries it to all the tissues of the body.

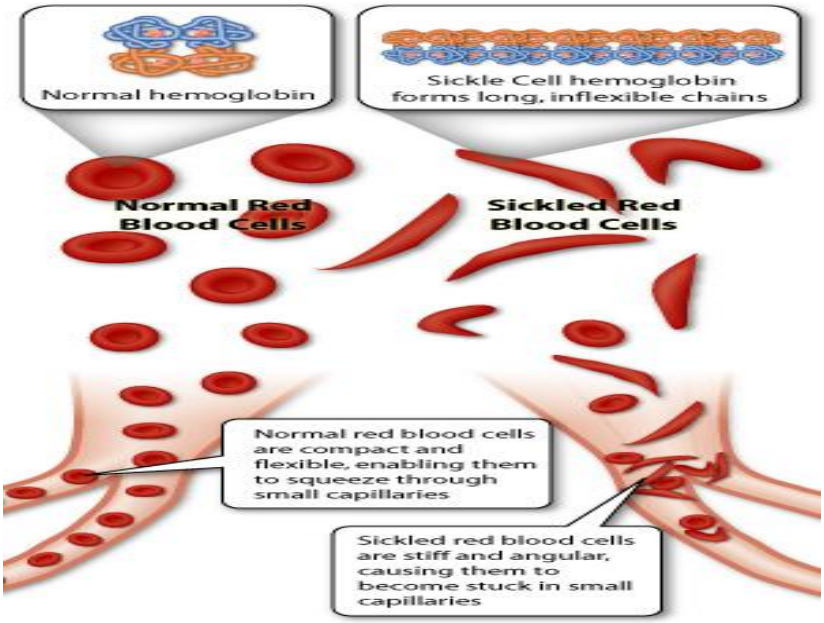
Red blood cells that contain normal hemoglobin are disc shaped. This shape allows the cells to be flexible so that they can move through large and small blood vessels to deliver oxygen(Figure 2.3.11).

Sickle hemoglobin is not like normal hemoglobin, because the beta-globin forms long, inflexible chains changing it into a crescent, or sickle shape instead of disc shape chains that found in normal hemoglobin (figure 2.3.11).

The RBC's of a person with sickle cell disease lose this elasticity component making it impossible for the sickled cells to pass through, leading to capillary blockage and eventually ischemia; restriction of blood supply to tissues (Ashley-Koch et al, 2000). This disadvantage is central to the pathophysiology of sickle-cell disease.

The actual anemia of the illness is caused by haemolysis, the destruction of the red cells because of their irregular "sickled" shape. A normal red blood cell lives for about 120 days in circulation, whereas a sickle cell lives for only 10 to 20 days.

Anemia is a condition in which the body does not have enough healthy red blood cells to provide oxygen to body tissues. The loss is then compensated by the production of new RBC's in the bone marrow but despite this effort, the rate of production does not match the rate of destruction which subsequently results in anemia (Ashley-Koch et al, 2000)



(Figure 2.3.11): Comparison between normal shape of RBCs and sickled shape of RBCs (Ashley-Koch et al, 2000)

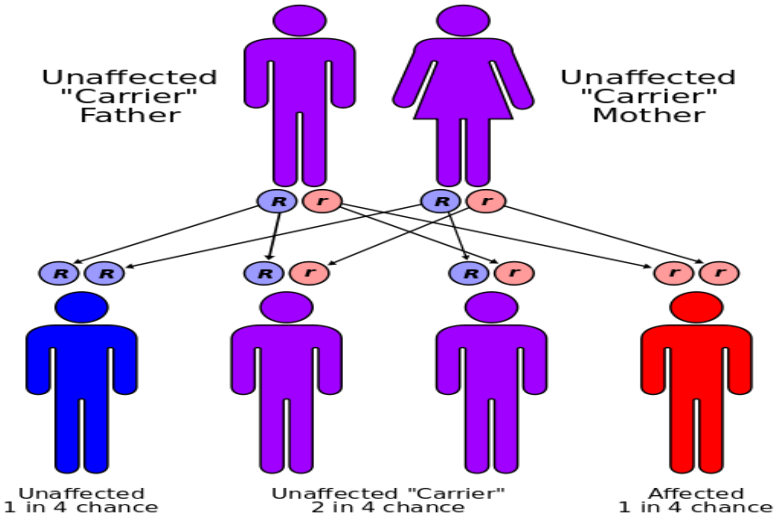
when one of the beta-globin subunits in hemoglobin is replaced with hemoglobin S the occurrence of the sickle cell trait is prevalent (Roach, 2005), but when both beta-globin subunits would have to be replaced by hemoglobin S the occurrence of the sickle cell disease is prevalent.

Both parents need to pass the abnormal hemoglobin gene to their child in order to their child to develop the disease (Ashley-Koch et al, 2000).

If both parents carry the defective gene, child have a 1 in 4 chance of inheriting the disease and becoming sick with it (Ashley-Koch et al, 2000) (figure 2.3.12).

If a child is born with one defective hemoglobin-beta gene, he may become a carrier of the disease (Roach, 2005). Carriers usually don't develop SCD symptoms. But, they can pass the disease on to future children if their partner also carries the sickle cell trait.

Sickle cell trait explains the geographic distribution of sickle cell disease. It makes patient more likely to survive a malaria infection. That's why sickle cell is more common in areas that have, or had, a high prevalence of malaria.



(Figure 2.3.12): Diagram showing the transfer of defective alleles from parents to offspring (Ashley-Koch et al, 2000)

Alleles: one of two or more alternative forms of a gene that arise by mutation and are found at the same place on a chromosome.

2.3.5 History of the disease

Sickle cell anemia was discovered in the year 1904 by James B. Herrick and Ernest Edward Irons (William, 1986). They were investigating the blood of a Grenadian native Walter Clement Noel; who was a 20 year old, first year dental student. They found that his red blood cells were peculiarly elongated and sickle-shaped in appearance. Walter was readmitted to the hospital on several occasions with muscular rheumatism and bilious attacks. He later returned to Grenada where he died of pneumonia in 1916 (William, 1986).

It was in 1922 that this unknown disease was named sickle-cell anemia by Vernon mason (William, 1986). Some of the symptoms of the disease had been traced back to places like Africa and Ghana before it was initially diagnosed.

The abnormality in the hemoglobin molecule was shown by Linus Pauling and colleagues in 1949 to cause the sickle-cell disease (William, 1986). This is a link between a genetic disease and the mutation of a protein; the first of the many milestones of molecular biology.

Sickle-cell disease is more common in people (or their descendants) from tropical and sub-tropical regions where malaria is or was common. In areas where malaria is common, there is a fitness benefit in carrying only a single sickle-cell gene (sickle cell trait). Those with only one of the two alleles of the sickle-cell disease, while not totally resistant, are more tolerant to the infection and thus show less severe symptoms when infected.

2.3.6 Epidemiology and prevalence of the disease in the world:

The highest frequency of sickle cell disease is found in tropical regions, particularly sub-Saharan Africa, tribal regions of India and the Middle-East, where malaria is or was common (Roberts and Montalembert, 2007).

2.3.6.1 Prevalence of the disease in the Africa

Three-quarters of sickle-cell cases occur in Africa. A recent WHO report estimated that around 2% of newborns in Nigeria were affected by sickle cell anaemia, giving a total of 150,000 affected children born every year in Nigeria alone. The carrier frequency ranges between 10% and 40% across equatorial Africa, decreasing to 1–2% on the north African coast and <1% in South Africa (Roberts and Montalembert, 2007).

2.3.6.2 Prevalence of the disease in the United States

The number of people with the disease in the United States is approximately 1 in 5,000, mostly affecting Americans of Sub-Saharan African descent, according to the National Institutes of Health (Roberts, and Montalembert, 2007). In the United States, about one out of 500 African-American children and one in every 36,000 Hispanic-American children have sickle-cell anemia (Radhakrishnan et al, 2005). It is estimated that sickle-cell disease affects 90,000 Americans (Mathew et al, 2006). Most infants with SCD born in the United States are now identified by routine neonatal screening.

2.3.6.3 Prevalence of the disease in the United Kingdom

In the United Kingdom (UK) it is thought that between 12,000 and 15,000 people have sickle cell disease (Kulozik et al, 1986) with an estimate of

250,000 carriers of the condition in England alone. As the number of carriers is only estimated, all newborn babies in the UK receive a routine blood test to screen for the condition (Roberts and Montalembert, 2007). Due to many adults in high-risk groups not knowing if they are carriers, pregnant women and both partners in a couple are offered screening so they can get counseling if they have the sickle cell trait (Kulozik et al, 1986).

2.3.6.4 Prevalence of the disease in the Middle East

In Saudi Arabia about 4.2% of the population carry the sickle-cell trait and 0.26% have sickle-cell disease. The highest prevalence is in the Eastern province where approximately 17% of the population carry the gene and 1.2% have sickle-cell disease (Jastaniah, 2011). In 2005 in Saudi Arabia a mandatory pre-marital test including HB electrophoresis was launched and aimed to decrease the incidence of SCD and thalassemia (Jastaniah , 2011).

In Bahrain a study published in 1998 that covered about 56,000 people in hospitals in Bahrain found that 2% of newborns have sickle cell disease, 18% of the surveyed people have the sickle cell trait, and 24% were carriers of the gene mutation causing the disease (Kulozik et al, 1986). The country began screening of all pregnant women in 1992 and newborns started being tested if the mother was a carrier. In 2004, a law was passed requiring couples planning to get married to undergo free premarital counseling.

2.3.6.5 Prevalence of the disease in the India

Sickle-cell disease is common in ethnic groups of central India who share a genetic linkage with African communities where the prevalence has ranged from 9.4 to 22.2% in endemic areas of Madhya Pradesh, Rajasthan and Chhattisgarh (Kulozik et al, 1986).

2.3.7 Types of sickle cell disease

Hemoglobin is the protein in RBCs that carries oxygen. It is made up of two alpha chains and two beta chains. These are made by the alpha and beta genes.

The four main types of sickle cell anemia are caused by different mutations in these genes (Yolanda and Pharm, 2015).

2.3.7.1 Hemoglobin SS Disease

Hemoglobin SS disease is the most common type of sickle cell disease. It occurs when you inherit copies of the hemoglobin S gene from both parents (Yolanda and Pharm, 2015). This forms hemoglobin known as Hb SS. As the most severe form of SCD, individuals with this form also experience the worst symptoms at a higher rate.

2.3.7.2 Hemoglobin SC Disease

Hemoglobin SC disease is the second most common type of sickle cell disease. It occurs when you inherit the Hb C gene from one parent and the Hb S gene from the other (Yolanda and Pharm, 2015). Individuals with Hb SC have similar symptoms to individuals with Hb SS. However, the anemia is less severe.

2.3.7.3 Hemoglobin SB+ (Beta) Thalassemia

Hemoglobin SB+ (Beta) thalassemia affects beta globin gene production (Yolanda and Pharm, 2015). The size of the red blood cell is reduced because less beta protein is made. If inherited with the Hb S gene, you will have Hemoglobin S Beta thalassemia.

2.3.7.4 Beta-Zero Thalassemia

Beta-Zero thalassemia is the second type of beta thalassemia. It has similar symptoms to Hb SS anemia. However, sometimes the symptoms of beta-zero thalassemia are more severe. It is associated with a poorer prognosis.

2.3.8 Risk people for sickle cell disease

Children are only at risk for sickle cell if both parents carry sickle genes(S, C or Trait) (Harvey, 2013).

People from regions that have endemic malaria are more likely to be carriers (Harvey, 2013). This includes people from Africa, India, the Mediterranean, and Saudi Arabia.

2.3.9 Symptoms of sickle cell disease

If a person has sickle cell disease (SCD), it is present at birth. But most infants do not have any problems from the disease until they are about 5 or 6 months of age (Schnog, 2004).Some countries require that all newborn babies receive screening for SCD. When a child has SCD, parents are notified before the child has symptoms. children have few or no symptoms if treatment is started early on.

The signs and symptoms of SCD will vary from person to person and can change over time.

Some children with SCD will start to have problems early on, and some later.

Early symptoms of SCD may include (Schnog, 2004):

Painful swelling of the hands and feet, known as dactylitis.

Fatigue or fussiness from anemia.

A yellowish color of the skin, known as jaundice, or whites of the eyes, known as icteris, that occurs when a large number of red cells hemolyze.

2.3.10 Common clinical manifestations of sickle cell disease:

2.3.10.1 Pain and acute sickle cell crisis

The hallmark of sickle cell disease is the sickle cell crisis (also sometimes known as a vaso-occlusive crisis), which is an episode of pain(Platt et al, 1991) . It is the most common reason for hospitalization in sickle cell disease.

The pattern may occur as follows (Platt et al, 1991) :

In general, the risk for a sickle cell crisis is increased by any activity that boosts the body's requirement for oxygen, such as illness, physical stress, or being at high altitudes. In more than half of episodes, however, the trigger is unknown.

Episodes typically begin at night and last 3 - 14 days, accelerating to a peak over several days and then declining.

The pain is typically described as sharp, intense, and throbbing. Severe sickle cell pain has been described as being equivalent to cancer pain and more severe than postsurgical pain. Shortness of breath is common.

Pain most commonly occurs in the lower back, leg, hip, abdomen, or chest, usually in two or more locations. Episodes usually recur in the same areas. Pain in the bones (usually occurring symmetrically on both sides) is common because blood obstruction can directly damage bone and because bone marrow is where red blood cells are manufactured.

The liver or spleen may become enlarged, causing pain in the upper right or upper left sides of the abdomen. Liver involvement may also cause nausea, low-grade fever, and increasing jaundice.

Males of any age may experience prolonged, often painful erections, a condition called priapism.

Episodes cannot be predicted, and they vary widely among different individuals. Episodes sometimes become less frequent with increasing age (Platt et al, 1991) . Generally, people can resume a relatively normal life between crises (Platt et al, 1991) . Most patients are pain-free between episodes although pain can be chronic in some cases.

2.3.10.2 Anemia due to SCD

Anemia is a significant characteristic in sickle cell disease (which is why the disease is commonly referred to as sickle cell disease).

Severe worsening of anemia: Children, adolescents, and possibly young adults may experience what is called splenic sequestration. This happens when a large amount of the sickled red blood cells collect in the patient's spleen (Bainbridge et al, 1985). Symptoms may include pain in the right abdomen below the ribs and a large mass (the swollen spleen) may be felt.

Chronic Anemia: Because of the short lifespan of the sickle red blood cells, the body is often unable to replace red blood cells as quickly as they are destroyed. This causes a particular form of anemia called hemolytic anemia

(Bainbridge et al, 1985)–. Most patients with sickle cell disease have a hemoglobin levels of 8 g/dL, much lower than people without sickle cell anemia. Chronic anemia reduces oxygen and increases the demand on the heart to pump more oxygen-bearing blood through the body. Eventually, this can cause the heart to become dangerously enlarged, with an increased risk for heart attack and heart failure (Bainbridge et al, 1985).

On occasion, patients may experience what is called an aplastic crisis. This happens when the cells in the bone marrow that are normally trying to make new red blood cells suddenly stop working. This sudden stopping is often triggered by a virus called human parvovirus B19 (Bainbridge et al, 1985).

2.3.10.3 Splenic complications

2.3.10.3.1 Autosplenectomy

The spleen is an important immunological organ that acts as a filter for red blood cells, triggers phagocytosis of invaders, and mounts an immunological response when necessary (Brousse et al, 2014). SCD cause lack of a spleen, called asplenia, occur by autosplenectomy or the surgical counterpart,

Autosplenectomy occurs when a disease damages the spleen to such an extent that it becomes shrunken and non-functional. Asplenia can increase susceptibility to infection (Brousse et al, 2014).

SCD where the misshapen cells block blood flow to the spleen, causing fibrosis and eventual atrophy of the organ (Brousse et al, 2014). 2.3.10.3.2

2.3.10.3.2 Splenomegaly and acute splenic sequestration crisis (ASSC)

The first person who conceptualized the term acute splenic sequestration crisis (ASSC) was Toppled in 1981, who defined it as acute splenic enlargement with a fall in the hemoglobin (Hb) level of at least 20 g/l (or 2 g/dL) and abnormal basal reticulocyte count (Poulin et al, 1986). It is also defined as the sudden onset of splenomegaly (greater than 2 cm from the steady-state level) or sudden enlargement of a preexisting splenomegaly in association with acute anemia, evidence of active bone marrow, and regression of splenomegaly after

blood transfusion. It is the result of rapid sequestration of RBCs in the spleen, which alters its functioning. ASSC is divided into major and minor (Poulin et al, 1986) .Minor ASSC refers to the moderate increase in splenic size and the decrease in Hb level of 2 to 3 g/dL; sometimes reaching a level as low as 2 to 3 g/dL, the spleen size regresses after blood transfusion, and there is evidence of active bone marrow.

Minor ASSC is referred as a moderate increase in splenic size and a decrease in Hb level of 2 to 3 g/dL; the spleen size regresses after blood transfusion, and there is evidence of active bone marrow.

Splenomegaly is the enlargement of the spleen. However, an enlarged or palpable spleen is not necessarily of clinical significance. Moreover, certain individuals with broadly splayed costal margins have readily palpable but small spleens. A spleen weight of 400–500 g indicates splenomegaly, and some authors consider spleens weighing more than 1000 g to have massive splenomegaly. Spleens that are prominent below the costal margin typically weigh 750–1000 g. Poulin et al. defined splenomegaly as moderate if the largest dimension is 11–20 cm and severe if the largest dimension is greater than 20 cm (Poulin et al, 1986). Hypersplenismrefers to splenomegaly and any combination of anemia, leucopenia, and thrombocytopenia, with compensatory bone marrow hyperplasia and tendency to normalization of blood parameters after splenectomy (Poulin et al, 1986) . Hyposplenism is defined as an acquired disorder caused by several hematological and immunological diseases and characterized by absent or reduced splenic function impairment (Poulin et al, 1986). The most common condition associated with hyposplenism is sickle cell anemia(Poulin et al, 1986) . RBC abnormalities, including the presence of inclusions, nucleated RBC, and target cells, are commonly present. Patients with hyposplenism are at increased risk of bacterial sepsis, especially due to infection by Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenza type b. Massive splenic

infarction (MSI) is the infarction involving more than 50% of the spleen size. It can develop spontaneously or be precipitated by other factors, namely, high altitude, acute chest syndrome, and severe stress in the form of septicemia or severe vasoocclusive crisis (Poulin et al, 1986).

ASSC is a serious and the earliest life-threatening complication seen in patients with SCA (Poulin et al, 1986). It may occur during the first weeks of life, and it could be the first symptom of the disease. Up to 75% of first cases occur before 2 years. ASSC is considered the second leading cause of death after infection in the first decade of life in these patients. These crises are usually seen in infants and young children commonly between 5 months and 2 years of age. Mortality is up to 3% in children and 10% of adults who die from hypovolemic shock given the lack of early transfusion. Other reports show mortality rates of 15%–44% (Poulin et al, 1986) Early neonatal screening and early parental education diminishes mortality rate up to 0.53%. .Between 10% and 30% of homozygous children have suffered a crisis of splenic sequestration before 3 years of age, and all patients with SCA and no fibrosis spleen are susceptible to ASSC. In homozygous patients, it usually occurs between 3 months and 3 years old, but it can occur at older ages in those treated early with hydroxyurea, delayed autosplenectomy, and also in double heterozygotes SC and S-thalassemia, in which it can occur even in adulthood. There is a recurrence in the 50% of those who survive a first episode of splenic sequestration (Poulin et al, 1986).

2.3.10.3.3 Spleen abscess

Patients with SCD are at greater risk of developing splenic sepsis(Al-Salem, 1998). Splenic abscess occurs secondary to infection of splenic infarcts. The association of splenic abscess with SCD was first reported by Beet in 1949 (Al-Salem, 1998). It is estimated that 12% of splenic abscesses occur in SCD patients, but the exact incidence of splenic abscess in SCD is unknown. Two predisposing factors were recognized:–(Al-Salem, 1998) repeated splenic

infarctions which are more likely to occur with splenomegaly and exposure to systemic bacterial infection to which SCD patients are susceptible as a result of hyposplenism. A culture of pus from the abscess may be negative as patients may be on a course of wide spectrum antibiotics prior to laparotomy. However, streptococcus milleri and other bacteria such as streptococci, staphylococci and salmonella have been isolated (Al-Salem, 1998).

Typical presentation is development of upper abdominal pain, usually at the left upper quadrant, fever and neutrophil leucocytosis. The spleen may be palpable and tender. Radiological studies such as ultrasonography and computerized tomography (CT) are crucial in the diagnosis of this condition and can be employed for guided percutaneous drainage.

SCA conditions that may require splenectomy are as follows:

Recurrent splenic sequestration crisis.

Discomfort and deterioration in quality of life secondary to hypersplenism and splenomegaly.

Splenic abscess.

Massive splenic infarction.

Splenomegaly with nonfunctioning spleen.

2.3.10.4 Hepatic complications:

The liver can be affected by a number of complications due to the disease itself and its treatment (Banerjee et al, 2001). In addition to the vascular complications from the sickling process, patients with sickle cell disease have often received multiple transfusions placing them at risk for viral hepatitis, iron overload, and (combined with the effects of chronic hemolysis) the development of pigment gallstones (cholelithiasis), choledocholithiasis and acute hepatic failure., all of which may contribute to the development of liver disease (Banerjee et al, 2001).

Disorders associated with the sickling process

Liver disease in patients with SCD can be conceptually divided into disorders caused by the sickling process, and those resulting from complications of the disease or its treatment. However, the distinction between these two categories is not always clear since both often exist concurrently.

Acute pain and jaundice — Acute presentation with pain and jaundice may be due to a several different causes, which may coexist (Ebert et al, 2010) . These include acute sickle hepatic crises, sickle cell intrahepatic cholestasis, acute viral hepatitis, cholecystitis, and choledocholithiasis with common bile duct obstruction (Ebert et al, 2010) . The diagnosis can usually be established by the medical history and specific laboratory and radiologic testing.

Acute sickle hepatic crisis — Patients usually present with acute right upper quadrant pain, nausea, low grade fever, tender hepatomegaly, and jaundice The serum total bilirubin concentration is usually <15 mg/dL (256.5 µmol/L (Hatton et al, 1985) . Liver histology may reveal sickle cell thrombi in the sinusoidal space with engorgement by red blood cells. Other features that have been described include Kupffer cell hypertrophy, mild centrilobular necrosis, and occasional bile stasis (Hatton et al, 1985) .The pathogenesis is probably related to ischemia caused by sinusoidal obstruction.

Hepatic sequestration crisis — . Patients with hepatic sequestration usually present with right upper quadrant pain, rapidly increasing hepatomegaly, and a falling hematocrit (Hatton et al, 1985) . A rapid fall in the hematocrit paralleled a dramatic increase in the liver size. Regression of hepatic size was associated with a rapid increase in hemoglobin from 4.2 to 7.5 g/dL (Hatton et al, 1985) .

Liver biopsies on patients with SCD show sinusoidal dilations, Kupifer cell hyperplasia and erythrophagocytosis (Hatton et al, 1985) .An autopsy study showed 34% of SCD patients have focal necrosis, 20% portal fibrosis and 16% micronodular cirrhosis.

The abnormalities in liver function tests tend to be more severe in vaso-occlusive episodes. Hepatocellular damage in SCD may be due to a variety of causes such as obstruction of sinusoids by sickled cells with subsequent hepatic infarction during vaso-occlusive episodes, cholelithiasis and cardiac failure. But by far the most common causes are those related to repeated blood transfusion such as haemosiderosis and viral hepatitis which lead to chronic liver disease (Hatton et al, 1985)

Disorders related to coexisting conditions

some specific medical treatments may also be associated with liver toxicity (Berry et al, 2007) .eg.

Iron overload, in patients who have received multiple transfusions, increased deposition of iron occurs within reticuloendothelial cells, including Kupffer cells.

Viral hepatitis,Chronic hepatitis B and Chronic hepatitis Calso occur in patients who have received multiple transfusions

Miscellaneous liver disorders

A number of liver abnormalities have been described in association with SCD including hepatic infarction, liver abscess

Hepatic infarction can occur when there is thrombosis or occlusion of the main hepatic artery due to skilling cells (Gauthier et al, 1985) ,

Single or multiple pyogenic abscesses can also occur if there is biliary disease (Chong et al,1993) .it have been described with an irregular shape on CT scan.

2.3.10.5 Bilary complications

Cholelithiasis. Patients with SCD are at high risk of developing pigmented gall stones due to chronic haemolysis (Schubert, 2013)

Gall stones may be asymptomatic or may present with repeated attacks of biliary colic or with acute cholecystitis (Schubert, 2013)

Choledocholithiasis. Choledocholithiasis can be caused by either primary or secondary bile duct stones. Although patients with sickle cell disease (SCD)

are at high risk of development of pigmented gallstones due to chronic hemolysis, primary choledocholithiasis in SCD is very uncommon (Schubert, 2013) .

2.3.10.6 Acute chest syndrome (ACS)

Acute chest syndrome (ACS) occurs when the lung tissues are deprived of oxygen during a crisis. It can be very painful, dangerous, and even life threatening–(Castro et al, 1994). It is a leading cause of illness among sickle cell patients and is the most common condition at the time of death. At least one whole segment of a lung is involved, and the following symptoms may be present-(Castro et al, 1994):

Fever of 101.3Â°F degrees (38.5Â°C) or above

Rapid or labored breathing

Wheezing or cough

Acute chest pain

Pain often lasts for several days. In about half of patients, severe pain develops about 2 - 3 days before there are any signs of lung or chest abnormalities (Castro et al, 1994). Acute chest syndrome is often accompanied by infections in the lungs, which can be caused by viruses, bacteria, or fungi. Pneumonia is often present-(Castro et al, 1994). A dull, aching pain usually follows, which most often ends after several weeks, although it may persist between crises (Castro et al, 1994).

2.3.10.7 Kidney problems

Sickle cell nephropathy is a type of nephropathy associated with sickle cell disease which causes kidney complications as a result of sickling of red blood cells in the small blood vessels. The hypertonic and relatively hypoxic environment of the renal medulla, coupled with the slow blood flow in the vasa recta, favors sickling of red blood cells, with resultant local infarction and papillary necrosis (Nath and Hebbel, 2015). Functional tubule defects in

patients with sickle cell disease are likely the result of partial ischemic injury to the renal tubules.

Also the sickle cell disease in young patients is characterized by renal hyperperfusion, glomerular hypertrophy, and glomerular hyperfiltration. Many of these individuals eventually develop a glomerulopathy leading to glomerular proteinuria and, in some, the nephrotic syndrome. Co-inheritance of microdeletions in the -globingene (thalassemia) appear to protect against the development of nephropathy and are associated with lower mean arterial pressure and less protein in the urine (Nath and Hebbel, 2015).

Mild increases in the blood levels of nitrogen and uric acid can also develop. Advanced kidney failure and high blood urea levels occur in 10% of cases (Nath and Hebbel, 2015). Pathologic examination reveals the typical lesion of "hyperfiltration nephropathy" namely, focal segmental glomerular sclerosis. This finding has led to the suggestion that anemia-induced hyperfiltration in childhood is the principal cause of the adultglomerulopathy (Nath and Hebbel, 2015). Nephron loss secondary to ischemic injury also contributes to the development of azotemia in these patients.

In addition to the glomerulopathy, kidney complications of sickle cell disease include cortical infarcts leading to loss of function, persistent bloody urine, and perinephrichematomas (Allon, 1990). Papillary infarcts, lead to an increased risk of bacterial infection in the scarred kidney tissues and functional tubule abnormalities. Functional tubule abnormalities such as nephrogenic diabetes insipidus result from marked reduction in vasa recta blood flow, combined with ischemic tubule injury. This concentrating defect places these patients at increased risk of dehydration and, hence, sickling crises–(Allon, 1990). Other tubule defects involve potassium and hydrogen ion excretion, occasionally leading to high blood potassium, metabolic acidosis, and a defect in uric acid excretion which, combined with increased urine synthesis in the bone marrow, results in high blood uric acid levels.

Kidney failure is a major danger in older patients and accounts for 10 - 15% of deaths in sickle cell patients (Allon, 1990). Renal medullary carcinoma is an aggressive, rapidly destructive tumor in the kidney that is rare but can occur as a result of sickle cell disease (Allon, 1990).

2.3.10.8 Other medical complications

Older children and adult patients with sickle cell are subject to other medical problems, including pulmonary hypertension, stroke, peptic ulceration, ischaemic colitis, leg ulcers, priapism, bone and joint problems, blindness and gum disease.

2.3.11 Pregnancy and sickle cell disease

Women with sickle cell disease who become pregnant are at higher risk for complications such as miscarriage, premature birth, and low birth weight (Al Jama et al, 2009). Sickle cell disease symptoms often worsen during pregnancy and pain crises become more frequent. However, with careful prenatal care and monitoring, serious problems can be avoided (Al Jama et al, 2009). Maternal mortality rates have dropped significantly over the past decades. Most women with sickle cell disease can now anticipate favorable pregnancy outcomes.

2.3.12 Diagnosis and imaging methods of sickle cell disease

Newborn baby should be evaluated by doing genetic testing screen for the condition before or after birth.

2.3.12.1 Screening before birth

Sickle cell disease can be diagnosed in an unborn baby by sampling some of the fluid surrounding the baby in the mother's womb (amniotic fluid) to look for the sickle cell gene (Clarke and Higgins, 2000).

2.3.12.2 Newborn screening

When a child has SCD, it is very important to diagnose it early to better prevent complications (Lee et al, 2000).

Every state in the United States, the District of Columbia, and the U.S. territories require that every baby is tested for SCD as part of a newborn screening program (Lee et al, 2000).

In newborn screening programs, blood from a heel prick is collected in "spots" on a special paper (Lee et al, 2000). The hemoglobin from this blood is then analyzed in special labs.

2.3.12.3 Children and adults investigation:

one or more of the following procedures may also be used to diagnose and follow up the complication of sickle cell disease:

2.3.12.3.1 Detailed patient history

This condition often first appears as acute pain in the hands and feet. Patients may also have:

severe pain in the bones, anemia, painful enlargement of the spleen, growth problems, respiratory infections, ulcers of the legs and heart problems

2.3.12.3.2 Lab blood tests

Several blood tests can be used to look for sickle cell anemia and used also on follow up (Bernard et al, 2006) ,(Clarke and Higgins, 2000)

blood counts can reveal an abnormal Hb level in the range of 6 – 8 g/dL

blood films may show RBCs that appear as irregularly contracted cells

Sickle solubility tests look for the presence of Hb S

Hb Electrophoresis: Hb electrophoresis is always needed to confirm the diagnosis of sickle cell. It measures the different types of hemoglobin in the blood.

2.3.12.3.3 Radiological investigation:

Radiological imaging are more used in follow up the sickle cell disease complications

2.3.12.3.3.1 Conventional x-ray : done routinely

requested for children and adult to detect more sickle cell disease complication (Ejindu et-al, 2004) like musculoskeletal complications, hand and foot

swelling, bone infarctions, acute chest syndrome, pneumonia, heart ventricular dilatation and some of the abdominal complications.

2.3.12.3.3.2 Ultrasound scanning: done routinely

Abdominal u/s used to diagnose manifestation of abdominal organs like hepatomegaly, liver lesions, splenomegaly, splenic abcess, splenic infarction, gall bladder stones, renal stones, renal necrosis, large kidney size or renal infarction (Ejindu et-al, 2004).

Doppler u/s used to show blood flow on vessels to search for many complications like thrombus and transcranial Doppler blood flow in stroke cases.

Echocardiography: search for pulmonary hypertension, atrium and ventricular dilatation or increasing in heart size.

2.3.12.3.3.3 CTA scan:

Cerebrovascular complications (Ejindu et-al, 2004)

Chest complications like pneumonia, acute chest syndrome and pulmonary disease (Ejindu et-al, 2004)

Abdominal organs complications (Ejindu et-al, 2004),

hepatobiliary like hepatic crisis, Acute hepatic failure ,hepatomegaly, Cholelithiasis, gall stones, Post-cholecystectomy complications and choledocholithiasis.

Spleen complications (Ejindu et-al, 2004) like Acute splenic sequestration crisis, Splenic abscess, splenic infarctions

Gastrointestinal complications (Ejindu et-al, 2004) like ischaemic colitis

Renal manifestations like kidney failure renal medullary carcinoma and so on.

CTA :neurological complication acute territorial infarction, silent ischemia, intracranial hemorrhage, pulmonary artery occlusion and collateral vessels at various organs (Ejindu et-al, 2004).

2.3.12.3.3.4 MRI and MRA:

MRI is used mainly in diagnosis of musculoskeletal and brain complications (Ejindu et-al, 2004).

MRA: Neurological complications

2.3.12.3.3.5 Scintigraphy scanning:

Different findings in Tc-99m MDP scintigraphy of patients with sickle cell disease (Ejindu et-al, 2004).

for e.g.

Pulmonary vascular occlusion and acute chest syndrome bone.

Bone infarction, osteomyelitis and bone marrow necrosis.

Splenic infarction, vaso-occlusive episodes in the kidneys, enlarged kidneys and increased activity in the spleen.

Penile scintigraphy for priapism.

2.4 CT physics and technique of the abdomen and chest

CT, or CAT scans, are special X-ray tests that produce cross-sectional images of the body using X-rays and a computer. CT scans are also referred to as computerized axial tomography. CT was developed independently by a British engineer named Sir Godfrey Hounsfield and Dr. Alan Cormack(Zatz, 1981).

It has become a mainstay for diagnosing medical diseases. For their work, Hounsfield and Cormack were jointly awarded the Nobel Prize in 1979(Zatz, 1981).

The x-ray images used to generate the tomographic images are generated first by exposing the patient to a fan-shaped x-ray beam and then detecting the projected image on a thin semicircular, digital x-ray detector. The patient is placed between the source and detector, and the detector is configured with its geometric center located at the x-ray source. Each image is an x-ray projection of a very thin transverse slice of the body(Zatz, 1981).

To collect the multitude of x-ray projections necessary to generate a tomographic CT image, both the x-ray source and detector are rotated about a

patient within a supporting gantry. While the source and detector rotate, images are collected and stored(Zatz, 1981).

As in a traditional x-ray, the signal levels in the image slice represent the relative radio density of the patient along a line from the x-ray source to the corresponding pixel location.

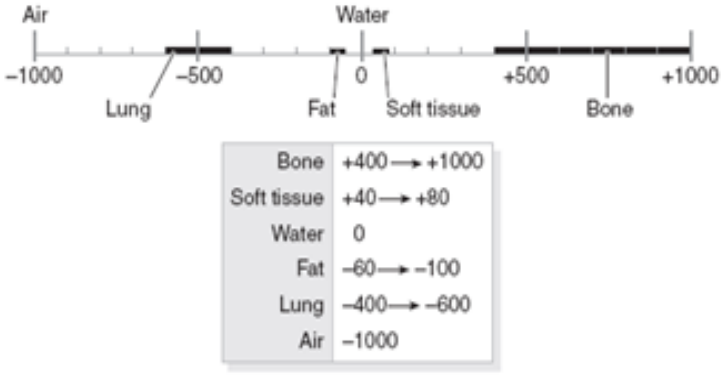
2.4.1Data acquisition:

Every acquired CT slice is subdivided into a matrix of up to 1024 ×1024 volume elements (voxels). Each voxel has been traversed during the scan by numerous X-ray photons and the intensity of the transmitted radiation measured by detectors. From these intensity readings, the density or attenuation value of the tissue at each point in the slice can be calculated(Pullan et al.1981). Specific attenuation values are assigned to each individual voxel. The viewed image is then reconstructed as a corresponding matrix of picture elements (pixels).

2.4.1.1Hounsfield unit or CT number:

Each pixel is assigned a numerical value (CT number), which is the average of all the attenuation values contained within the corresponding voxel. This number is compared to the attenuation value of water and displayed on a scale of arbitrary units named Hounsfield units (HU) after Sir Godfrey Hounsfield(Pullan et al,1981)(figure 2.4.1).

This scale assigns water as an attenuation value (HU) of zero. The range of CT numbers is 2000 HU wide although some modern scanners have a greater range of HU up to 4000. Each number represents a shade of grey with +1000 (white)and –1000 (black) at either end of the spectrum(Pullan et al,1981)



(Figure 2.4.1):The Hounsfield scale of CT number(Pullan et al,1981).

2.4.1.2Window level (WL) and window width (WW)

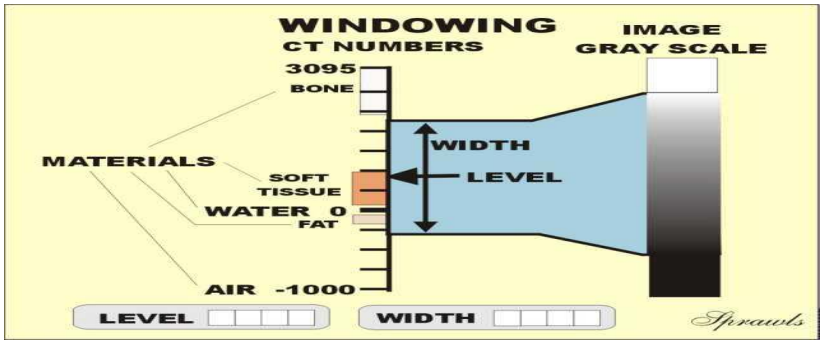
Whilst the range of CT numbers recognized by the computer is 2000, the human eye cannot accurately distinguish between 2000 different shades of grey.

Therefore to allow the observer to interpret the image, only a limited number of HU are displayed. A clinically useful grey scale is achieved by setting the WL and WW on the computer console to a suitable range of Hounsfield units, depending on the tissue being studied(Pullan et al,1981).

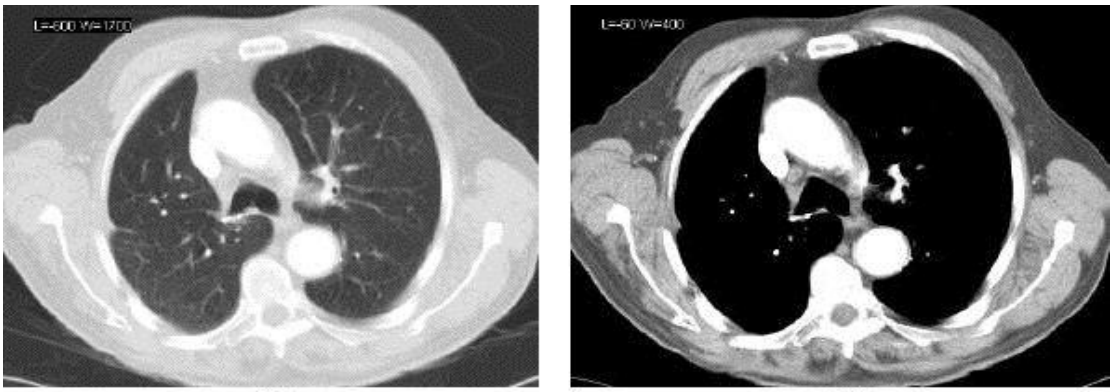
The term 'window level' represents the central Hounsfield unit of all the numbers within the window width(Pullan et al,1981).

The window width covers the HU of all the tissues of interest and these are displayed as various shades of grey (figure 2.4.2). Tissues with CT numbers outside this range are displayed as either black or white(Pullan et al,1981). Both the WL and WW can be set independently on the computer console and their respective settings affect the final displayed image.

For example, when performing a CT examination of the chest, a WW of 350 and WL of +40 are chosen to image the mediastinum (soft tissue) (Figure 2.4.3 a),whilst an optimal WW of 1500 and WL of –600 are used to assess the lung fields (mostly air) (Figure 2.4.3 b).



(Figure 2.4.2): Windowing CT numbers(Pullan et al,1981)



(Figure 2.4.3):Effect of window width and level: (a) Level = -600; Width = 1700. (b) Level = -60; Width = 400. Image (a) displays the lung tissue more clearly, while image (b) can be used to highlight any pulmonary lesions(Pullan et al,1981).

2.4.2Abdominal CT scan:

2.4.2.1Indications:

To evaluate cystic disease of abdominal organs.

To evaluate solid tumors of abdominal organs such as Hepatocellular Carcinoma, Adenocarcinoma, Haemangioma etc.

To demonstrate inflammatory changes of abdominal organs such as cirrhosis, abscess, cholecystitis, cholelithiasis, pancreatitis, ascitis, peritoneal metastasis, pyelonephritis etc.

In case of trauma of abdominal organs such as renal trauma, splenic trauma, peritoneal trauma etc.

Planning of radiation therapy for cancer of abdominal organs.

Guiding the passage of needle used to obtain a tissue sample.

Initial staging of GIT neoplasms.

Detecting and staging post operative recurrence of tumor.

2.4.2.2 General consideration about routine adult abdominal CT technique

All CT scans must be closely monitored by a radiologist, who may modify these procedures as needed. According to hospital and Medical Group compliance guidelines, a CT of the abdomen does not include the pelvis unless the requesting

clinician has ordered both "abdomen and pelvis." (Shaw and Prokop, 2015)

2.4.2.2.1 Patient preparation:

Patient is asked to wear comfortable, loose fitting clothing for CT scan.

Come with empty stomach for about 6 hours before scanning for CECT.

Anything that might interface with imaging abdomen such as belts, keys should be removed (Shaw and Prokop, 2015).

The patient must be instructed to void and empty the urinary bladder 1 hour before the start of the exam (Shaw and Prokop, 2015).

Patient is asked to arrive 1 hour before the scanning and should be given oral contrast first dose 45 minutes before study, second dose 30 minutes prior to the study and third dose just before scanning (Shaw and Prokop, 2015).

Explain the patient about the CT machine and the breathing commands as the patient must be familiar oneself with the procedure and be able to co-operate during the examination (Shaw and Prokop, 2015).

2.4.2.2.2 Patient positioning:

Patient is asked to lie down on the couch in supine position.

Arms are usually positioned above the head to eliminate artifact and instruct patient not to move during scanning (Shaw and Prokop, 2015).

Patient is positioned into the gantry with the help of laser light accurately.

Height and position of table is fixed and cleared to make table position zero (Shaw and Prokop, 2015).

2.4.2.2.3 Technique:

Patient data is entered into the register in the computer.

Scanogram of the abdomen is taken with the following parameters (Shaw and Prokop, 2015):

Scan collimation 5 mm, Scan length 500 mm, Filter 2, Mode PA, Tube orientation Inward, KV/mA 120 KV/100mA, Matrix 512

Routine abdomen CT is performed in axial axis.

Slices are started from the top level of dome of diaphragm to the iliac crest in case of upper abdomen and for pelvic cavity from iliac crest to symphysispubis (Shaw and Prokop, 2015).

Slice thickness varies but routine study slices are of 8-10 mm thick.

Field of view is adjusted according to the size of the body.

Normal scan is started with following protocol (Shaw and Prokop, 2015):

Thickness 10 mm, mA 200, FOV 350 mm, Index 10, Scan time 1 sec

KV 120, Matrix 512, Filter 3

After finishing the plain normal scan CM is injected through the median antecubital vein according to the dose required for patient (80-100ml) (Shaw and Prokop, 2015).

In general CM is injected for indication which includes determining the vascular characterization of mass, differentiation of a vascular anomaly or abnormality from a neoplasm and maximizing lesion detectability.

After scan is finished, scan is stopped and couch is taken out from the gantry and gantry is parked at its original position.

All the images with topogramis printed with proper WW (240) and WC (40) on 14"x17" film in 5x6 format. Then film is developed or may receive as dry film by dry silver image processor (Shaw and Prokop, 2015).

But radiation exposure during a CT scan depends on the parameters used for the scan, such as the kilovoltage (kVp) and milliamperage (mA) selected, as well as factors such as speed of tube rotation, speed of table advancement, and the volume of tissue scanned(Shaw and Prokop, 2015).

A patient with a large body habits represents a challenge, as the exposure parameters need to be increased to generate images of adequate diagnostic quality, with a resultant increase in absorbed dose.

Notes about some previous techniques.

2.4.2.2.4 Breath hold technique

If possible, all abdominal CT scanning should be done during a single breath hold (Shaw and Prokop, 2015). It is often helpful to coach the patient regarding breathing, and hyperventilating the patient prior to scanning.

Emphasize to the patient that it is important that he or she does not breathe or move during the study.

If it is absolutely necessary to let the breath out early, tell them to let it out slowly and evenly because this causes less motion artifact. Instruct the patient to take a deep breath in and out several times. Prior to scanning, ask the patient to take a medium-sized breath in and hold it. When performing a multiphase study such as a triple-phase liver or pancreas protocol, instruct the patient to try to take the same sized breath with each scanning phase (Shaw and Prokop, 2015). With 16 slice scanners and above, quite shallow breathing may be best approach (Shaw and Prokop, 2015).

2.4.2.2.5 Image reconstruction

Certain indications may require that images be reconstructed in coronal and/or sagittal planes.

Very thin images may need to be reconstructed to serve as source images for the sagittal and/or coronal reformatted images.

Creation, use, and archival of these additional images are at the discretion of the supervising radiologist and/or departmental policy. Very large datasets may result from these additional reconstructions.

2.4.2.2.6 Radiation dose management

AEC should be used whenever possible (Kim and Pickhardt, 2011).

Be careful attention to the values selected to define the desired level of image quality (eg, noise index, quality reference mAs, standard deviation) (Kim and Pickhardt, 2011).

Each manufacturer will have recommendations unique to their systems and system features.

Be sure to work with your CT equipment manufacturer and a qualified medical physicist to ensure safe and appropriate operation of AEC systems (Kim and Pickhardt, 2011).

If more than one CT localizer radiograph is acquired, AEC systems from different manufacturers can differ with respect to which one is used to determine mA and/or kV settings.

2.4.2.2.7 Basics protocol of contrast-enhancement CT abdomen

During contrast enhancing abdominal computed tomography examinations, patients asked to take a special contrast agent (orally, rectally or via injection) (Rubin, 2014). Intravenous, oral and rectal CT contrast are pharmaceutical agents (liquids) and are sometimes referred to as "dye". CT contrast is used to make specific organs, blood vessels and/or tissue types "stand out" with more image contrast to better show the presence of disease or injury.

2.4.2.2.7.1 Intravenous contrast agent

Iv contrast scans can be classified as single-phase, multiphase, or special.

Single-phase scans are typically used to evaluate acute abdomen or suspected abdominal infections, with imaging usually in the portal venous phase (Rubin, 2014). It is usually combined with administration of oral contrast. Oral or intraluminal contrast enhances the evaluation of the bowel.

Multiphase scans consist of precontrast and combinations of arterial phase, portal venous phase, and delayed imaging, depending on the organ of interest (Rubin, 2014).

Special phases include:

CT cystography uses water-soluble dilute iodinated contrast introduced via a catheter into the bladder, typically to evaluate for bladder rupture or leak (Vaccaro and Brody, 2010) CT enterography combines a negative contrast agent (Volumen) and multiphase scanning to evaluate bowel, arterial supply, and mesenteric and portal venous integrity (Ilangovan et al, 2012) CT colonography uses a noncontrast protocol in supine and prone positions after insufflation of the prepared large bowel with gaseous carbon dioxide at a controlled pressure.

2.4.2.2.7.2 Phases of enhancement

The purpose of contrast-enhanced CT (CECT) is to find pathology by enhancing the contrast between a lesion and the normal surrounding structures (Ilangovan et al, 2012).

Sometimes a lesion will be hypovascular compared to the normal tissue and in some cases a lesion will be hypervascular to the surrounding tissue in a certain phase of enhancement.

So it is important to know in which phase a CT should be performed depending on the pathology that is looking for.

Scroll through the images to see the enhancement in the different phases.

Non-enhanced CT (NECT) helpful in detecting calcifications, fat in tumors, fat-stranding as seen in inflammation (Ilangovan et al, 2012) like appendicitis, diverticulitis, omental infarction etc.

Early arterial phase - 15-20 sec or immediately after bolustracking. This is the phase when the contrast is still in the arteries and has not enhanced the organs and other soft tissues (Ilangovan et al, 2012).

Late arterial phase - 35-40 sec or 15-20 sec after bolustracking. Sometimes also called "arterial phase" or "early venous portal phase", because some enhancement of the portal vein can be seen. All structures that get their blood supply from the arteries will show optimal enhancement (Ilangovan et al, 2012).

Hepatic or late portal phase - 70-80 sec or 50-60 sec after bolus tracking. Although hepatic phase is the most accurate term, most people use the term "late portal phase". In this phase the liver parenchyma enhances through blood supply by the portal vein and should see already some enhancement of the hepatic veins (Ilangovan et al, 2012).

Nephrogenic phase - 100 sec or 80 sec after bolus tracking. This is when all of the renal parenchyma including the medulla enhances. Only in this phase will be able to detect small renal cell carcinomas (Ilangovan et al, 2012).

Delayed phase - 6-10 minutes or 6-10 minutes after bolus tracking. Sometimes called "wash out phase" or "equilibrium phase". There is wash out of contrast in all abdominal structures except for fibrotic tissue, because fibrotic tissue has a poor late wash out and will become relatively dense compared to normal tissue (Ilangovan et al, 2012).

2.4.2.2.7.3 Timing of CECT

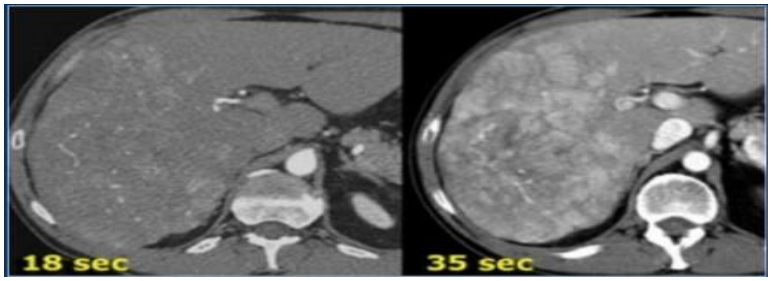
Timing of CT-series is important in order to grab the right moment of maximal contrast differences between a lesion and the normal parenchyma (Rubin, 2014).

The CT-images show an early arterial phase in comparison to a late arterial phase.

The CT-images are of a patient who underwent two phases of arterial imaging at 18 and 35 seconds (Rubin, 2014).

In the early arterial phase nicely see the arteries, but only see some irregular enhancement within the liver.

In the late arterial phase can clearly identify multiple tumor masses (Rubin, 2014) (figure 2.4.4).



(Figure 2.4.4):Hypervascular lesion is best seen in late arterial phase (Rubin, 2014).

Should have to adapt the protocol to the type of scanner, the speed of contrast injection and to the kind of patient that are examining.

If have a single slice scanner, it will take about 20 seconds to scan the liver.

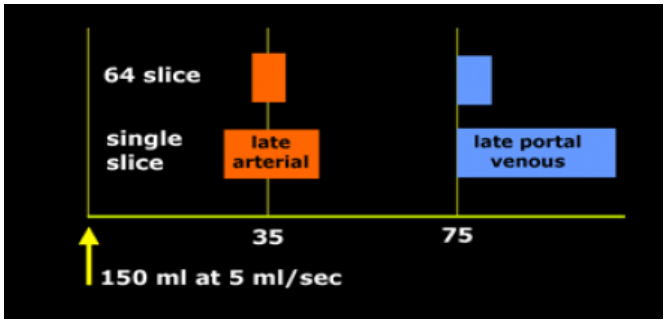
For late arterial phase imaging 35 sec is the optimal time (Rubin, 2014), so starts at about 25 seconds and end at about 45 seconds.

However if have a 64-slice scanner, will be able to examine the whole liver in 4 seconds (Rubin, 2014). So starts scanning at about 33 seconds, which is much later.

In arterial phase imaging the time window is narrow, since have only limited time before the surrounding liver will start to enhance and obscure a hypervascular lesion.

For late portal venous phase imaging it is different. Here don't want to be too early, because want to load the liver with contrast and it takes time for contrast to get from the portal vein into the liver parenchyma (Rubin, 2014). Besides have more time, because the delayed or equilibrium phase starts at about 3-4 minutes (Rubin, 2014).

So starts at 75 seconds with whatever scanner have (figure 2.4.5).



(Figure 2.4.5): Late arterial and late portal venous phase at the various scanning types (Rubin, 2014)

2.4.2.2.7.4 Total amount of contrast

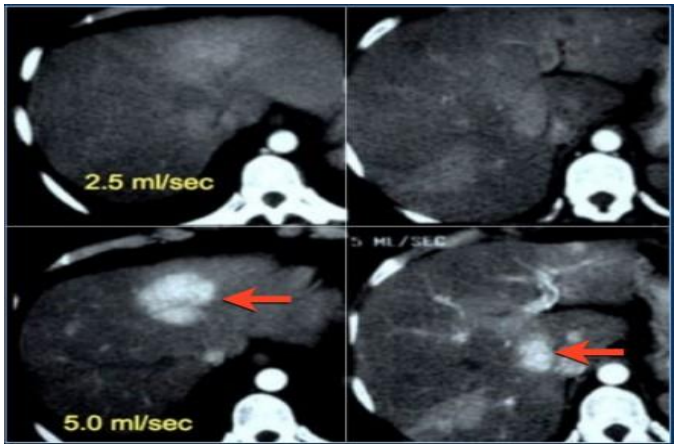
In many protocols a standard dose is given related to the weight of the patient (Amera et al, 2015):

Weight < 75kg : 100cc

Weight 75-90kg: 120cc

Weight > 90kg : 150cc

In some protocols always want to give the maximum dose of 150cc, like when looking for a pancreatic carcinoma or liver metastases (figure 2.4.6).



(Figure 2.4.6): Patient with liver cirrhosis and multifocal HCC injected at 2.5ml/sec (left) and at 5ml/sec (right) (Amera et al, 2015)

2.4.2.2.7.5 Injection rate

5cc/sec through a 18 gauge i.v. catheter

For all indications, but especially for GI-bleeding, liver tumor characterization, pancreatic carcinoma, pulmonary emboli.

Use for instance a green venflon. Test by fast injection of 10cc NaClmanually (Amera et al, 2015).

Hold the arm stretched.

3-4cc/sec through a 20 gauge pink venflon

If 5cc/sec is not possible or not needed because only interested in the late portal phase.

The upper images are of a patient with liver cirrhosis and multifocal hepatocellular carcinoma examined after contrast injection at 2.5ml/sec(Amera et al, 2015).

Because of poor enhancement the examination was repeated at 5ml/sec. There is far better contrast enhancement and better tumor detection (Amera et al, 2015).

2.4.2.2.8 Oral contrast agent

Some prefer to give positive oral contrast to mark the bowel (Koo et al, 2008).

This however has some disadvantages (Koo et al, 2008) :

Usually only a portion of the bowel is filled with contrast.

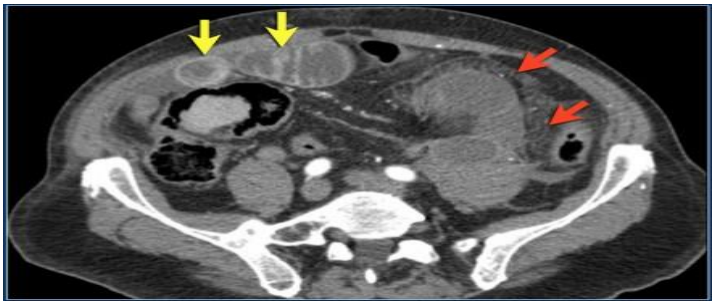
More radiation is needed in areas of positive contrast to get the same quality of images.

Enhancement of the bowel wall is obscured.

Use fat containing milk as negative oral contrast or if the patient doesn't drink milk simply use water (Koo et al, 2008).

Polyethylene glycol (PEG) is also used, and Volumen, which is a low density barium suspension.

PEG and Volumen have the advantage that there is better bowel distension.



(Figure 2.4.7): The CT-image shows nice enhancement of the normal bowel wall (yellow arrows) and no enhancement of the infarcted bowel (red arrows). This would not be visible if positive oral contrast was given (Koo et al, 2008).

2.4.2.2.9 Rectal contrast

Rectal contrast is given in cases of suspected bowel perforation or anastomosis leakage.

Use positive contrast: 750 cc water with 50 cc non-ionic water soluable contrast.

2.4.2.3 General consideration about routine pediatric abdominal CT technique

Pediatric protocols differ from adult protocols (Shrimpton and Wall, 2000) for the following reasons:

Radiation dose is only one reason.

Safety issues (medication, sedation).

Children do not cooperate until they understand and feel safe.

The pathology we look for is often different.

Children have congenital anomalies and infections much more commonly than adults

When children have cancer, they have sarcomas whereas adults have carcinomas. These cancers occur in different places and act differently.

2.4.2.3.1 Patient preparation:

Child should wear comfortable, loose-fitting clothing to the exam. He or she given a gown to wear during the procedure (Shrimpton and Wall, 2000).

Metal objects have to be removed prior to exam. Child asked not to eat or drink anything for several hours, especially if a sedative or anesthesia will be used in the exam. Should also inform physician of any medications which child is taking and if he/she has any allergies, especially to intravenous (IV) or oral contrast materials.

Also inform the doctor of any recent illnesses or other medical conditions that child may have, and if there is a history of heart disease, asthma, diabetes, kidney disease or thyroid problems. Any of these conditions may influence the decision on whether contrast material will be given to the child for the examination (Shrimpton and Wall, 2000).

2.4.2.3.2 Patient positioning:

The technologist begins by positioning the patient on the CT examination table, lying flat on his/her back, feet first (Shrimpton and Wall, 2000). Straps and pillows may be used to help the patient maintain the correct position and to hold still during the exam.

2.4.2.3.3 Technique:

(Table 2.4.1): Technical parameters of pediatric abdominal CT scan (Shrimpton and Wall, 2000):

Technical parameters	**parameters**
KVp	120
Time (rotation)	0.33 sec
Average acquisition time	4-5 sec
Collimation	64 x 0.6mm
Pitch value	2.5-3.0
Scan direction	Craniocaudal
Comments: The effective mAs is adjusted using guidelines based upon the patient's body habits, weight, and age.	

2.4.2.3.4 Image reconstructions:

(Table 2.4.2): Reconstruction parameters of pediatric abdominal CT scan (Shrimpton and Wall, 2000):

Reconstruction parameters	**Soft tissue**
Slice thickness	3mm
Reconstruction spacing	3mm
Reconstruction algorithm	B30f
Window width and level	410 / 10
Reconstruction comments: coronal and sagittal reconstructions are performed	

2.4.2.3.5 Contrast-enhancement

2.4.2.3.5.1 Oral contrast agent

Types: Water, water soluble contrast, about 1.5% to 3 % concentration

Reason for oral contrast for abdomen: less intraabdminal and pelvic fat in the pediatric group and un-opacified bowel loop like a mass or abnormal fluid collection.

2.4.2.3.5.2 IV contrast

Check allergic history, asthma, previous reaction and consent from parents

(Table 2.4.3): Intravenous and oral contrast agent (total amount of contrast and injection rate) (Shrimpton and Wall, 2000).

Contrast parameters	**parameters**
Contrast type	Non ionicomnipaque
Contrast volume	weight based
Saline flush	N/A
Injection rate	1.5-3ml / sec
Oral contrast	Non ionic water soluble
Contrast volume	weight based
Comments: The scan delay is determined both in part by patient age, IV access, and injection rate.	

Other Comments: IV contrast is given when indicated to patients based upon their weight1.5ml per kg. The ratio of 1ml/lb is used up to 120ml. Images should be acquired during peak portal venous enhancement, which will vary based upon patient age, weight, and IV access.

(Table 2.4.4): The amount of oral contrast is determined by the patient's weight (Shrimpton and Wall, 2000):

Weight (kg)	**Contrast**
1-7 kg	40-60 ml
8-11 kg	110-160 ml
12-15 kg	165-240 ml
16-42 kg	250-360 ml
Over 42 kg	480 +

2.4.2.3.5.3 Phases of enhancement

Arterial phase(CTA)

Smart prep for arterial phase,

CTA is performed with a fast contrast injection and then flushing the contrast medium with equally fast saline injection

When examining babies, the injection rate of 1–1.5 ml/s is usually enough, and with older children 2–3 ml/s. An injection rate of 4–5 ml/s may be sometimes needed but usually only when imaging teenagers.

The arterial phase begins 15 to 25 secs after the start of contrast injection

Portal venous phase

Scan immediately after arterial phase

It begins 45 to 50 secs after the start of contrast injection

The contrast agent volume and flow rate are the same as described above.

Delay image

It consider very important technique because Infants have shorter circulation time due to: Faster heart rate and shorter distance than adult.

Scan delay depends on the child's size, the cannula used and the injection rate. As general scan delay time is 50 to 60 secs after contrast administration.

2.4.2.3.5.3 Rectal contrast

It's very rarely given.

Reason for not using rectal contrast in children: pain, uncooperative

2.4.2.3.6 Radiation dose management

(Table 2.4.5): The effective mAs for a pediatric abdomen CT is calculated using the following table (Strauss et al, 2009).

Weight (kg)	Effective mAs	Care dose
<15	45-65 mAs	
15-24	70-85 mAs	
25-34	85-95 mAs	
35-44	100-110 mAs	
45<	Care dose	125 ref mAs

General guidelines about reduction of the dose (Parker, 2001)

ALARA principle, lower mA and kVp, modulation automatic exposure control-~65% lower dose as compared with fixed tube current, collimation and pitch, limit the scanning range and in-plane bismuth shielding.

2.4.2.3.7 Breath hold

A > 5 years single breath holding (Shrimpton and Wall, 2000)

B <5 Unable to co operate Quiet respiration may require anesthesia or sedation (Shrimpton and Wall, 2000)

2.4.2.3.8 Technique of sedation

2.4.2.3.8.1Orally or rectally

Thirty minutes to one hour before the procedure (Malviya et al, 2000).

(Table 2.4.6): Amount of sedation in different age/weight pedia (Malviya et al, 2000):

Age / Weight	**Sedation**
< 1 month old	Comfort by feeding and wrapping the Child
Under 1 year old or up to 10kg	75mg/kg chloral hydrate
10 kg – 15 kg or up to 3 years of age	100mg/kg chloral hydrate
> 15 kg and/or over 3 years of age	Sedation unlikely to be effective, to be assessed on individual basis, if unable to undertake procedure without sedation consider a general anaesthetic

2.4.2.3.8.2 Intravenously

propofol, dexmedetomidine, ketamine, or etomidate.

IV short-acting barbiturates (eg, pentobarbital or methohexital) or midazolam , 5mg/kg to a maximum dose of 200mg (Malviya et al, 2000).

Children older than 5 years of age will cooperate after verbal reassurance and explanation of the procedure (Malviya et al, 2000).

Neonates and small infants scan during sleeping after feeding (Malviya et al, 2000).

2.4.2.4 Benefits of the abdomen and pelvis CT scan

Viewing a CT scan, an experienced radiologist can diagnose many causes of abdominal pain with very high accuracy, enabling faster treatment and often eliminating the need for additional, more invasive diagnostic procedures.

When pain is caused by infection and inflammation, the speed, ease and accuracy of a CT examination can reduce the risk of serious complications such as those caused by a burst appendix or ruptured diverticulum and the subsequent spread of infection.

CT scanning is painless, noninvasive and accurate.

Unlike conventional x-rays, CT scanning provides very detailed images of many types of tissue CT examinations are fast and simple; in emergency cases, they can reveal internal injuries and bleeding quickly enough to help save lives.

CT has been shown to be a cost-effective imaging tool for a wide range of clinical problems.

CT is less sensitive to patient movement than MRI.

CT can be performed if you have an implanted medical device of any kind, unlike MRI.

CT imaging provides real-time imaging, making it a good tool for guiding minimally invasive procedures such as needle biopsies and needle aspirations of many areas of the body, particularly the lungs, abdomen, pelvis and bones.

A diagnosis determined by CT scanning may eliminate the need for exploratory surgery

No radiation remains in a patient's body after a CT examination.

X-rays used in standard CT scans have no immediate side effects.

2.4.2.5 Risks of the abdomen and pelvis CT scan

There is always a slight chance of cancer from excessive exposure to radiation (Brenner and Elliston, 2004). However, the benefit of an accurate diagnosis will generally outweigh the risk.

The effective radiation dose for this procedure varies(Brenner and Elliston, 2004) .

Women should always inform their physician and x-ray or CT technologist if there is any possibility that they are pregnant.

CT scanning is, in general, not recommended for pregnant women unless medically necessary because of potential risk to the baby(Brenner and Elliston, 2004) .

The risk of serious allergic reaction to contrast materials that contain iodine is extremely rare, and radiology departments are well-equipped to deal with them (Radhakrishnan et al, 2005).

2.4.3 HRCT imaging technique

Two techniques have been used (Sundaram et al, 2010):

2.4.3.1 Spaced Axial

Thin sections are acquired with an interval of 1-2 cm between the two sets of images (Sundaram et al, 2010). It has been considered sufficient to detect abnormalities in diffuse lung diseases. This technique is most useful when single detector CT is being used (Sundaram et al, 2010). The patient dose is less as compared to volumetric imaging.

2.4.3.2 Volumetric HRCT

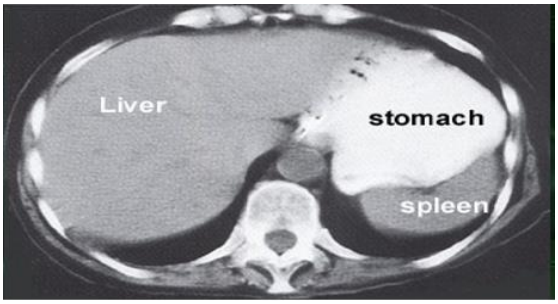
Thin sections are acquired continuously using multidetector row CT scanners in a single breath hold. Volume imaging with thinner slices allows detection of a greater degree of pathology and also allow reconstruction in any plane (Sundaram et al, 2010). Patient dose is higher compared to axial imaging.

Fundamental technical protocols (Sundaram et al, 2010)

Slice thickness: 0.625-1.25 mm, Scan time: 0.5-1 second, kV: 120, mAs: 100-200, Collimation: 1.5-3 mm, Matrix size: 768 x 768 or the largest available, FOV: 35 cm, Reconstruction algorithm: high spatial frequency, Window: lung window, Patient position: supine (routinely) or prone (if suspected ILD), Level of inspiration: full inspiration (routinely recommended) expiratory HRCT scans at three or more levels in patients with obstructive lung diseases.

2.5 Normal appearance CT features of certain abdominal organs regarding to study:

2.5.1 Liver:



(Figure 2.5.1): Unenhanced, axial scan: A normal liver scan (Henderson et al, 1981)

2.5.1.1Normal liver length

Liver length is used to measure at the level of lower third of T9 which is the point of biggest liver length, & it measures from mid hepatic point (MHP) in max AP direction to the liver tip. M.HP: from anterior to posterior margin of the liver at the level of main portal vein (Henderson et al, 1981).

Normal liver length in CT image is varies depending on human age.

In children (from 1 month to 12 years) (Henderson et al, 1981):

(Table 2.5.1): Liver length differs according to children ages:

Age	liver length
1-3 months	6.5 cm
3-6 months	7.1 cm
6-12 months	7.5 cm
1-2 years	8.6 cm
2-4 years	9 cm
4-6 years	10 cm
6-8 years	10.3 cm
8-10 years	10.5 cm
10-12years	10.6 cm

Increasing over any of those previous regular severally values is considered to be hepatomegaly.

In adults (up to 12 years):

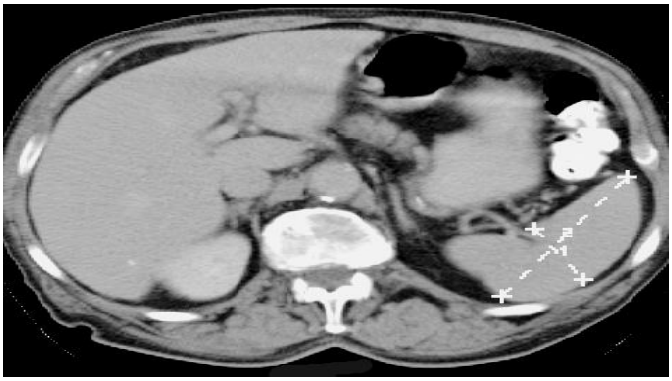
Liver length is range from 10.7-12.5 cm in craniocaudal length (Henderson et al, 1981). The liver size increased progressively from birth to 13 years with accelerated growth in the first year. Up to 15.5 cm length in adults consider hepatomegaly.

2.5.1.2 Normal liver CT number (HU unit)

Normal Hounsfield unit of the liver is used to measure at the center of the RT lobe in free lesion area after enhancing contrast media, the normal Hounsfield values of the liver has being ranged from(55-65 HU)before contrast enhancing (Kodama et-al, 2007) and it will be increase more than this after enhancing.

Any decreasing in liver CT number –before contrast– away from this range is considered to be abnormal.

2.5.2 Spleen



(Figure 2.5.2): CT examination: Unenhanced, axial scan: A normal-sized, smooth-contoured, homogenous spleen is visible (marked axes) on the left side (Henderson et al, 1981).

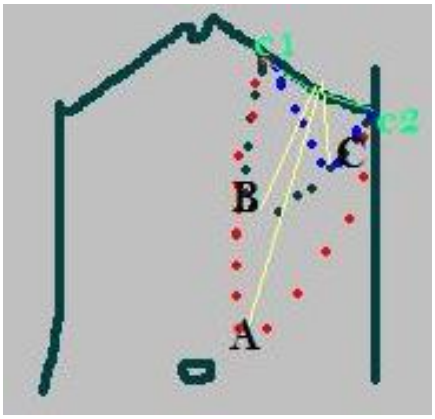
2.5.2.1 Normal length& width of the spleen

Normal measurements of spleen are always done at the level of lower third of T9 which is the highest point of the spleen (Henderson et al, 1981).

The correct way to measure spleen length is the length from the tip of the spleen along the long axis, at the midpoint of green line C, the line that joins

the points c1 and c2, that are the points where spleen gets retrocostal (Henderson et al, 1981) (figure 2.5.11).

From dome to tip through the hilum (craniocaudal direction). Measurement of the width of the spleen was made at the hilum.



(Figure 2.5.3): Way of spleen measurements (Henderson et al, 1981)

Normal length and width of the spleen in CT image are vary depending on human age.

In children (from 1 month to 12 years) (Henderson et al, 1981):

(Table 2.5.2): Length of spleen differs according to children ages (Henderson et al, 1981):

Age	**Spleen length**	**Spleen width**
1-3 months	4.9 cm	3.45 cm
3-6 months	5.4 cm	3.7 cm
6-12 months	6 cm	4 cm
1-2 years	6.4 cm	4.2 cm
2-4 years	6.9 cm	4.45 cm
4-6 years	7.4 cm	4.7 cm
6-8 years	7.9 cm	4.95 cm
8-10 years	8.2 cm	5.1 cm
10-12years	8.7 cm	5.35 cm

Increasing over any of those previous regular severally values is considered to be splenomegaly.

In adults: (up to 12 years) (Henderson et al, 1981).

Spleen length is ranged from 12-13 cm and normal width is about 7 cm.

Up to 13cm length and 7cm width in adults consider splenomegaly.

2.5.2.2 Normal shape & location of the spleen:

Shape:

The shape is influenced by adjacent organs, but the commonly shape is fist shape and has medial concavity (Piekarski et al, 1980) .

Change in shape will considered to be abnormal for e.g.

If the spleen is showing enlarged or loss it's medial concavity or appear in pyramidal shape this indicate presence of splenomegaly.

If the spleen is showing atrophied or very small or shrunken and totally calcified this confirm presence of disorder.

Location: LT hypochondrum, between fundus of stomach and diaphragm (Piekarski et al, 1980).

Change in location also will considered to be abnormal for e.g.

If the spleen is appear extend to the lower third of LT kidney this give signal to presence of splenomegaly.

2.5.2.3 Normal CT number of the spleen:

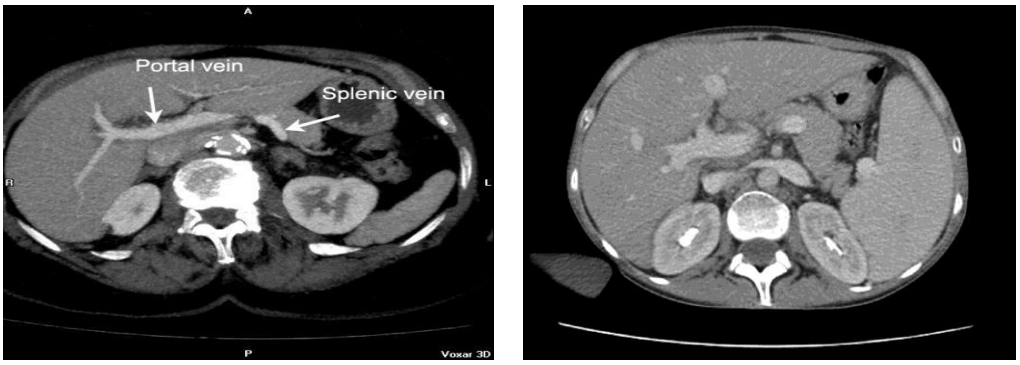
Normal Hounsfield unit of the spleen is have to range from (40-60 HU) before contrast enhance (Kodama et-al, 2007). On contrast-enhanced, arterial-phase CT images, the spleen typically shows a heterogeneous enhancement pattern due to variable flow rates of contrast-enhanced blood through the sinuses of the red pulp. On contrast-enhanced, portal venous-phase CT images, healthy splenic parenchyma has a homogenous appearance and give measuring over 60 HU (Kodama et-al, 2007).

Any decreasing in CT number –before contrast– away from this range is considered to be abnormal.

2.5.2.4 Splenic vein diameter:

Diameter of splenic vein measures at the level of L1, posterior to the neck of pancreas-(Anakwue, 2009).

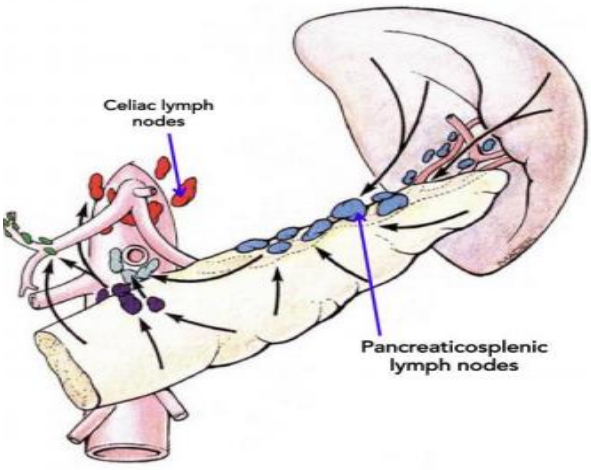
The normal diameter of splenic vein in CT is about <10mm (Anakwue, 2009), So increasing in splenic vein diameter more than this range diagnosed as splenic vein dilatation (figure 2.4.12b), which may occur due to thrombosis, vein obstruction, portal hypertension, splenomegaly, liver disorderor other causes.



(Figure 2.5.4): a, Normal splenic vein b, dilated splenic vein (Anakwue, 2009)

2.5.2.5 Spleen lymph node

lymph nodes of the spleen are small, oval or kidney-shaped (Hegde and Kohli, 2005). They vary in size from 0.1 to 0.4 cm in length (Hegde and Kohli, 2005).



(Figure 2.5.5): Splenic lymphnodes (Hegde and Kohli, 2005)

Presentation of spleenic lymph nodes enlargement in CT :

CT usually shows a huge round or lobular mass (>0.8 cm in size) (Hegde and Kohli, 2005) and tend to have a lower attenuation than that of surrounding organs with a homogeneous density and uniform enhancement.

2.6 CT findings of some abdominal organs complication in patients with sickle cell disease:

2.6.1 CT appearance of spleen complications in SCD:

Sickle cell clots cause ischemic vascular occlusion, which frequently affects different parts of the abdominal structures. The most commonly involved organ is the spleen, which is affected in almost all patients with SCA (Adler et al, 1986) .

2.6.1.1 Spleen infarction and abscess

Splenic infarction usually presents with abscess formation over the splenic area. CT imaging appearance of splenic infarction and abscesses depends on the timing of imaging and the size of the infarct. In well-established cases both ultrasound and CT are almost equally sensitive, however in early acute stage, contrast enhanced CT scan is the most sensitive tool of imaging. The typical infarct is seen as a hypodense non- or poorly enhancing wedge(figure 2.6.1 A) and (fig. 2.6.3) , with apex pointing toward the hilum. Later on, these infarcts may resolve completely or leave a permanent scar seen as contracted segment, or liquefy with possible abscess formation. Also, multiple small infarcts or global infarct of the whole spleen may reported in the imaging findings (Adler et al, 1986) .

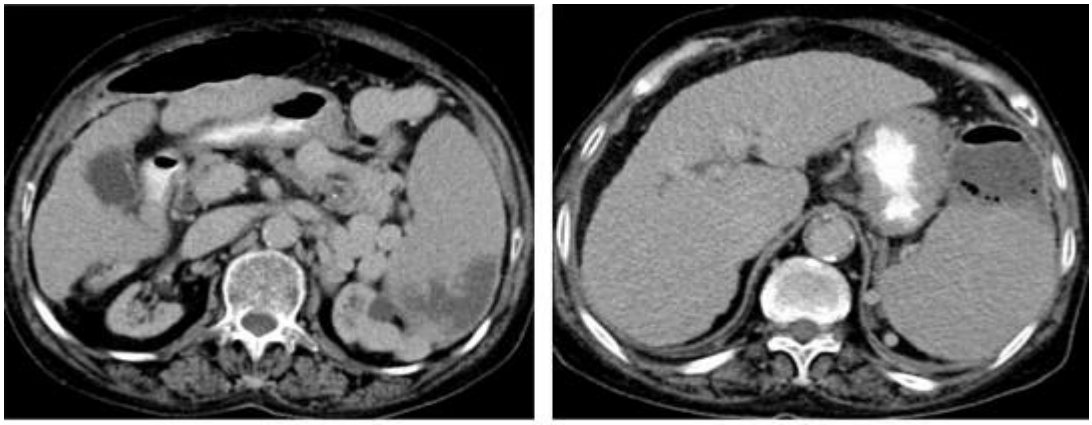


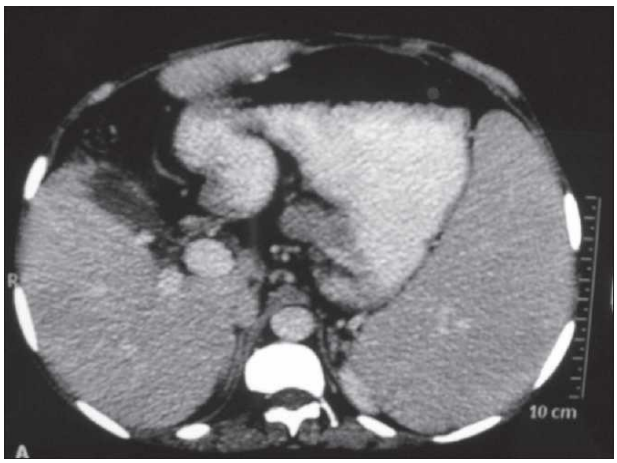
Figure (2.6.1): Non contrast CT scan in two different SCA patients showing splenic infarct (A), seen as capsular based irregular triangular shaped hypodense patch (Arrow) and splenic abscess (B), seen as splenic cystic swelling showing air fluid levels (arrow) (Adler et al, 1986) .

2.6.1.2 Splenomegaly and spleen sequestration syndrome

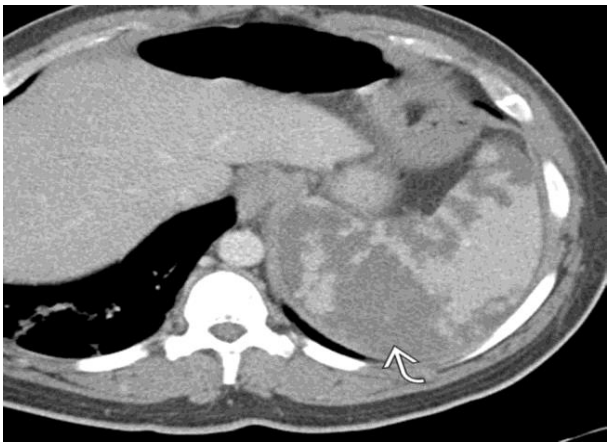
Another splenic complication of SCD is known as sequestration syndrome. It is characterized by rapid pooling of blood within a solid organ, with resulting intravascular volume depletion and dropping hematocrit values (Poulin et al, 1986). When sequestration syndrome is mild, the child may experience minimal pallor, lethargy, splenic enlargement, tachycardia, and left upper quadrant pain. Sequestration syndrome may be quite severe, however, and severely affected children present with a rapidly enlarging spleen, splenic vein dilatation and enlargement of lymph nodes (Adler et al, 1986) (Poulin et al, 1986).The condition may progress rapidly (within hours) to cardiovascular collapse and death. Therefore, the diagnosis of sequestration syndrome must be considered in a child with any of the above symptoms and signs. Treatment consists of transfusion; occasionally splenectomy is performed, especially in those patients with recurrent sequestration syndrome.

sequestration syndrome has been described in older children and adults; therefore, a spleen larger than expected in any patient with SCA should prompt an evaluation for this possibly life-threatening complication.

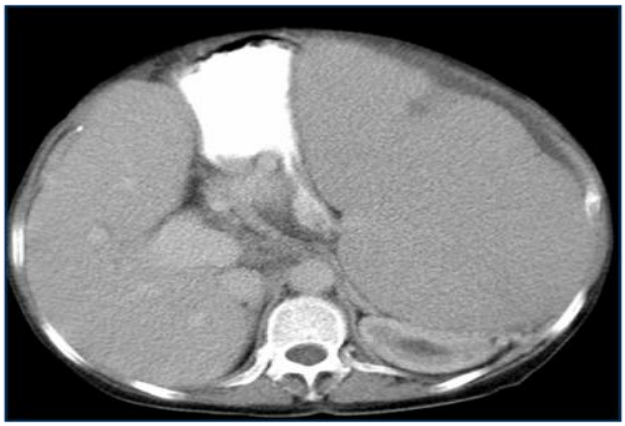
At CT imaging, the spleen is appear larger (figure 2.6.2) than expected>14 cm length in adult and may loss its normal medial concavity or appear in a pyramidal shape with irregular out line and may also extended below lower third of the LT kidney (Ahmed, 2010) (figure 2.6.4). It appears as Low CT attenuation number than normal with dilatation of splenic vein and lymph nodes enlargement will be seen at CT(Ahmed, 2010).



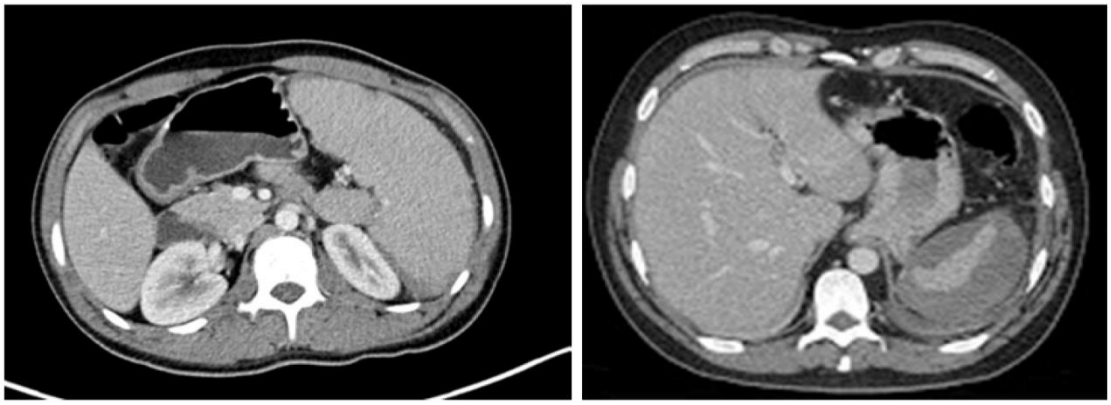
(Figure 2.6.2): CT scan of abdomen showing massive splenomegaly with a dilated splenic vein in pt with sickle cell disease (Ahmed, 2010).



(Figure 2.6.3): (Left) Axial CECT in a sickle cell patient demonstrates an enlarged spleen with multiple wedge-shaped acute splenic infarcts image (Adler et al, 1986)



(Figure 2.5.4): Contrast enhenced axial CT of abdomen in sicklerpt shows compressed left kidney by splenomegaly (Adler et al, 1986) .



A B

(Figure 2.6.5): (A) Enlarged spleen with subcapsular infarction in the posterior pole, suggestive of ASSC. (B) Enlarged spleen that enhances heterogeneously with calcifications, suggestive of ASSC in fibrotic phase (Adler et al, 1986) .

2.6.2 CT appearance of hepatobiliary complications in SCD:

Multiple hepatobiliary complications occur in the patients with SCD due to the increased risk of hepatic injury from sickling: most complications reported in the liver is Hepatomegaly, focal necrosis, hepatic infarction , abcesses and cysts. CECT considered the most sensitive technique in detecting those liver complications.

2.6.2.1 Hepatomegaly

Liver may appear larger (figure 2.6.6) than normal size(hepatomegaly) in the image >16cm in length and give low attenuation values than normal in the non contrast image (Jessie et al, 2006).

2.6.2.2 Hepatic infarction

Infarction typically presents as an well-defined wedge-shaped based area of hypo attenuation which is mostly peripheral without pressure effect on adjacent structures in post-contrast images (Gauthier et al, 1985) (figure 2.6.7).

2.6.2.3 Liver abscess

Appearance of liver abscesses in sickle cell patient on CT is variable (Chong et al,1993) , In general, they appear as peripherally enhancing, centrally hypoattenuating lesions (Chong et al,1993) (figure 2.6.9). Occasionally they appear solid or contain gas .Segmental, wedge-shaped (Chong et al,1993) or circumferential perfusion abnormalities, with early enhancement, may be seen.

2.6.2.4 Hepatic focal necrosis

Hepatic focal necrosis in sickler may appear in a multitude of ways on CT scans. The majority of them are hypovascular (hypoattenuating) in comparison with surrounding parenchyma; (figure 2.6.8) therefore, on nonenhanced CT scans, most lesions appear either hypoattenuating or isoattenuating relative to the surrounding parenchyma (Markowitz et al, 1980).

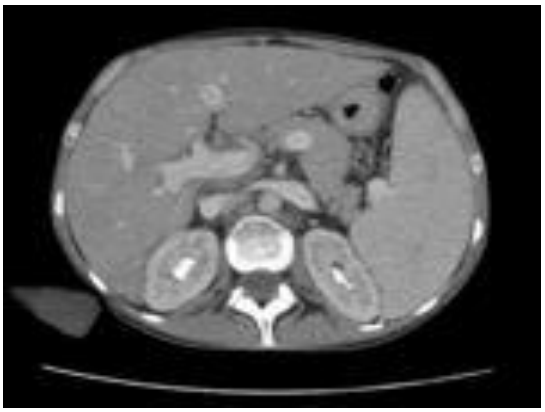
2.6.2.5 Cholelithiasis

A high incidence of gall bladder is a multiple pigmented gall stones (cholelithiasis) are clearly demonstrated among SCA patients due to high bilirubin levels. And the way of appearance in CT image is depending on if it's calcified or not, Pure cholesterol stones are hypoattenuating to bile, and calcified gallstones are hyperattenuating to bile (figure 2.6.10).

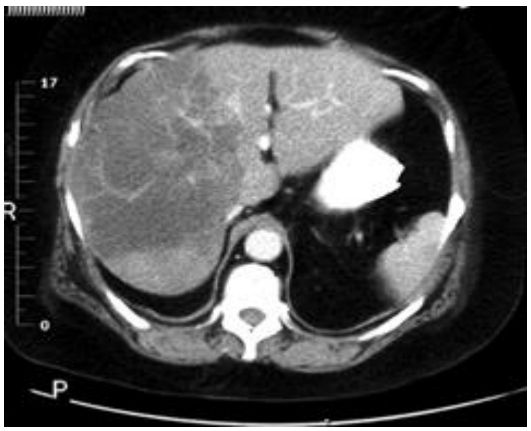
2.6.2.6 Acute pancreatitis

Acute pancreatic inflammationis the one of sickle cell complication, it may be a result of gallstone or microvascular occlusion and ischemic injury. Non-

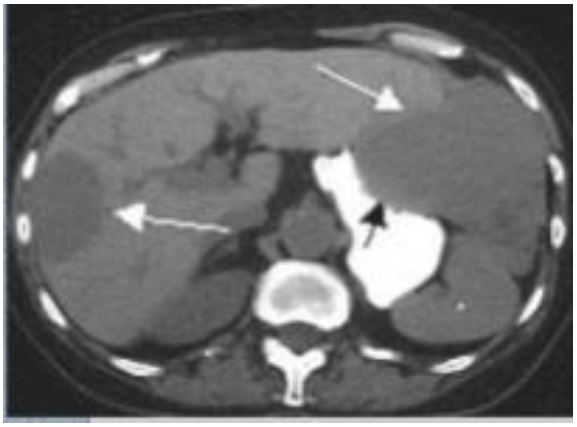
doubtfully, CECT scan is the most reliable imaging tool of acute pancreatitis (Sheehan et al, 1993). Characteristic findings of acute pancreatitis in sickler patients on contrast-enhanced CT (CECT) are some edema of the pancreatic head, tail or edema in the peripancreatic fat consistent with interstitial pancreatitis (Sheehan et al, 1993) (figure 2.6.11).



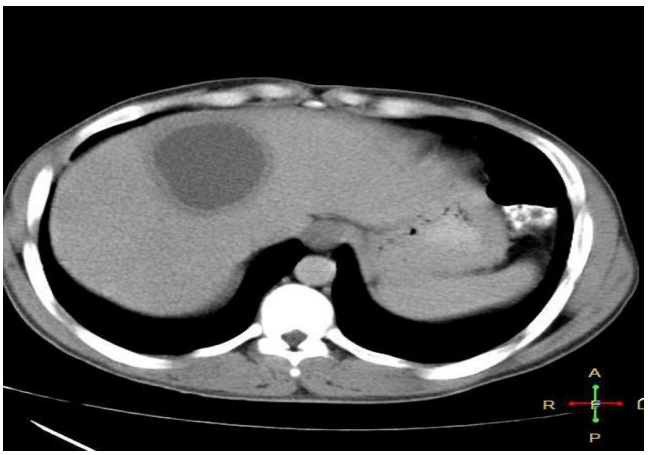
(Figure 2.6.6): CT scan of the abdomen showing hepatomegaly, splenomegaly and dilated portal and splenic veins in pt with sickle cell disease (Jessie et al, 2006)..



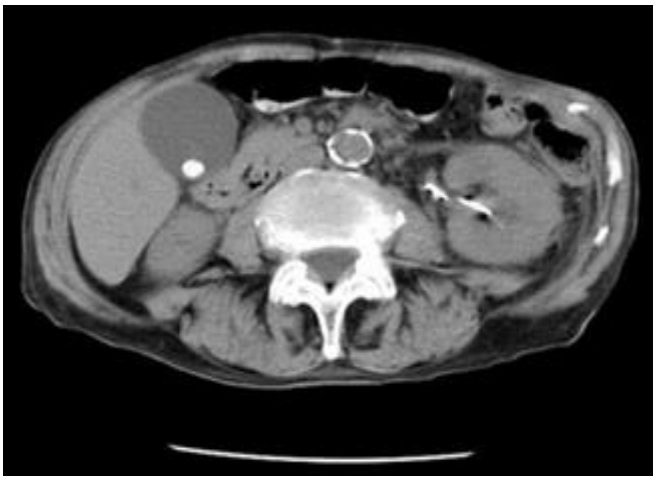
(Figure 2.6.7): CT scan of the abdomen obtained prior to the arteriogram demonstrates a large wedge-shaped area of decreased attenuation consistent with a hepatic infarct in patient with sickle cell disease (Gauthier et al, 1985) .



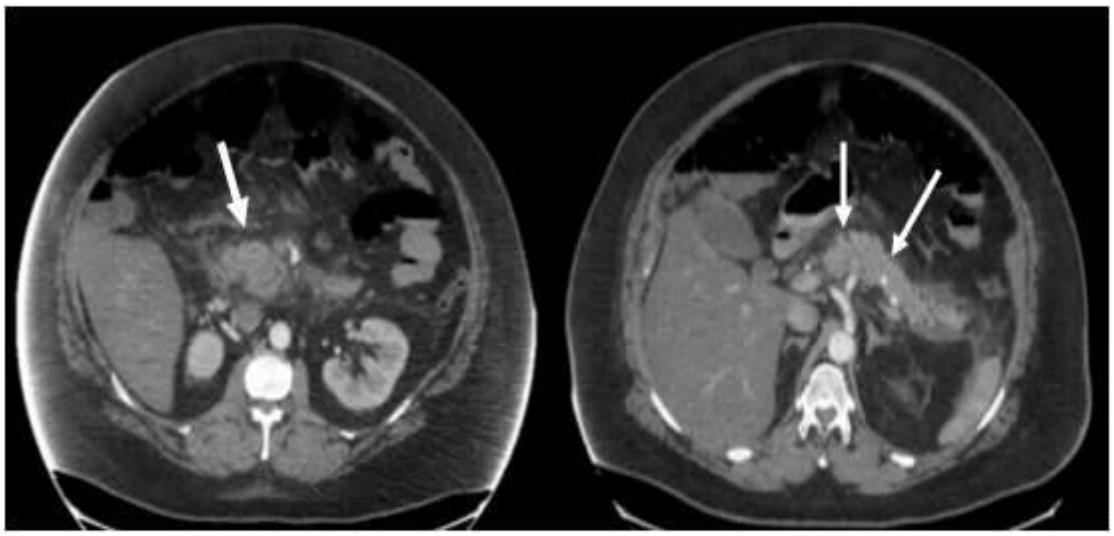
(Figure 2.6.8): Post contrast CT demonstrates hypovascular hepatic focal necrosis in sickle cell pt (Markowitz et al, 1980).



(Figure 2.6.9): Axial CT in portal venous phase demonstrate peripherally enhancing, centrally hypoattenuating liver abscess in sickle cell pt (Chong et al,1993) .



(Figure 2.6.10): Noncontrast CT demonstrates calcified gallstone in asickler pt (Sheehan et al, 1993)



(Figure 2.6.11):Two axial CECT images in a sickle cell disease pt, Notice the inflammation and edema surrounding the pancreas caused by acute pancreatitis (Sheehan et al, 1993).

2.6.3 CT image appearance of pulmonary complications in SCD:

Patients with SCD may develop obstructive or restrictive lung diseases, when there is a progressive decline in the pulmonary functions after a preceding history of several attacks of acute chest syndrome. This may be explained by established fibrotic lung changes from repeated episodes of pulmonary infective and vaso-occlusive events. The most pulmonary complications in SCD are pleural effusion, lung fibrosis, pneumonia and consolidation (Martin and Buonomo, 1997) **,** (Kim et al, 1999).

CT is a sensitive method capable of imaging the lung with excellent spatial resolution, providing anatomical detail similar to that seen by gross pathological examination (Martin and Buonomo, 1997)**.**

High resolution CT scan (HRCT) shows these SCD pulmonary changes very clearly (Kim et al, 1999).

2.6.3.1 Pleural effusion

Infarction of lung, local abscess, and heart, kidney, or pancreas problems are among the many causes of pleural effusion in sickle cell disease. CT scanning is excellent at detecting small amounts of fluid and is also often able to

identify the underlying causes. A pleural effusion appears on CT as a dependent sickle-shaped opacity with a CT number lower than that of any adjacent pleural thickening (Martin and Buonomo, 1997) (figure 2.6.12).

2.6.3.2 Pulmonary fibrosis

Patients with sickle cell disease (SCD) are suspected to have more pulmonary fibrosis. High resolution computerized tomography can detect interstitial fibrosis. HRCT of pulmonary fibrosis appearing as reticular opacities with honey combing appearance- (Kim et al, 1999) (figure 2.6.13, 2.6.14).

2.6.3.3 Pneumonia

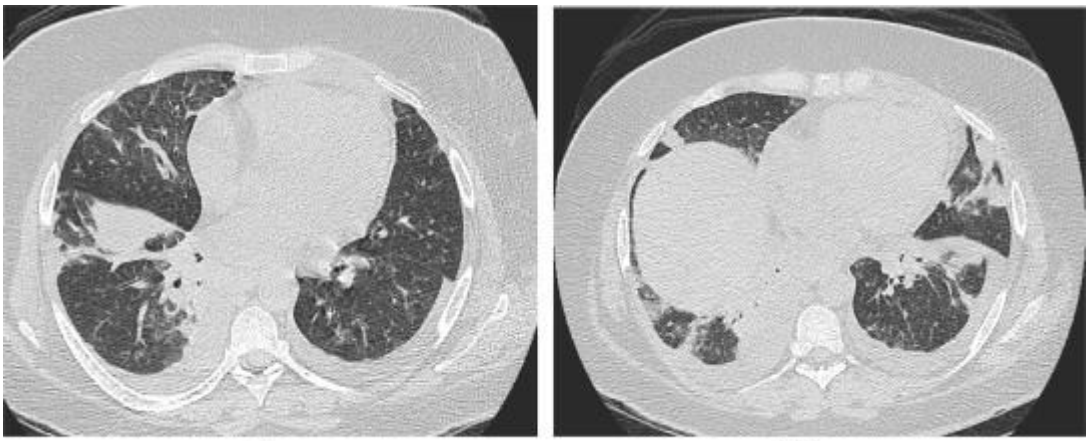
Lung infection (pneumonia) is extremely common in children with sickle cell anemia and is also the most common reason for hospitalization. The type of bacteria that is frequently the cause of pneumonia is called the pneumococcus. (This is, in part, due to the increased susceptibility to this particular bacteria when the spleen is poorly functioning). HRCT of pneumonia has a pattern of focal ground-glass opacity in a lobar(Figure 2.6.15)or segmental pattern (Kim et al, 1999). This is due to incomplete filling of alveoli and consolidation. At other times there can be dense opacification of the entire lobe.

2.6.3.4 Pulmonary consolidation

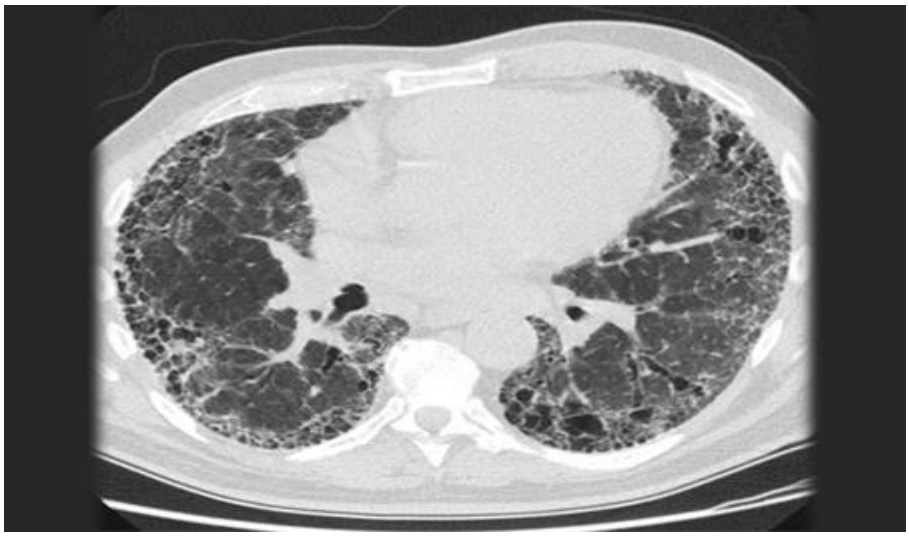
Acute Chest Syndrome more frequently presented on CT as a consolidation pattern. In CT scan studies it presents as increased attenuation of the lung parenchyma causing obscuration of pulmonary vessels (figure 2.6.16). Air bronchograms can also be found.

The current results suggest that high-resolution computed tomography examination and/or noninvasive assessment of haemolysis might facilitate identification of sickle cell disease patients with respiratory function impairment-(Kim et al, 1999). These tests may be particularly useful in those patients unable to complete pulmonary function tests. More of the patients had abnormalities on high-resolution computed tomography than on lung function testing, which suggests that high-resolution computed tomography is a more

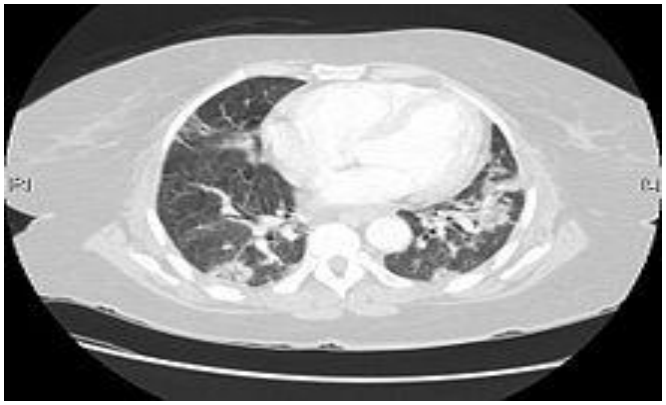
sensitive detector of respiratory abnormalities than lung function testing. This hypothesis merits testing by serially assessing sickle cell disease patients to determine whether those with only high-resolution computed tomography abnormalities subsequently develop lung function abnormalities.



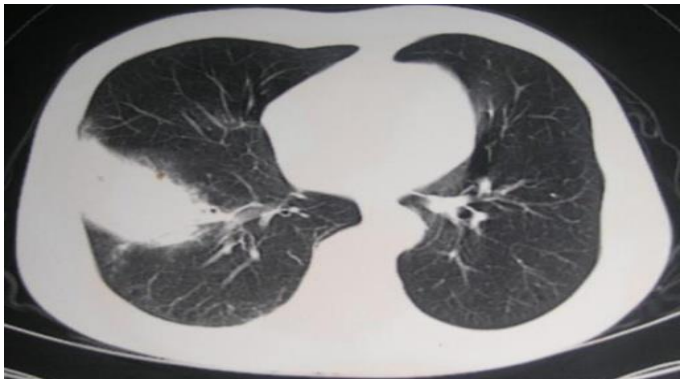
(Figure 2.6.12): HRCT scan (A and B) showing bilateral multiple infiltrates of ACS as well as bilateral pleural effusion (Martin and Buonomo, 1997).



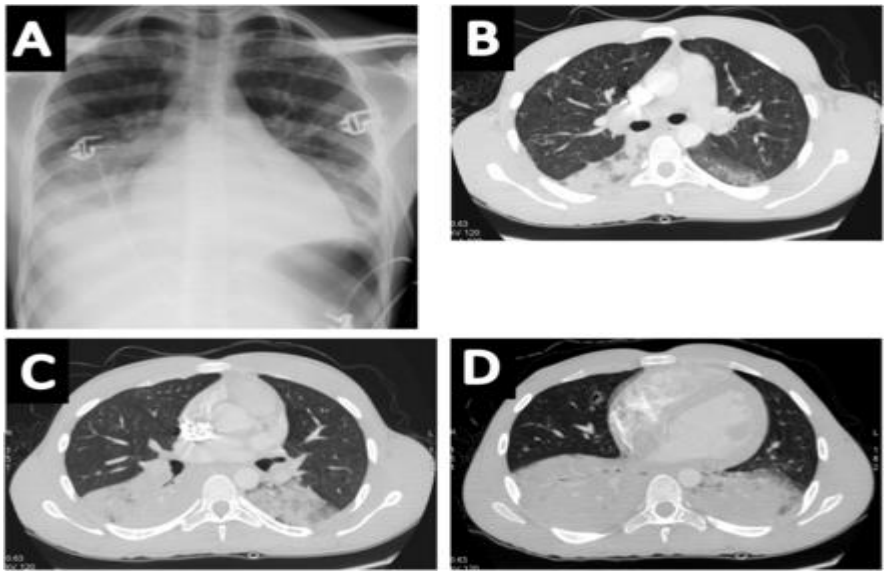
(Figure 2.6.13):HRCT scan of patient with SCD showing bilateral pulmonary fibrosis (Kim et al, 1999)



(Figure 2.6.14): CT scan of SCD pt, pneumonia seen on CT scan. Honeycomb fibrosis is seen at the bases of both lungs-(Kim et al, 1999).



(Figure 2.6.15): Computed tomography scan of the thorax in SCD pt. showing features of lobar pneumonia (Kim et al, 1999).



(Figure 2.6.16): Example of a patient with acute chest syndrome and bilateral consolidations predominating at lung bases on chest radiograph (panel A) and CT (panels B, C and D) (Kim et al, 1999).

2.6.4 CT appearance of renal complications in SCD:

In patients with SCD, certain functional and structural changes in the kidney can be observed. These affect the entire nephron, from the glomerulus to the renal papilla. Due to a high consumption of oxygen during cellular metabolism, the kidney is highly affected in the setting of vaso-occlusive crises (Allon, 1990), which are characteristic of SCD. The environment surrounding the renal medulla is characterized by acidosis, hypertonicity, and hypoxia, and these factors contribute to the sickle cell crisis that is responsible for the occlusion of the renal vessels. The most important consequence of these crises is damage to the renal tubules; this causes atrophy or dilation of the tubules, the presence of protein cylinders, and iron deposition along with degeneration of the tubule epithelium (Allon, 1990), (Koshy, et al, 1989)

Sickle cell nephropathy, which develops as a result of sickling of RBCs in renal circulation, leads to renal stones &ischemia which causing renal infarctions and papillary necrosis, as well as renal vein thrombosis and finally renal failure. CT scan is a good diagnostic imaging modality for nephropathicchanges (Kenneth and Eugene, 2000). Kidneys in patient with SCD are generally give low attenuation values than normal one.

2.6.4.1 Renal infarctions

Sickling of red blood cells (RBCs), which significantly decreases renal medullary blood flow through vaso-occlusion is the cause of renal infarction in SCD because it results in complete occlusion of the main renal artery.

Renal infarcts are most easily identified on post contrast CT images, preferably in the cortical/arterial phase. One or more focal, wedge-shaped parenchymal defects that involve both the cortex and medulla and extend to the capsular surface are demonstrated (figure 2.6.17). In cases where the main renal artery is occluded, then the entire kidney fails to enhance (Kenneth and Eugene, 2000).

2.6.4.2 Renal papillary necrosis

The renal medulla contains the vasa rectae, that is, the renal tubules and blood vessels located therein. Low oxygen tension, low pH, and high osmolality characterize the normal renal medullar environment. All of these conditions predispose to RBC sickling, especially with severe intravascular volume depletion. The resulting increased blood viscosity contributes to ischemia and eventual infarction that involves the renal microcirculation.

Medullary ischemia and infarction cause papillary necrosis. Sloughed papillae may obstruct urinary tract outflow, leading to renal papillary necrosis.

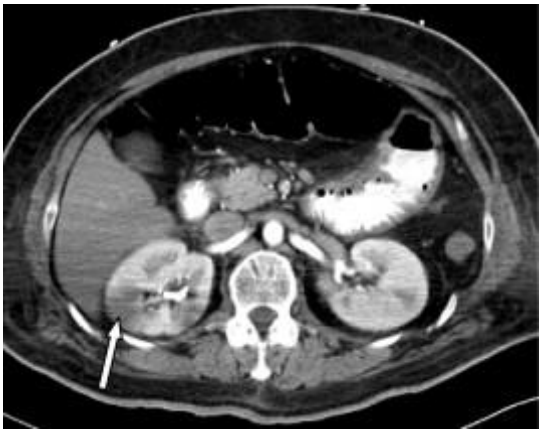
Renal papillary necrosis is visible when excreted contrast material, at Contrast enhanced CT during the excretory phase fills a necrotic cavity located centrally or peripherally in the papillae can depict necrosis as clearly and thus allow accurate diagnosis of the condition (Falk, 1992) (figure 2.6.18).

CT urography typically demonstrates multiple small collections of contrast material in the papillary regions peripheral to the calyces. The entire papilla may become necrotic. The papillary defects may eventually become peripherally calcified (Falk, 1992). Sloughed papillae appear as filling defects in the collecting system and ureters and may obstruct them and cause renal colic (Kenneth and Eugene, 2000), (Falk, 1992).

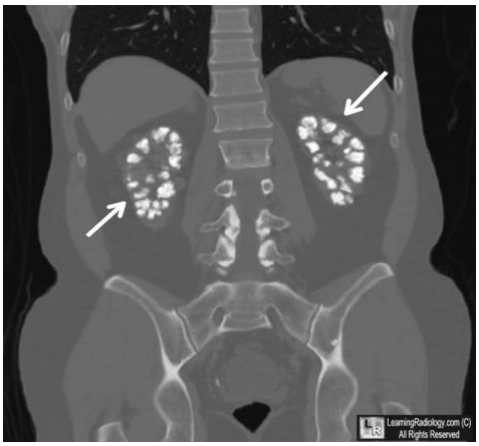
2.5.4.3 Renal stones:

All previous pathological conditions may result in an accumulation of dissolved minerals on the inner lining of the kidneys and so excessively acidic environment conducive to the formation of kidney stones in a SCD patient.

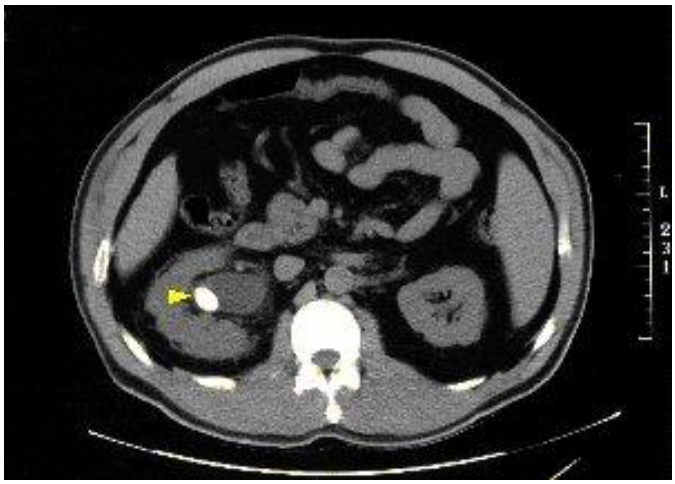
Ninety-nine percent of renal tract calculi are visible on a non-contrast CT(Kenneth and Eugene, 2000) (figure 2.6.19).On CT almost all stones that appear are opaque, but vary considerably in density according to their component. Radiolucent and usually undetectable on non-contrast CT characterized on delayed phase as a filling defect in the ureter.



(Figure 2.6.17): Nephrographic phase contrast enhanced CT scan shows right renal wedge shaped cortical infarct (arrow) (Kenneth and Eugene, 2000).



(Figure 2.6.18): Coronal CT reconstruction in Excretory Phase of SCD pt shows amorphous, coarse calcifications throughout both kidneys (white arrows) diagnosed as a renal papillary necrosis (Falk, 1992).



(Figure 2.6.19): Non contrast axial CT image of SCD pt demonstrates RT renal caculi (Kenneth and Eugene, 2000)

2.7 Previous studies:

Many studies had been done about diagnosis of SCD because it discovered from 1910 and so it categorize as an old disease, here is some of the studies done about certain abdominal and chest organs in patients with sickle cell disease using multidetector computed tomography.

Study done by **Ali et al.** (in sep 2002) about Characterization of CECT spleen in children with sickle cell disease. And abstracted that, sickle cell disease can affect any part of the body and one of the most common and an early organ to be affected in SCD is the spleen, CT scan is consider one of the most important imaging modality that can shows clearly spleenic complications in sickle cell disease. 50 SCD children ranged from one to ten years in age was studied, all of them were show spleenic changes in CT scan, 80% of children that ranged from 1-4 years old their spleen appeared as enlarge in size and shape with location changed and extend to the lower portion of the LT kidney with splenic vein dilatation, additional to gave splenic Hounsfield number lower than the normal. 14 cases of all 50 children were present with splenic lesions either abscess or cyst- with majority of abscess more than cyst-most of abscess were appear clearly in the venous and delay phase, and conversely arterial phase was give us cleared showing for cystic lesions. A hypovascular splenic infarction was present in 60% of children which were ranged from 8 to 10 years old and all of their infarction were appear more clearly in delay phase.

In other study done by **Mouzan et al.** (June 2004) about Clinical and radiological features(CT and MRI) of sickle cell disease-splenic manifestation in eastern Saudi Arab children, and abstracted that, the clinical features of sickle cell disease (SCD) in Saudi Arab children of eastern origin are presented. One hundred and seventy-three children were diagnosed from 3 months to up to 4 years of age. There were 87 boys and 86 girls. Genotype distribution included 146 sickle cell anemia, 24sickle hemoglobin C disease,

two sickle beta +-thalassemia and one sickle beta 0-thalassemia. Of our patients, 27% complain abdominal pain presented in the first 12 months of age and 50% present with abdominal pain and noticeable swelling those aged from 1 year to 3 years, remained asymptomatic at 4 years. CT and MRI in imaging was done and result that splenic complication of sickle cell disease is enlargement of low spleenic intensity and low signal intensity in CT and MRI respectively was the most common initial complication , followed by splenomegaly with formation of splenic abscess lesion/s, abscess formation without splenic enlargement appear/s in venous phase, and splenic infarction showing in delay phase, occurring in 60%, 31.6%, 6.7%, and 1.7% of the patients, respectively. None of the patients presented with severe bacterial infections. During this study, 173 sickle cell disease were documented, but only 16 (9.1%) required hospital admissions. There were no deaths in this series. High hemoglobin F levels correlated with delayed clinical presentation and reduced number of crises. We conclude that SCD in children of eastern origin is clinically milder than earlier descriptions from the Eastern Province of Saudi Arabia due to earlier diagnosis of complications due to advancement of the imaging tool (CT and MRI).

There is study also done by **Priya and Tracy,** in (August 2001), who studied computed tomography of the children's spleen and liver with sickle cell disease and abstracted that, the spleen was assessed in 27 patients between one to twelfth years old with sickle cell disease studied with computed tomography (CT) for abdominal pain and/or unexplained fever. 10 Patients with sickle cell anemia were found to have small, densely calcified spleens with occasional low-density infarcts appear clearly in delay phase. Five of six had hepatomegaly, and there was one case each of hepatic abscess, infarcts, and hemochromatosis. All remaining patients were found to have splenomegaly, with a variety of findings that appear clearly in venous and delay phase including changing in spleen shape and location , low splenic attenuation,

abscess formation, splenic vein dilatation, acute and chronic infarcts, rupture, and possible sequestration. It was concluded that CT is useful for evaluating the status of the spleen and liver in symptomatic patients with sickle cell disease.

A unique study by **Rani Al-Senan,** (2001), studied acute splenic sequestration crisis in children with sickle cell disease: US, CT, and MR imaging findings and abstracted that, Acute splenic sequestration crisis (ASSC) is a common complication in children with sickle cell disease that is diagnosed clinically by means of splenic enlargement and a rapid fall in hemoglobin. 13 cases of ASSC in children ranged between 3 months to 3 years of age with homozygous sickle cell disease (sickle cell- hemoglobin SS and sickle cell-hemoglobin SC disease) were studied with use of duplex Doppler ultrasound (US), computed tomography (CT), and magnetic resonance (MR) imaging. In all thirteen cases, US showed enlargement of the splenic vein and multiple hypoechoic lesions on the periphery of an enlarged spleen that were of low attenuation on CT scans and hyperintense on both T1- and T2-weighted MR images. These findings were believed to be suggestive of subacute hemorrhage. Further study is needed to determine the role of imaging in the diagnosis and treatment of ASSC.

Ahmed et al, (2005), they studied characterization of splenic infarction and abscess of Sickle Cell Disease patient- CECT assessment and abstracted that, This is a report of our experience with 20 cases of splenic infarct/s and 20 cases of abscess in patients with sickle cell disease (SCD). All presented with fever and abdominal pain and were found to have a tender enlarged spleen. Although both ultrasound and CT-scan of the abdomen were of diagnostic value, we found CT-scan more accurate and reliable in the diagnosis of splenic infarct/s and abscess. Contrast enhancing CT-scan in various phases is used. And noted that splenic abscesses was appear as single, irregularly marginated lesions with low attenuation before enhancing, but a rim enhancement was

seen on contrast-enhanced scans specifically on portal venous phase whereas rim-enhancement of the outside-facing portion of the abscesses wall was appear clearly. The inside-facing portions of the wall was show less-enhancing or non-enhancing components, which represent fibrous and proteinaceous material. The content of abscess was appear inhomogeneous with density values ranging from 20 to 40 HU. Gas formations within the abscess was encounter in 12 cases of all 20 cases of splenic abscess and confirmed the diagnosis of abscess. The other 20 sickle cell disease cases which was diagnosed as splenic infarct, they were poorly visualize on non-enhanced CT. After intravenous iodine contrast administration, especially in venous and delay phases, they appeared as peripheral, wedge-shaped non-enhancing defects. Concluded that CT is considered the most important imaging investigation of choice in diagnosing of splenic abscess and infarcts in sickle cell disease, and ideally performed during the portal venous phase in detecting of splenic abscess formation and in delay phase in infracted lesion cases. but in less typical cases, splenic infarcts may mimic with abscesses or tumours, this requiring clinical correlation, or if necessary, percutaneous fine-needle aspiration biopsy can be done.

Magid et al, in **(May 2014),** studied Abdominal pain in sickle cell disease and the role of CT and abstracted that, patients with either homozygous or heterozygous sickle cell disease may have frequent episodes of abdominal pain and/or fever of uncertain cause. While many of these episodes represent a so-called sterile crisis, the possibility of gross organ infarction and rupture, infection, or other complication cannot be ignored. Computed tomography (CT) was used to evaluate 30 such patients. Virtually all patients had splenic abnormalities, 14 patients had splenomegaly and spleen of 8 patients is totally infracted and shrunken and 5 patients are found with splenic abscess, remaining three patients had splenic vein dilatation as a result of vein thrombus .In 14 patients hepatic abnormalities were found, including six case

of hepatomegaly, three cases found with multiple liver infarction, four of hepatic abscess, and one of retained intrahepatic gallstones after cholecystectomy. Ten patients had significant acute renal abnormalities, including four case of renal papillary necrosis, three case of interstitial nephritis from renal stones and one of renal vein thrombosis, remaining two patient are present with renal abscess. One patient had a ruptured periappendiceal abscess and one a pericolonic abscess. One patient had an abscess around a total hip replacement. CT was found to be an excellent and relatively noninvasive means of both initial investigation and subsequent follow-up.

Carly et al, (September 2010) studied CT abdominal imaging findings in patients with sickle cell disease: acute vaso-occlusive crisis, complications, and chronic sequelae and abstracted that, Sickle cell disease (SCD) is the most prevalent hemoglobinopathy. Survival in patients with SCD has improved over the past few decades. These patients experience a lifetime of repeated acute pain crises, which are thought to result from sickling and microvascular occlusions; acute abdominal pain is common. Moreover, repeated crises often lead to organ dysfunction, such as asplenia, hepatic failure, and renal failure. The spleen, liver, biliary system, kidneys, and gastrointestinal tract can all be affected. Patients may undergo CT to further direct clinical management. We reviewed the spectrum of CT imaging findings of abdominal manifestations in 35 patients with SCD, from the acute microvascular occlusive pain crisis to the potential complications and chronic sequelae. And result that all patients which had splenic problems were present with hepatic problems, splenomegaly is present in 60% of cases and they were present also with hepatomegaly and hepatic abscesses 40% and 20% respectively. And splenic abscess was discovered in 10% of cases and all of them also present with hepatic abscess and cysts. 30% of spleen of the remaining sickle cell patient were totally infarcted with some small liver infarctions was also existed. Renal

disorders were found in 30% of all cases and diagnosed as renal stones and hydronephrosis, Renal vein thrombosis, renal papillary necrosis and renal infarctions and failure, diagnosed in 13%, 7%, 6%, 4% of renal disordered patients respectively. CT scan is a sensitive modality for evaluation of the sickle cell disease complications in the abdominal organs.

Jebbin and Adotey (2011 Apr), excogitate the presence of the abdominal complications of the sickle cell disease in different age groups , and assessed that People with sickle cell disease (SCD) start to have signs of the disease during the first year of life, usually around 5 months of age. Symptoms and complications of SCD are different for each person and can range from mild to severe. The reason that infants don't show symptoms at birth is because baby or fetal hemoglobin protects the red blood cells from sickling. When the infant is around 4 to 5 months of age, the baby or fetal hemoglobin is replaced by sickle hemoglobin and the cells begin to sickle.SCD is a disease that worsens over time. Treatments are available that can prevent complications and lengthen the lives of those who have this condition. 90 patients who had abdominal complications from sickle cell disease in different age groups were studied by using contrast CT scan in diagnosing. And result that the patients whose aged from six months to ten years old (30 patients) were present with splenomegaly, hepatomegaly, hepatic abscess, Ischemic colitis and normal kidney showing, in 24, 12, 6, 3 and 30 patients respectively and the patients whose aged range from eleven to twenty years old (30 patients) are showed splenomegaly, splenic abscess and splenic infarct in 10,4 and 2 patients respectively. And showed hepatomegaly, liver abscess and hepatic necrosis in 2,5 and 1 patients respectively. And present with some renal problems, renal vein thrombosis in 2 patients and renal stones in another 2 patients. One patient was present with acute pancreatitis and another one patient was present with gall stones and dilated common bile duct, two patients had duodenal ulcer. The last age group are ranged from 22 to 30 years old (30 patients) they

were present with splenic infarction (17 pts), hepatic infarct and hepatic necrosis (5, 2 pts), renal infarct and renal failure (2, 1 pts), bowel infarction in one pt and acute pancreatitis in 3 patients.

The early discovering of the abdominal complications of sickle cell is the very important, in order to prolonged the lives of many patients who are now living into adulthood.

Christoph et al, (2013 Feb), they studied Hounsfield attenuation number of the some affected abdominal organs with sickle cell disease. and abstracted that Hounsfield values are depend on a combination of factors including the presence or absence, as well as the phase, of IV contrast administration. A 55 cases of patients -whose had abdominal manifestations from sickle cell disease- their CT number of each affected organ were studied. And generally noted that, before administration of contrast media, organs whose influenced by sickle cell disease were give low attenuation values than the normal. After contrast administration, any infracted abdominal organ are gave very low attenuation values in the delay phase, which was range from (20- 22Hu) in cases of splenic and renal infarction, increased fewer in infracted liver until 30 Hu although the normal range of those organ is 30, 40 and 55 for kidneys, spleen and liver respectively. Abscess which was discovered in the most influenced abdominal organ with sickle cell (spleen, liver and renal) were give attenuation values between 30- 35 Hu in the portal venous phase. Any case presented with spleen enlargement or hepatic enlargement ,their CT number were measure lower than the healthy spleen and liver.

Dr. Abdulla (2004 Sep), excogitate the Pulmonary manifestations of sickle cell disease in eastern Saudi Arab patients- using HRCT and assessed that Pulmonary complications account for significant morbidity and mortality in patients with sickle cell disease. Clinical lung involvement manifests in two major forms: the acute chest syndrome and sickle cell chronic lung disease. Acute chest syndrome is characterised by fever, chest pain, and appearance of

a new infiltrate on chest radiograph. Sickle cell chronic lung disease, on the other hand, manifests as radiographic interstitial abnormalities, impaired pulmonary function, and, in its most severe form, by the evidence of pulmonary hypertension. Progress has been made in understanding the pathophysiology and management of these complications. In this review we studied the more common pulmonary complications from sickle cell disease in 60 patients in the eastern Saudi Arab. And we found that the more frequent complication which diagnosed in HRCT was pleural effusion, found in 40% of patient sample followed by bronchiectasis in 21%, lung fibrosis in 19% of cases, pulmonary consolidation in 9% and pulmonary artery thrombosis in 11% of patients. High-resolution computed tomography (HRCT) has a central role in the diagnosis and follow up the pulmonary problems that caused by sickle cell disease.

Chapter Three

Material and Method

3.1. Material:

3.1.1 Place and duration of the study:

This study was done in Aseer and Gizan states (south of Saudi arabia), in Ballasmar general hospital and king Fahad central hospital CT departments.

Data were collected in the period from (6.6.2014) to (12.6.2016).

3.1.2 Study population:

Random samples of (67) patients who were investigating as sickle cell disease, undergo for chest and abdomen CT examination.

patients were registered (age, sex, area, type of sickle cell disease, CT axial, coronal and/or sagittal sections findings was recordings)

28 patients are females, while the 39 are males and their ages are ranged from 10 months to 28 years old.

3.2 Method:

3.2.1 Machine used:

For all scanning techniques (axial, coronal and/or sagittal), American, general electric (GE) Hispeed 64 multidetector CT scanner was used, made by GE Healthcare Manufacturer, in years of 2009.

Tube 2.0 MHU MX 135, 3.9 million mAs, Software level 6.03, Fast scan 1.0 sec, Helical plus, 3D max, Power 200 mA, Max 1mm thickness, Acquisition, Helical 60 Max, Smart pre, DICOM MOD. It has voltage from 70- 150 Kvp and four options of mA, High (110), medium (77), low (55), and extra low (22). Has three options of slice thickness: 1mm, 3mm and 5 mm. Similar scan interspaces, Scan time of 4.8 sec, and construction algorithm of normal option (soft tissue), high frequency (bony)and HRCT (for lungs).

Images given in CD drive and store in special bacs system of the hospital.

Figure (3.1): Shows Ballasmar general hospital multidetector Hispeed (GE) CT scanner machine.

Figure (3.2): Shows Fahad king hospital multidetector Hispeed (GE) CT scanner machine.

3.2.2. Technique used

We are used two types of scanning techniques, for adults and other for pedia.

CT scans typically obtained for visualizing all abdominal organs and should include axial, coronal and/or sagittal cuts.

Proper positioning of the patients abdomen was done to obtain symmetrical image for each sections.

3.2.2.1. Abdominal technique used in pediatric: (from 0-12 years)

3.2.2.1.1. Sedation:

Patient between ages of 6 months and 5 years was preparing for sedation.

They are given IV pentobarbital sodium, 5mg/kg to a maximum dose of 200mg

3.2.2.1.2. Immobilization:

For patient under 5 years old.

We used a comfortable device that secures patient's arms beside the head with adhesive straps.

For larger children, used adhesive straps putted under the mattress and over the patient.

3.2.2.1.3. Scanning protocols:

Scans was obtain with patient supine, feet first, patient centered with gantry and scan taken from chest to symphsis pubic for abdomen.

Thinner slices of 5mm used for children 2 years and under 10mm slice for children 3 years and older.

A 120 kvp with mA ranged from 150-230 mA was used.

Higher pitch of 1 to 2 was used to reduce patient dose , and window of soft tissue was chosen.

3.2.2.1.4. Contrast:

A plain axial sections (sections before contrast) was taken firstly.

Oral contrast media:

The nonsedated patients was given dilute hypaque sodium which has concentration of 40% drunk immediately before examination

The amount of oral contrast needed per patients was determining by ages as follow:

From 6 months to 1 year given 175ml

From 1-5 years given 250ml

From 6- 12 years given 500-700ml

IV contrast agents:

Given 1-2ml/sec omino-obaque through automatic injector just before examination and took three stages of scanning :

Early arterial phase, later venous phase and very delayed venous phase

3.2.2.2. Abdominal techniques which used in adults: (over 12years)

3.2.2.2.1. Scanning protocols:

Scans was obtained with patient supine, feet first, patient centered and instructed to be hold his/her breath at end of inspiration.

Scan ranged from lower of the chest to iliac crest, and thinner slices of 1,2 to 4mm collimation with 1,2 to 4mm intervals are used.

Rotation time was 0.5sec with pitch of 1.37 and kv of 120 with auto mA range 100-400 and the table feed interval was 27.5mm.

Window setting which used to display images was for evaluation of soft tissue, window width (ww) of 350-400 Hounsfield unit (HU) and window level (wl) of 35-50 HU.

Images are reconstructed in coronal and/or sagittal planes.

Used very thin images (1mm) to be reconstructed to serve as source images for coronal and/or sagittal reformatted images.

3.2.2.2.2. Contrast:

A plain axial sections (sections before contrast) was taken firstly.

Oral contrast media:

Dilute barium sulfate solution (350-500)ml of contrast media was given to drink immediately before examination.

Intravenous contrast agents:

A (2 to 6 ml) of omino-obaque per second, concentration of 60% was given to the patient just before examination by automatic injector, and took three stages of scanning:

The early one was arterial phase scan with typical scan delays of 20-30sec,

The later venous phase scans with delays of 60-80sec and the last one is

Very delayed scans 1 to 4 hours.

3.2.3. HRCT technique:

Thin sections are acquired continuously using multi-detector row CT scanners in a single breath hold. Thinner slices are used to allow detection of a greater degree of pathology and also allowed reconstruction in any plane.

technical protocols were use:

Slice thickness: 1-1.25 mm, scan time: 0.5-1 second, kV: 120, mAs: 100-200, collimation: 1.5-3 mm, matrix size: 768 x 768

FOV: 35 cm, reconstruction algorithm: high spatial frequency, window: lung window, patient position: supine and the level of inspiration, in the full inspiration

3.2.4 Images evaluation:

All images (axial, coronal and /or sagittal) were evaluate by two radiologist and three technologist, and all patients were evaluated to identify any changes occurred within some abdominal organ and chest as a complication of sickle cell anemia.

3.2.5 Data collection

The data were collect from CT reports and then collected in data sheet which prepared specially for this task. Also CT images were collect in CDs after each scan as documentation for that scan.

2.2.6 Data Analyses

Data were analyze using Microsoft excel and statistical Package of Social Sciences (SPSS) (Inc., Chicago, Illinois version 16). The data obtained were analyzed statistically and data were presented as frequency and percentages. Paired t-test was used for testing the differences between the variables. The difference at value of $P < 0.05$ will be considered significant.

Chapter Four
Results

Table (4.1): Shows distribution of sickle cell disease patients age in the study sample in frequencies and percentages (%).

Range of patients age	Frequency	Percentage
3 mon-10.5years	36	53.73%
11-20 years	22	32.84%
21-30 years	9	13.43%
Total patients	67	100%

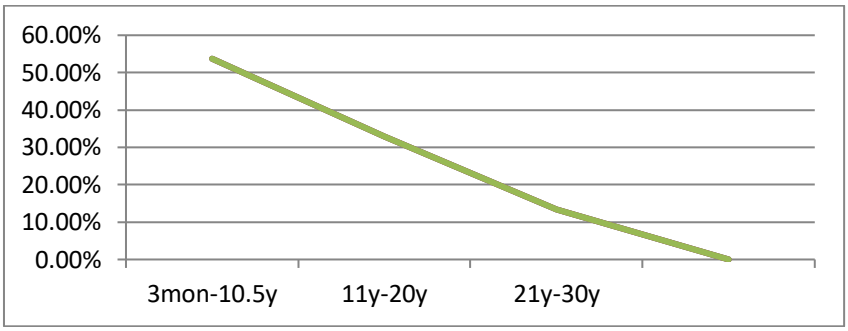


Figure (4.1): Percentage of patient's age

Table (4.2): Shows distribution of sickle cell disease patients gender in the study sample in frequencies and percentages (%).

Gender	Frequency	Percentage
Male	38	56.72%
Female	29	43.28%
Total	67	100%

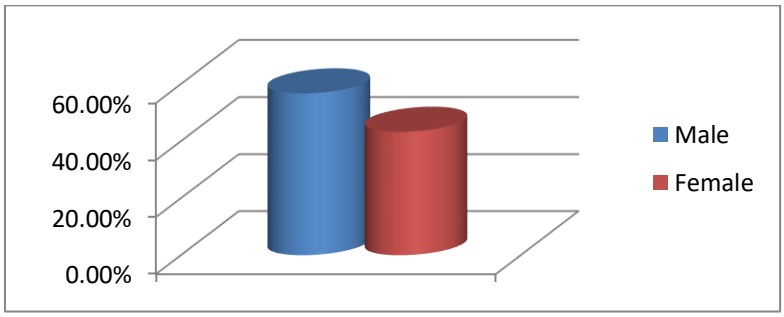


Figure (4.2): Percentage of patient's gender

Table (4.3): Distribution of sickle cell disease (SCD) types in the study sample in percentages (%).

SCD type	Percentage
Hemoglobin SS (Hb SS)	61.20 %
Hemoglobin SC (Hb SC)	16.40 %
Hemoglobin SB + (Beta) Thalassemia	7.50 %
Beta-Zero Thalassemia	10.40 %

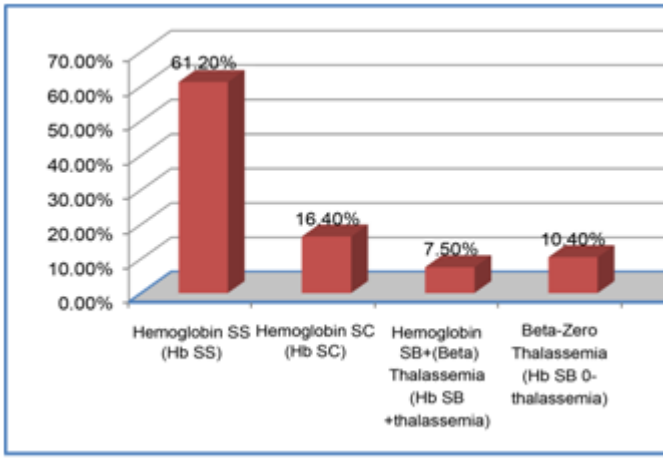


Figure (4.3): Shows distribution of sickle cell disease (SCD) types in the study sample in percentages (%).

Table (4.4):Characterization of spleen locations in patient affected with sickle cell disease in frequencies and percentages.

Spleen location	Frequency	Percentage
Normal location	21	31.3
Extend to left kidney	16	23.9
Extend below lower third of the left kidney	10	14.9
Atrophy	18	26.9
Spleen is not seen	2	3.0
Total	67	100.0

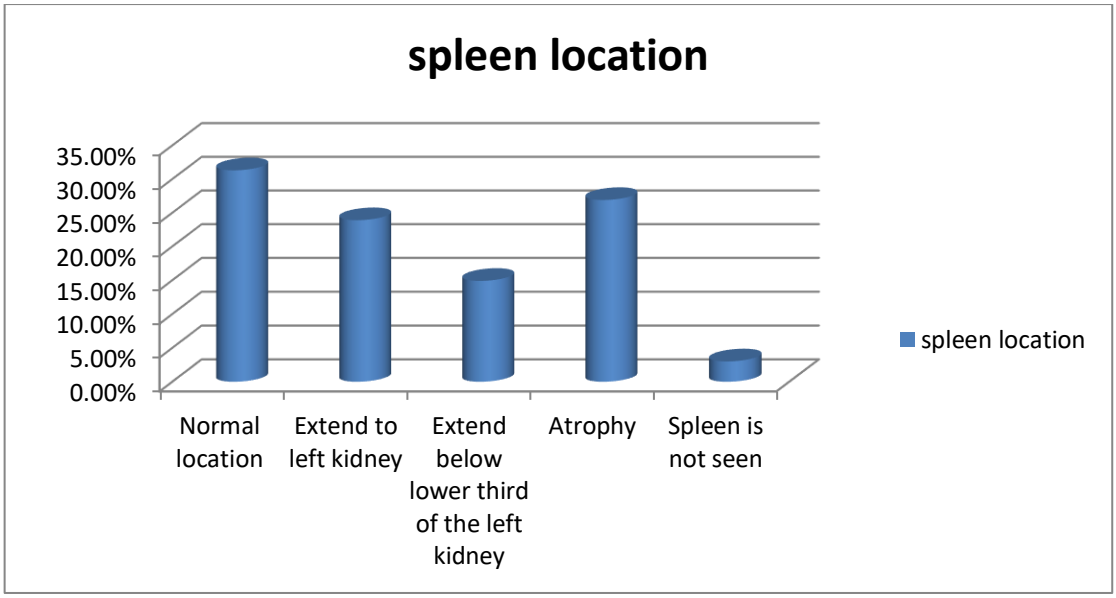


Figure (4.4): Shows distribution of spleen locations in patient affected with sickle cell disease in percentages.

Table (4.5):Shows distribution of spleen size in patient affected with sickle cell disease in frequencies

Size of spleen	Splenomegaly	Shrunken or very small size	Normal size
frequency	31	24	12

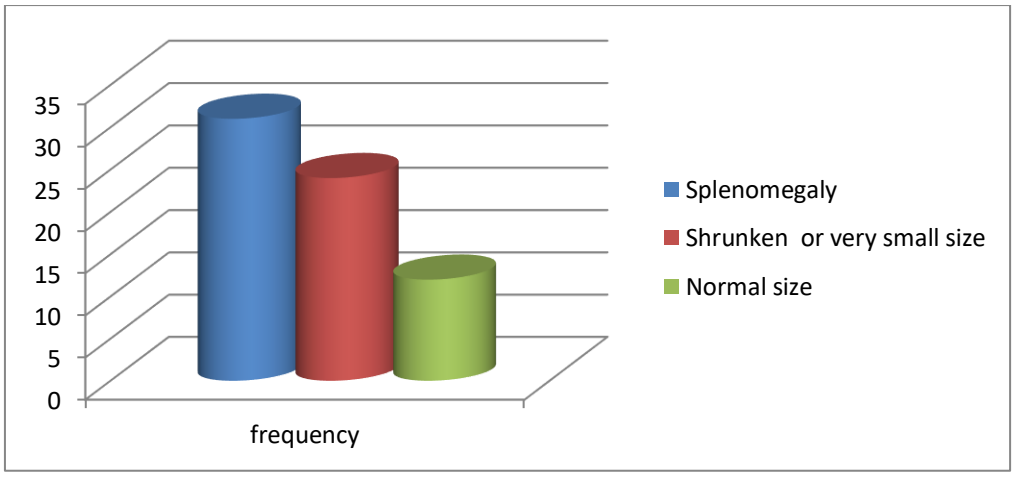


Figure (4.5): Shows distribution of spleen size in patient affected with sickle cell disease in frequencies

Table (4.6):Characterization of spleen size and shape in patients affected with sickle cell disease (SCD), frequency and percentages.

Spleen Size/Shape	Frequency	Percentage
Normal size and shape	21	31.3
Enlarged/normal shape	5	7.4
Enlarged, oval shape	7	10.4
Enlarged, irregular out line	4	6.0
Enlarged, pyramidal shape	6	9.0
Enlarged & loss it's medial concavity	4	6.0
Atrophied	18	26.9
Very small tissue like & totally calcified or autosplenectomy	2	3.0
Total	67	100.0

Table (4.7): Classification of sickle cell disease patient's age according to their spleen size in frequencies:

Range of the age	Splenomegaly	Shrunken or very small size	Normal size
3 mon – 10.5y	28	5	3
11y – 20y	2	11	9
21y – 30y	1	8	-

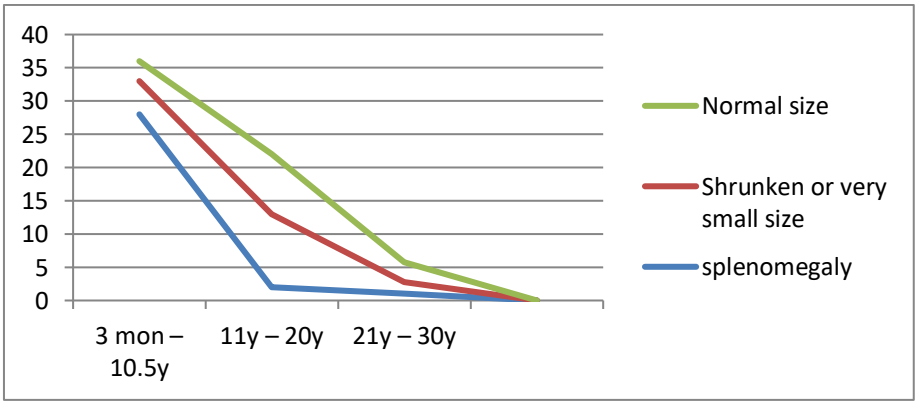


Figure (4.6): Classification of sickle cell disease patient's age according to their spleen size in frequencies

Table (4.8): Classification of sickle cell disease patient's age according to presence of spleen lesion:

Range of the age	Presence of lesion	No lesion
3 mon – 10.5y	13	23
11y – 20y	12	10
21y – 30y	4	5

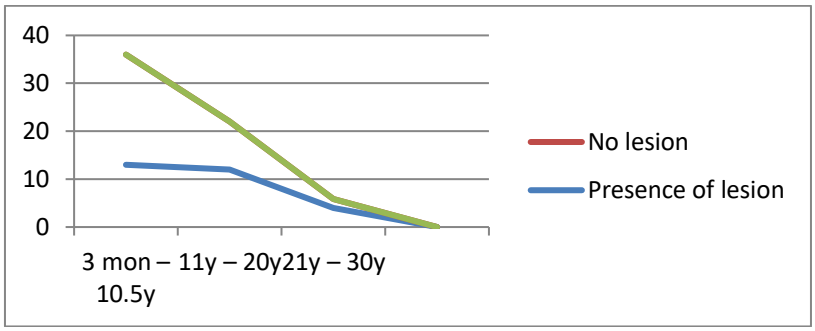


Figure (4.7): Classification of sickle cell disease patient's age according to presence of spleen lesion

Table (4.9):Shows the classification of spleen size and the normality of spleen CT number in patients affected with sickle cell disease (SCD).P ≤0.004

Size of Spleen	Less than 36 HU (Abnormal)	40 - 60 HU (Normal)	Spleen Doesn't Seen
Splenomegaly	12	19	-
Shrunken Spleen	19	3	2
Normal Spleen Size	1	11	-

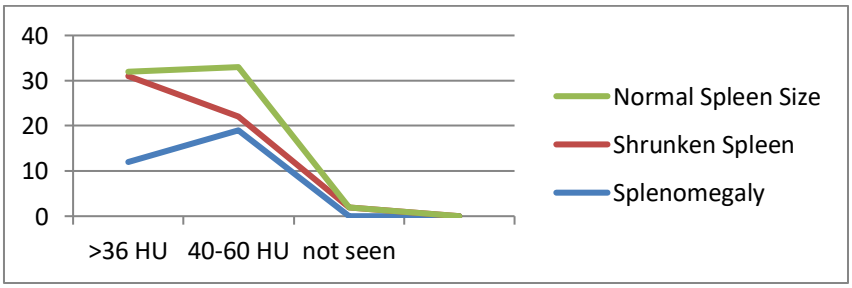


Figure (4.8): Shows the classification of spleen size and the normality of spleen CT number in patients affected with sickle cell disease (SCD).

Table (4.10):Shows the classification of spleen size according to the lesion type in patients affected with sickle cell disease (SCD).P ≤0.010

Size of Spleen	Infarction	Cyst	Abscess	Calcification
Splenomegaly	2	1	7	-
Shrunken Spleen	5	2	0	3
Normal Spleen Size	2	5	5	-

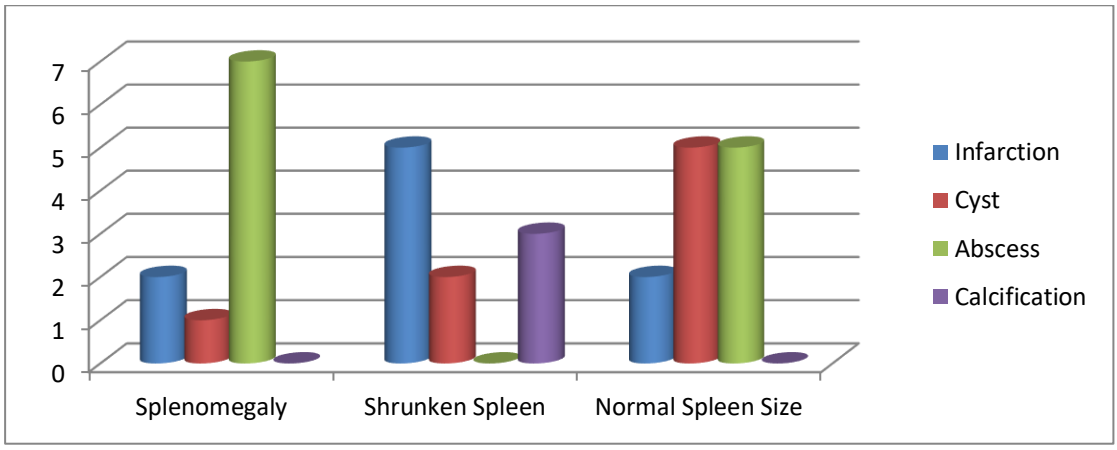


Figure (4.9): Shows the classification of spleen size according to the lesion type in patients affected with sickle cell disease (SCD).

Table (4.11): Findings in the spleen vein in patients affected with sickle cell disease (SCD).

Characterization of spleen vein	Percentage
Normal splenic vein	32.80 %
Dilated splenic vein	17.90 %
Multiple vein collaterais	4.50 %
Thrombus (filling defect)	25.40 %
Splenic vein is not seen	14.90 %
Dilated splenic vein + Multiple vein collaterais	4.50 %

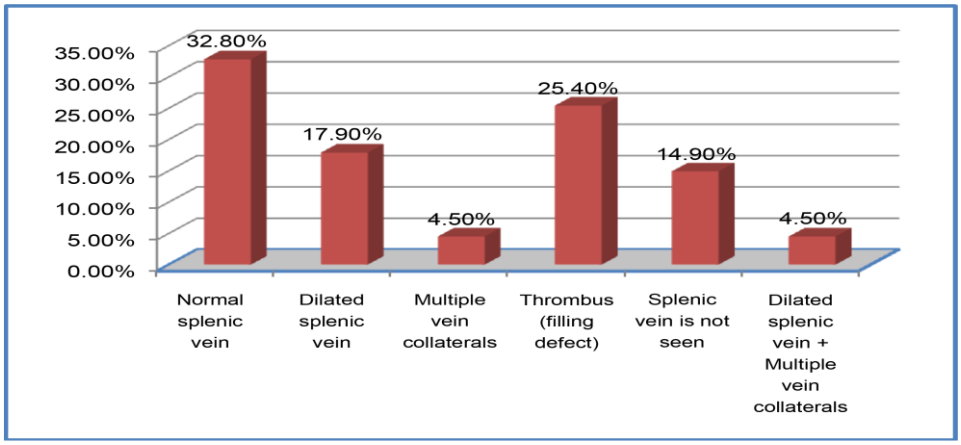


Figure (4.10): Shows findings in the spleen vein in patients affected with sickle cell disease (SCD).

Table (4.12):Shows the classification of spleen size and enlargement of spleen lymph nodes in patients affected with sickle cell disease (SCD).

Size of Spleen	Enlarge Lymph Nodes	Normal	Not Seen
Splenomegaly	22	9	-
Shrunken spleen	1	1	22
Normal spleen size	6	6	-

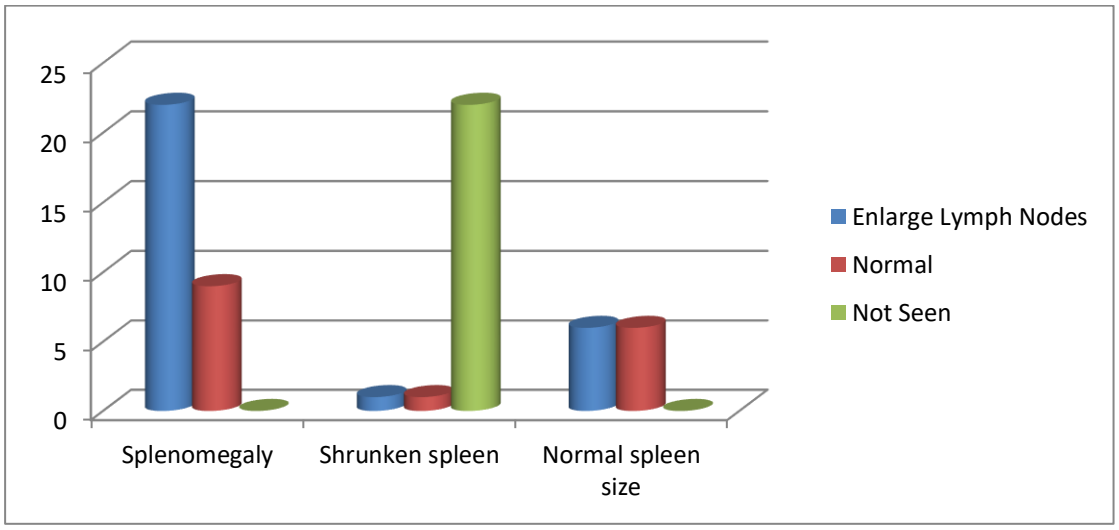


Figure (4.11): Shows the classification of spleen size and enlargement of spleen lymph nodes in patients affected with sickle cell disease (SCD).

Table (4.13):Shows the cross tabulation between spleen vein diameter and spleen lymph nodes characteristics, spleen size, spleen lesion type in patients affected with sickle cell disease (SCD).

	Dilated Spleen Vein Diameter	**Normal Spleen Vein Diameter**	**Not Seen**
Size of Spleen P ≤0.000			
Splenomegaly	23	8	-
Shrunken spleen	9	-	15
Normal spleen size	2	10	-
Lymph Nodes Condition P ≤0.000			
Normal lymph nodes	9	9	0
Enlarged lymph nodes	20	12	2
Lymph nodes not seen	0	0	15
Lesions Affected the Spleen P ≤0.024			
Infarction	5	1	3
Cyst	5	6	0
Abscess	5	7	0

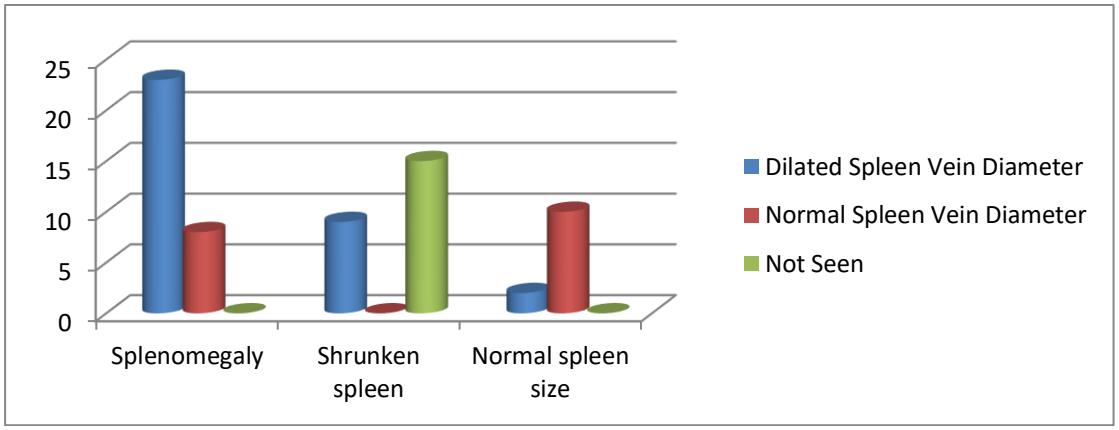


Figure (4.12): shows relations between spleen vein diameter and spleen size in patients affected with sickle cell disease (SCD).

Table (4.14):Characterization spleen lesions in all of the enhancement phase in patients affected with sickle cell disease (SCD). P ≤0.000

Degree of lesions enhancement	Before CM	Arterial phase	Venous phase	Delay
Well defined	0	8	15	19
Mild defined	0	1	8	1
Ill defined	11	15	6	2
Not appear	18	5	0	7

Table (4.15): Visibility of spleen abscess in all of the enhancement phase in patients affected with sickle cell disease (SCD).P ≤0.000

Degree of abscess enhancement	Before CM	Arterial phase	Venous phase	Delay
Well defined	0	1	8	9
Mild defined	0	0	4	1
Ill defined	2	9	0	2
Not appear	10	2	0	0

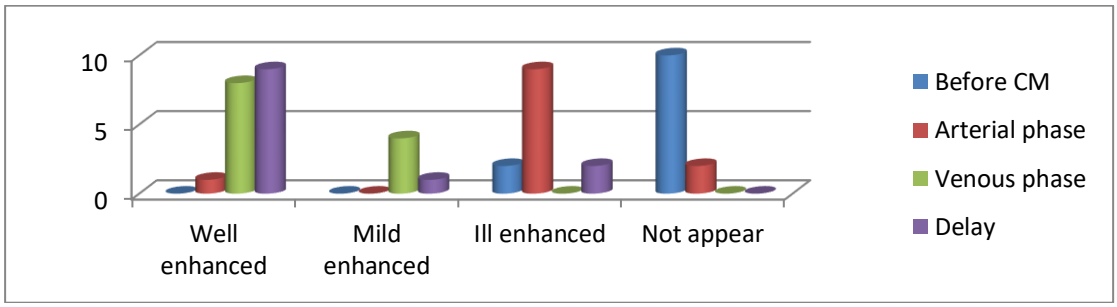


Figure (4.13): Shows visibility of spleen abscess in all of the enhancement phase in patients affected with sickle cell disease (SCD).

Table (4.16): Visibility of spleen cyst in all of the enhancement phase in patients affected with sickle cell disease (SCD).P ≤0.000

Degree of cyst enhancement	Before CM	Arterial phase	Venous phase	Delay
Well enhanced	0	7	3	1
Mild enhanced	0	1	0	0
Ill enhanced	7	0	5	0
Not appear	1	0	0	7

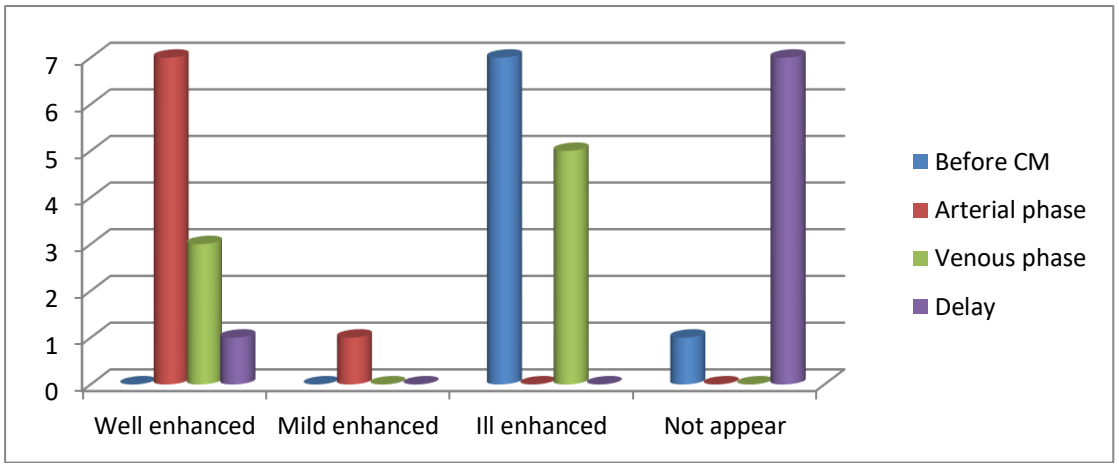


Figure (4.14): Shows visibility of spleen cyst in all of the enhancement phase in patients affected with sickle cell disease (SCD).

Table (4.17): Visibility spleen infarction in all of the enhancement phase in patients affected with sickle cell disease (SCD).P ≤0.000

Degree of infarction enhancement	Before CM	Arterial phase	Venous phase	Delay
Well defined	0	0	4	9
Mild defined	0	0	4	0
Ill defined	2	6	1	0
Not appear	7	3	0	0

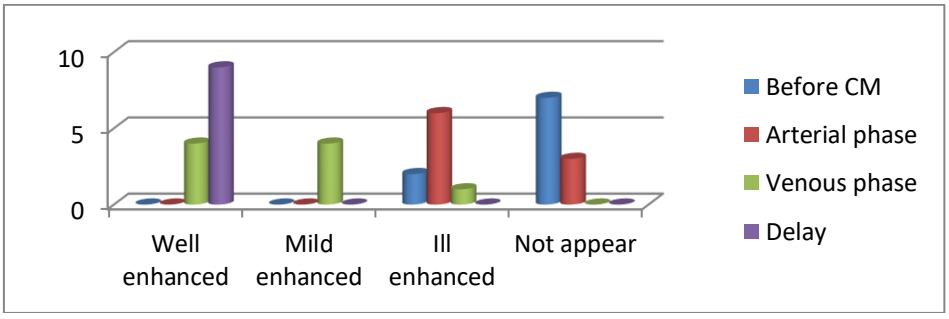


Figure (4.15): Shows visibility spleen infarction in all of the enhancement phase in patients affected with sickle cell disease (SCD).

Table (4-18): Spleen abscess, either single or multiple, CECT appearance characteristics found in SCD patients of studied sample in frequencies and percentages

Appearance characteristics of the lesion in CE CT	frequency	percentage
peripherally enhancing, centrally hypoattenuating lesions (ring enhancement)	7	58.3%
Segmental, wedge-shaped solid or contain gas	3	25%
early enhancement of circumferential perfusion abnormalities	2	16%
Total	12	100%

Table (4-19): Spleen Cyst ,either single or multiple, CECT appearance characteristics found in SCD patients of studied sample in frequencies and percentages

Appearance characteristics of the lesion in CE CT	frequency	percentage
Regular outline circle/s of good enhanced area	5	62.5%
Very small enhanced capsule with a little air bubble within the lesion	2	25%
Enhanced bean shape with regular outline	1	12.5%
Total	8	100%

Table (4-20): Spleen infarcts CECT appearance characteristics found in SCD patients of studied sample in frequencies and percentages

Appearance characteristics of the lesion in CE CT	frequency	percentage
well-defined wedge-shaped based area of hypo attenuation which is peripheral with apex pointing toward the hilum without pressure effect on adjacent structures	6	66.6%
Capsular based irregular triangular shaped hypodense patch	2	22.2%
Irregular bean shape peripherally of hypodense area	1	11%
Total	9	100%

Table (4.21):Characterization spleen lesions before CM in patients affected with different type sickle cell disease types (Hb SB + thalassemia, Hb SB 0-thalassemia, Hb SC and Hb SS) P-value = 0.047

Type of Sickle	Hb SB + thalassemia	Hb SB 0-thalassemia	Hb SC	Hb SS	Total
Not appear	-	3(9.4%)	5(15.6%)	13(40.6%)	21 (65.6%)
Ill defined lesions	-	1 (3.1%)	-	4 (12.5%)	5 (18.8%)
Well defined calcifications	1 (3.1%)	1 (3.1%)	-	1 (3.1%)	3 (9.4%)
Well defined nodules	1 (3.1%)	-	1 (3.1%)	-	2 (6.3%)
Total	2 (6.3%)	5 (15.6%)	6 (18.8%)	18(56.3%)	31(100.0%)

Table (4.22):Characterization spleen lesions in arterial phase in patients affected with different type sickle cell disease (Hb SB + thalassemia, Hb SB 0-thalassemia, Hb SC, Hb SS, SCT).P-value = 0.085

Type of Sickle	Hb SB + thalassemia	Hb SB 0-thalassemia	Hb SC	Hb SS	Total
Well Enhanced Lesion& Calcifications	1 (3.1%)	3 (9.4%)	-	1 (3.1%)	5(15.6%)
Well Enhanced Nodules	1 (3.1%)	-	-	1 (3.1%)	2(6.3%)
Well Enhanced Cysts	-	-	1 (3.1%)	-	1(3.1%)
Ring Enhancement	-	-	-	1 (3.1%)	1(3.1%)
Peripheral Enhancement with Ill Enhanced Lesion	-	-	-	3 (9.4%)	3(9.4%)
Ill Enhanced Lesion	-	2 (6.3%)	4 (12.5%)	6 (18.8%)	12(37.5%)
Not Enhanced	-	-	1 (3.1%)	4 (12.5%)	5 (15.6%)
Total	2(6.3%)	5(15.6%)	6(18.8%)	18(56.3%)	31(100.0%)

Table (4.23):Characterization spleen lesions venous phase in patients affected with different type sickle cell disease Hb SB + thalassemia, Hb SB 0-thalassemia, Hb SC, Hb SS, SCT. P-value = 0.037

Type of Sickle	Hb SB + thalassemia	Hb SB 0-thalassemia	Hb SC	Hb SS	Total
Well defined enhanced lesion	-	-	1(3.1%)	2(6.3%)	3(12.5%)
Well defined non enhanced lesion (hypo dense)	-	2(6.3%)	3(9.4%)	10(31.3%)	15(46.9%)
Multiple well defined non enhance lesions	-	-	-	2(6.3%)	2(6.3%)
Peripheral hypo dense enhanced lesion	-	-	-	1(3.1%)	1(3.1%)
Hypo dense lesion surround by enhancing calcification	-	1(3.1%)	-	-	1(3.1%)
Homogenous hypo dense with well defined peripheral enhancement	-	-	-	2(6.3%)	2 (6.3%)
Heterogeneous pattern	-	-	1(3.1%)	-	1(3.1%)
Ill defined non enhanced lesion (hypo dense)	2(6.3%)	2(6.3%)	1(3.1%)	1(3.1%)	6(18.8%)
Total	2 (6.3%)	5 (15.6%)	6 (18.8%)	18(56.3%)	31(100.0%)

Table (4.24):Characterization spleen lesions in delay phase in patients affected with different type sickle cell disease Hb SB + thalassemia, Hb SB 0-thalassemia, Hb SC, Hb SS, SCT.P-value = 0.055

Type of Sickle	Hb SB + thalassemia	Hb SB 0-thalassemia	Hb SC	Hb SS	Total
Well defined enhanced lesion	-	-	1 (3.1%)	1(3.1%)	2 (9.4%)
Well defined hypo dense lesion	-	3(9.4%)	3(9.4%)	12(37.5%)	18 (56.3%)
Well defined peripheral enhance with unenhanced hypo dense lesion	-	-	-	2(6.3%)	2 (6.3%)
Ill defined unenhanced lesion	1 (3.1%)	-	2 (6.3%)	1(3.1%)	4 (12.5%)
Washout CM (not seen)	1 (3.1%)	2 (6.3%)	-	2 (6.3%)	5 (15.6%)
Total	2 (6.3%)	5 (15.6%)	6 (18.8%)	18(56.3%)	31(100.0%)

Table (4.25): frequencies of the affected certain abdominal and chest organs in patients with sickle cell disease:

Organ	Frequency
Liver	59
Kidney	55
Lung	56
Spleen	67
Pancreas	5
gallbladder	22

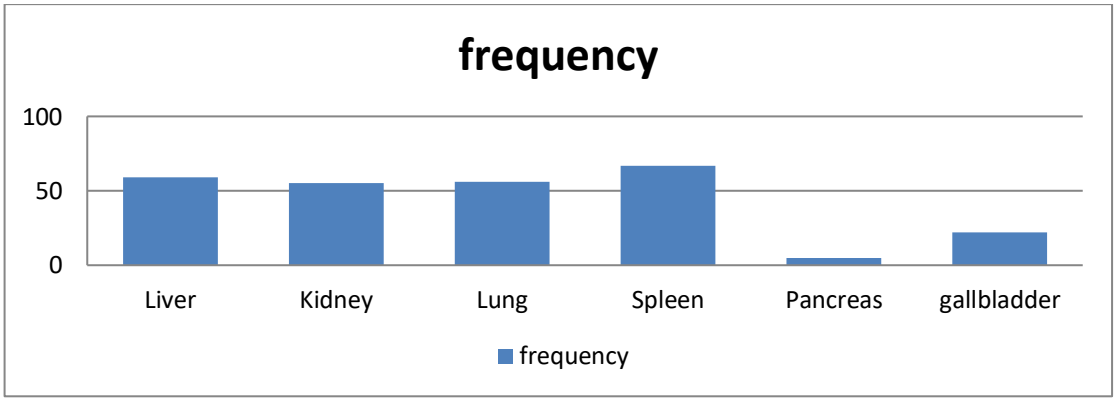


Figure (4.16): Shows frequencies of the affected certain abdominal and chest organs in patients with sickle cell disease.

Table (4.26): Cross tabulation between patients age and spleen CT manifestation in SCD :

Range of the age	Spleno megaly	Splenic cyst	Splenic Abscess	Splenic infarction	Splenomegaly+cyst	Splenomegaly+abscess
3 mon – 7y	15	3	-	3	1	6
8 y – 17 y	6	2	4	9	1	1
18y – 28y	2	0	1	11	0	2

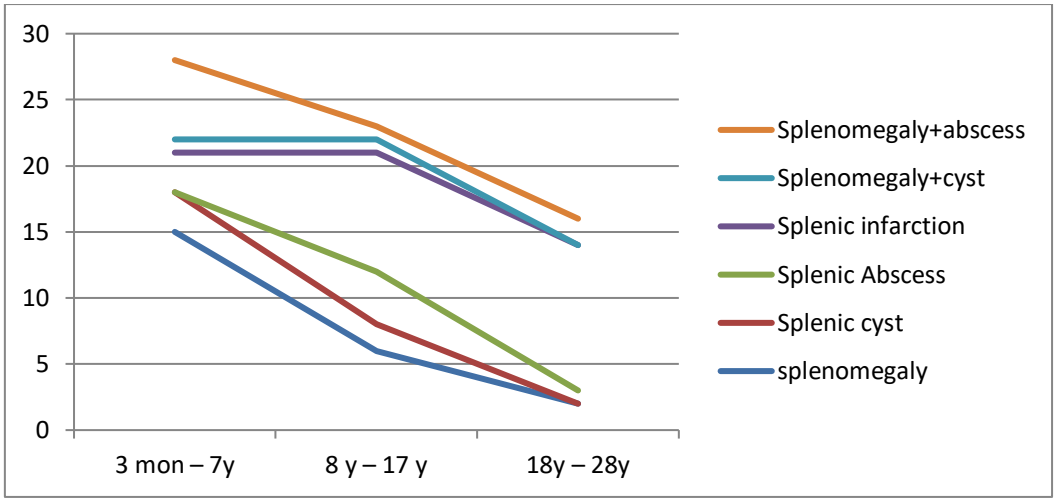


Figure (4.17): Shows relation between patients age and spleen CT manifestation in SCD

Table (4.27):Cross tabulation between patients age and liver CT manifestation in SCD

Range of the age	Normal	Focal necrosis	Hepato megaly	Hepatic abscess	Hepatic cyst	Hepatic infarction
3 mon – 7y	4	3	12	3	5	1
8 y – 17 y	4	2	5	5	4	3
18y – 28y	0	3	2	4	1	6

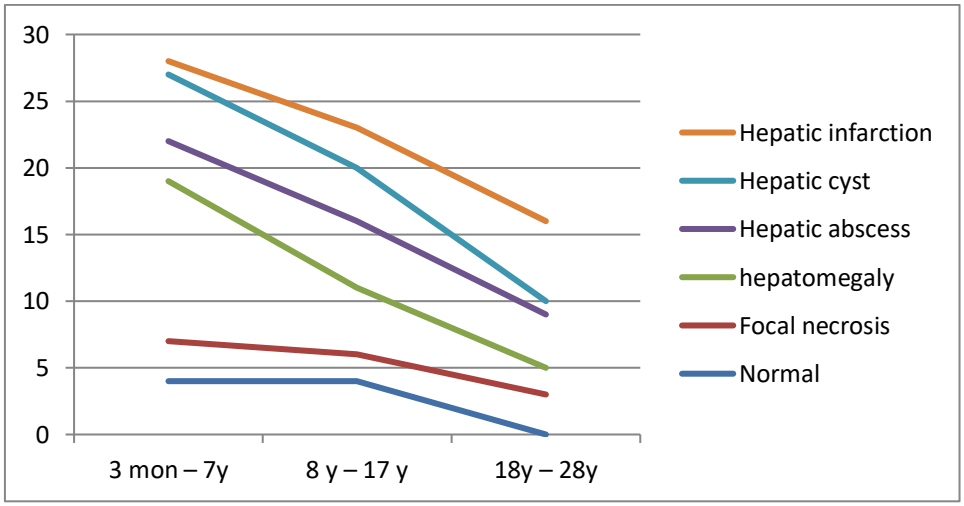


Figure (4.18): Shows relation between patients age and liver CT manifestation in SCD

Table (4.28):Cross tabulation between patients age and lungs CT manifestation in SCD :

Range of the age	Normal	Pleural effusion	Pneu-monia	Atelec-tasis	Ground glass nodules	Consolidation	fibrosis	Lung abscess
3 mon – 7y	8	9	5	3	1	2	0	0
8 y – 17 y	3	3	1	1	4	5	2	4
18y – 28y	0	4	0	0	0	1	8	3

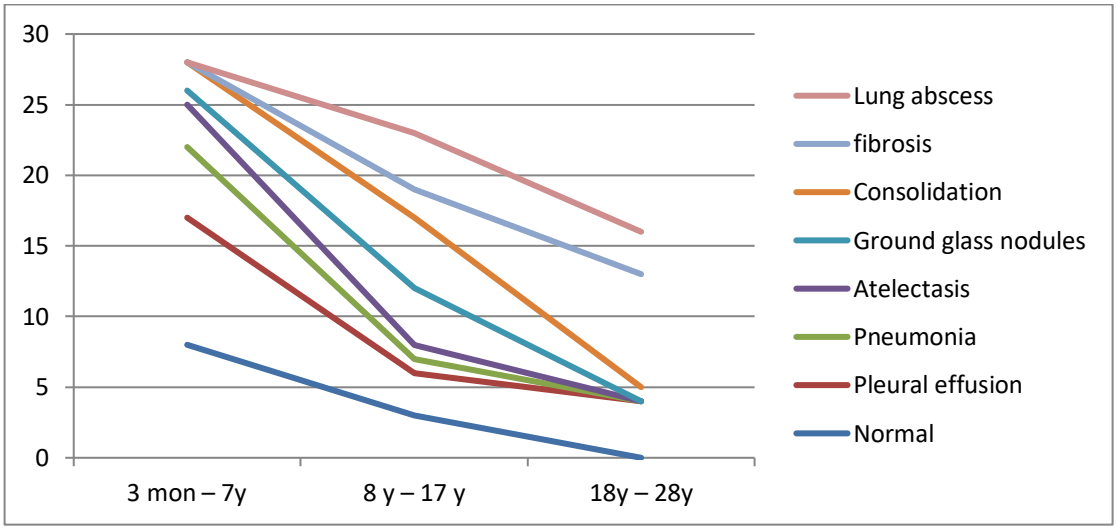


Figure (4.19): Shows relation between patients age and lung CT manifestation in SCD

Table (4.29):Cross tabulation between patients age and kidney CT manifestation in SCD

Range of the age	Normal	Papillary necrosis	Renal abscess	Stones &hydronephrosis	Renal vein thrombosis	Renal failure	Renal infarction
3 mon – 7y	8	9	2	8	1	0	0
8 y – 17 y	4	4	5	2	2	1	5
18y – 28y	0	2	0	1	1	6	6

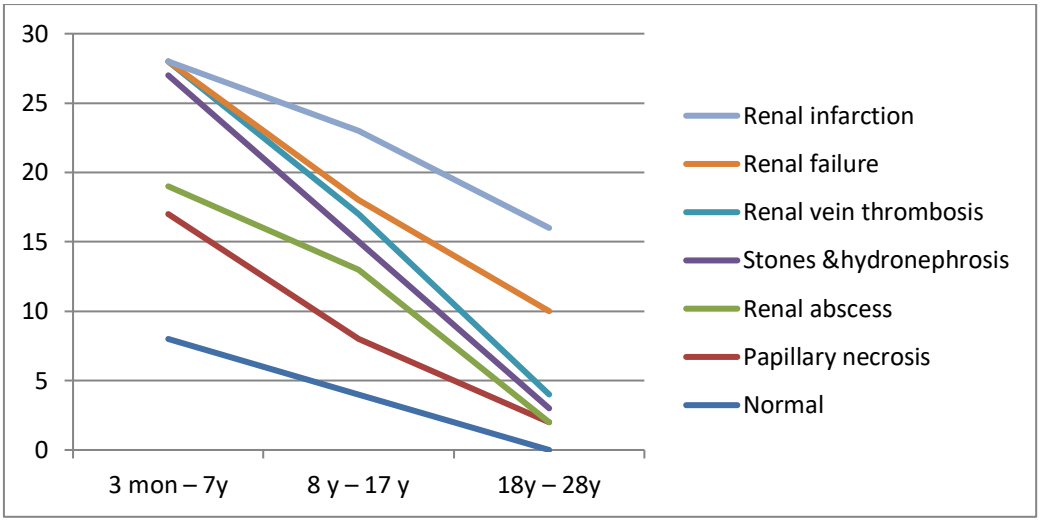


Figure (4.20): Shows relation between patients age and kidney CT manifestation in SCD

Table (4.30):Cross tabulation between patient's age , gall bladder and pancreas CT manifestation in SCD

Range of the age	Cholelithiasis	Gall stones and dilated common bile duct	Acute pancreatitis
3 mon – 7y	0	3	0
8 y – 17 y	3	5	2
18y – 28y	4	7	3

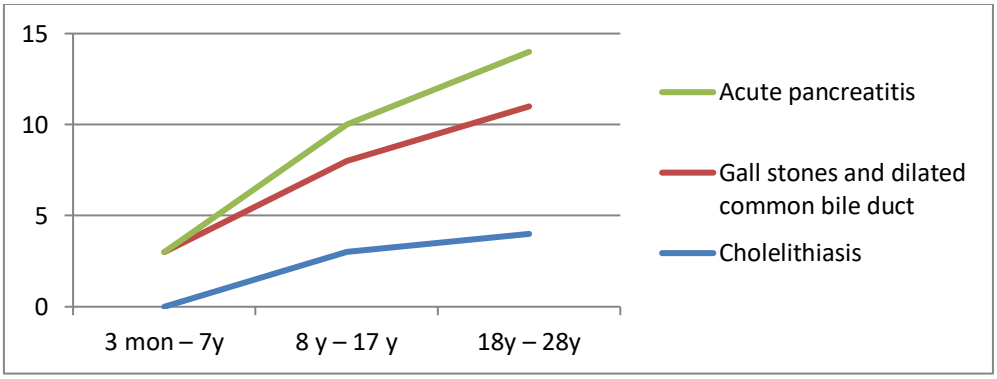


Figure (4.21): Shows relation between patients age and gall bladder and pancreas CT manifestation in SCD

Table (4.31): Relation between spleen CT manifestation in SCD and type of SCD

Type of SCA	splenomegaly	Splenic cyst	Splenic Abscess	Splenic infarction	Splenomegaly +cyst	Splenomegaly +abscess
Hb SS	21	3	3	13	2	8
Hb SC	0	2	1	5	0	0
Hb SB 0-thalassemia	0	0	0	4	0	1
Hb SB+ thalassemia	2	0	1	1	0	0

Table (4.32): Relation between liver CT manifestation in SCD and type of SCD

Type of SCA	Normal	Focal necrosis	hepatomegaly	Hepatic abscess	Hepatic cyst	Hepatic infarction
Hb SS	7	4	17	5	7	5
Hb SC	1	1	0	4	2	3
Hb SB 0-thalassemia	0	3	1	1	1	1
Hb SB+ thalassemia	0	0	1	2	0	1

Table (4.33):Relation between lung CT manifestation in SCD and type of SCD

Type of SCA	Normal	Pleural effusion	Pneu-monia	Atelec-tasis	Ground glass nodules	Consolid-ation	fibrosis	Lung abscess
Hb SS	9	13	6	4	3	6	5	3
Hb SC	1	2	0	0	1	1	2	2
Hb SB 0-thalassemia	1	1	0	0	0	0	2	1
Hb SB+ thalassemia	0	0	0	0	1	1	1	1

Table (4.34):Relation between kidney CT manifestation in SCD and type of SCD:

Type of SCD	Normal	Papillary necrosis	Renal abscess	Stones &hydronephrosis	Renal vein thrombosis	Renal failure	Renal infarction
Hb SS	10	13	5	8	3	4	6
Hb SC	1	1	1	1	1	2	2
Hb SB 0-thalassemia	1	0	0	1	0	1	2
Hb SB+ thalassemia	0	1	1	1	0	0	1

Table (4.35):Relation between gall bladder and pancreas CT manifestation in SCD and type of SCD:

Type of SCD	Cholelithiasis	Gall stones and dilated common bile duct	Acute pancreatitis
Hb SS	5	13	4
Hb SC	1	1	1
Hb SB 0-thalassemia	0	1	0
Hb SB+ thalassemia	1	0	0

Chapter Five

Discussion, Conclusion and Recommendations

5.1 Discussion

Sickle cell disease is a condition in which there aren't enough healthy red blood cells to carry adequate oxygen throughout the body(Vichinsky, 2016).

Sickle cell disease can affect any and all major organs system in the body and can lead to many complications.

It represents one of the most common hereditary blood disorders in Saudi Arabia. According to the latest statistics of the Saudi Arabia population for three years before the existence of many cases infected and carriers of genetic blood diseases by the equivalent of 3 million people, or 35% of the population(Siva, 2013).

and mostly are children and young people, which result in a shortage of working forces in the country and great impact on the economy and different fields of production in the country. If patients are starting good treatment, they can prevent complications.

Computed tomography (special X-ray tests that produce cross-sectional images of the body using X-rays and a computer(Herman and Gabor, 2009)) is noninvasive, safe and well-tolerated technique that provide greater clarity and reveal more details diagnostic modality, it represents the most widely applied cross-sectional abdominal imaging technique and is considered the imaging modality of choice for the evaluation and diagnosis of sickle cell disease complications from early stages(Ekeh et al, 2008).

The spleen is one of the most common and early organs to be affected in SCD(Al-Salem, 2006) . It is commonly enlarged during the first decade of life but then undergoes progressive atrophy and infarcted leading to autosplenectomy(Al-Salem, 2006) . Other abdominal and chest organs are also common influenced by the disease.

This study revealed about how spleen and certain abdominal(liver, kidneys, gallbladder and pancreas) and chest organs can appear when affected by any types of this disease in CT image, to be able to manage and treated complications. Random samples of (67) patients, 38 males and 29 females, who were investigating as sickle cell disease -in Aseer and Gizan areas (south of Saudi Arabia)-were undergo for chest, abdomen CT examination.

The characteristic of the all variables in the studied sample were describe as frequencies and percentages.

67 SCD patients ranged from 3 months to 28 years in age was studied, 53.73% of patients are ranged from 3 mon-10.5 years old, followed by 32.84% are ranged from 11-20 years old and finally ages from 21-30 years old were represent 13.43% (Table 4-1)

The most common type of SCD affected the Saudi patients in the study is hemoglobin SS disease (Hb SS) representing 41 (61.2%). Followed by hemoglobin SC Disease (16.40%), hemoglobin beta-zero thalassemia (10.40%) and hemoglobin SB+ (Beta) thalassemia (10.4%) of the patient sample. This was presented in (Table 4.3)**.**

Our study characterize the spleen locations in the patients affected with SCD; 26 (38.8%) are extend to the left kidney and below the lower third of the left kidney where 18 (26.9%) are atrophied spleen, this was presented in (Table 4.4).

Characterization of spleen size and shape were done in all of the affected sample with SCA, the shape can be changed to be an oval, irregular, blurred out line, pyramidal, loss it's medial concavity. The changes in size may become enlarged or atrophied or very small like tissue or shrunken, totally calcified or autosplenectomy; the changes occur were found to be of wide-range of variation, this was presented in (Table 4.6). And the most age group which affected by splenomegaly were ranged from (3 mon to10.5y), and

atrophied and shrunken spleen were occur in age groups who ranged from 11-30 years old (Table 4.7), agree with previous study done by (Ali et al, 2002). Studies mentioned that in SCD, the spleen size changes were due to repeated attacks of vaso-occlusion and infarction, however sometimes splenomegaly may occur (Vancauwenberghe et al, 2015), this justify our findings of the presence of various spleen features.

The spleen hilur region was evaluated and the splenic vein was measured 12 (17.9%) have dilated splenic vein, the presence of multiple vein collaterals, thrombus (filling defect) were also been detected in patients with SCD. This was presented in (Table 4.11).

Spleen vein dilatation in patients affected with SCD has significant relations in patients with splenomegaly and those with enlarged lymph nodes, however similar measurements (dilated) were found equally in patients affected with cysts, abscess or infarctions, these were noticed in (Table 4.13).

(Table 4.9) demonstrates the classification of spleen size and the normality of spleen CT number in patients affected with SCD it was found that 12 patients with splenomegally have abnormal attenuation values less than 36 HU and those with shrunken spleen were 19 patients, this may be due to the affection with cysts and abscess, infarction and inflammation that reduced the attenuation of the spleen, the reduction of the HU was significantly correlated with the changes of the spleen size at $P \leq 0.004$, which confirmed studies done by (Mouzan et al, 2004), and other study (Rani, 2001).

Enlargement of spleen lymph nodes in patients affected with SCD were seen in 22 of patients with Splenomegaly with significant relation at $P \leq 0.000$ between the spleen size changes and the enlargement of lymph nodes, this was presented in (Table 4.12).

Study characterize such cases in the contrast enhanced CT that show a total absence or heterogeneous enhancement pattern within the spleen related to partial or total infarction. Findings of infarction on unenhanced CT are low

attenuation of the spleen relative to the liver, a hyperdense intraluminal filling defect in the splenic vessels indicating an acute thrombus, and high density of the splenic capsule compared with the parenchyma. Immune-deficiency states due to disease or during immune suppression have emerged as a new, common predisposing cause of spleen abscess (Smith et al, 1993). Persistence of splenomegaly in SCA patients predisposes them to the development of complications (Wilson-Okoh et al, 2006).

The classification of spleen size according to the lesion type in patients affected with sickle cell anemia was done. The infarction affected 9 patients where cysts were found in 8, and abscess in 12 patients with significant relations between the type of the complications and the changes in the spleen measurements at $P \leq 0.010$. In the current study (Mouzan et al, 2004).; splenomegaly was observed in 10 patients (70%) with spleen abscess, other findings were observed significantly associated with enlarged spleen in patients with SCD including infarctions and cysts (Table 4.10).

CT scan pre and post contrast enhancement showed well characteristics of these lesions and differentiated the infarction from the cysts and abscesses.

Spleen abscess in all of the enhancement phase in patients affected with sickle cell disease is well defined in both venus and delay phase, and majority of them are peripherally enhanced with hypodensity in the center of lesion (table 4-18), where most of the abscess are ill defined in the arterial phase. Cysts are well enhanced in the arterial phase and most of them characterized by full regular circle enhancement (table 4-19), while spleen infarction showed well defined wedge-shaped based area of hypo attenuation which was mostly peripheral without pressure effect on adjacent structures in the delay phase this explained in table (4-20). On non-enhanced CT and arterial enhancement, infarcts are poorly visualized.

Previous studies mentioned that these patients should be evaluated substantially by ultrasound and if in doubt by CT scan of the abdomen

(Ahmed et al, 2005), Although ultrasound and CT scan are the best methods for the diagnosis of spleen abscess (Ralls et al,1982), (Nelken et al,1987)

We used CT scan because it allows more accurate anatomical localization of the abscess because of the presence of the contrast enhancement techniques. Similarly (Nelken et al, 1987) reported a 96% accuracy using CT-scan for the diagnosis of spleen abscess (Nelken et al,1987).

The study characterized the spleen hypo attenuation lesions (abscess, cyst and infarction) in all of the CT procedures pre contrast, arterial phase, venus phase and delay phase. The diagnostic difficulty in patients with SCD is the differentiation between spleen abscess and large spleen infarct, which can also present with a large spleen. The importance of characterization of the lesion type is to reach to early diagnosis of the spleen complications because if not recognized spleen abscess may rupture locally into the peritoneal cavity, into the adjacent bowel, or into the pleural space, leading to increased mortality, these points also were recommended in other previous studies (Urban and Fishman, 1998)The CT appearance of the spleen lesions depends on the timing of intravenous bolus administration of contrast material (Urban and Fishman, 1998) It may be heterogeneous with variable in appearance patterns include arciform, focal, and diffuse heterogeneity (Donnelly et al,1999) (Table 4.14) showed that the well enhanced lesions appears well in both venous and delay phase and the difference in enhancement characteristics were significantly related with the scanning phase $P \leq 0.000$. Studies mentioned that in most of pediatric CT examinations, splenic heterogeneity is resolved within 70 seconds of the beginning of contrast material injection; hence, low-attenuation lesions that are seen after this time should raise suspicion for a disease process. Helical CT scans obtained during the portal venous phase usually demonstrate homogeneous attenuation throughout the spleen (Donnelly et al,1999). Spleen abscess in all of the enhancement phase in patients affected with sickle cell disease is well enhanced in both venus and delay phase, where most of the

abscess were ill enhanced in the arterial phase, the current study showed the significant correlations at P ≤ 0.000 between degree of abscess enhancement and timing of contrast administration. Cysts are well enhanced in the arterial phase, Spleen infarction showed well defined in the delay phase and were correlated significantly P ≤ 0.000 and 0.000 respectively. This was presented in (Tables 4.15,16&17), that agree with study done by (Ahmed et al, 2005). The absence of wall-thickening, intralesional solid components or contrast-enhancement is in favor of benign lesions (Vancauwenberghe et al, 2015). At CT, cysts manifest as rounded, well-demarcated no enhancing lesions with near water attenuation similar description was mentioned previously (Karlo et al, 2013). These characterizations of cyst in contrast enhancement protocol help us in distinguishing a benign cystic lesion from a malignant lesion. The presence of the infarction in our patients with sickle cell disease was justified that erythrocytes are rigid and frequently occlude the small lesions (Vancauwenberghe et al, 2015). When we apply the contrast material, it becomes visible as small, disseminated hypodense, ill-defined lesions. It was present in early and late course of the disease, within enlarged spleen however in some cases the spleen shrinks and become calcified. Therefore, in patients with sickle cell disease, the presence of multiple small hypodense splenic lesions, is strongly suggestive of sickle cell-induced splenic infarctions. When we characterize patient with splenic infarction, The CT appearance of infarcts was found to be reliant on the time elapsed since the insult. On non-enhanced CT, infarcts are poorly visualized. In the hyper acute phase, the spleen demonstrates a mottled texture secondary to hemorrhagic infarction with intravenous administration of contrast material. When the entire spleen is infarcted, it results in diffuse splenic hypodensity, leaving a residual rim of enhancing capsule. This appearance was described in the study done by (Taylor et al, 1991) as known as the rim sign (Taylor et al, 1991). Over time, the lesions become better defined. Infarctions are peripheral and wedge-shaped

non-enhancing defects; however some cases have an irregular margin, at delay phase the lesions were resolved (wash out), leaving the cortical defect, calcification and the rim of enhancing capsule. The diagnosis and characterization of infarction is very critical because some infarcts may mimic other splenic lesions, including abscesses or tumors, requiring clinical correlation, or percutaneous fine-needle aspiration biopsy (Taylor et al, 1991). The current study characterized 3 cases of atrophied spleen with calcifications; in the noncontract films CT represented this dense splenic calcification. The current study justify this finding as it thought to be secondary to a combination of hemosiderin deposition, fibrosis as mentioned by (Lieven et al,1996) . Splenic abscess formation was also been detected At CT, abscesses typically manifest irregularly marginated lesions with low attenuation. Rim enhancement was seen on contrast-enhanced scans, this is also described by (Urrutia et al, 1996) . The enhancement pattern in different type of SCD were seen in all of the CT scanning phase, in arterial, venus and delay phase as well as scanning before contrast, the results showed a significant relation between the character of the lesions and degree of enhancement with the scanning technique used (pre contrast, venous and delay phase) in different SCD types that means it may have an impact on the lesions enhancement however the correlation in characterizing or defining lesion is found to be frail at $p \leq 0.085$ in the arterial phase, that means we have to consider the other phases in confirmation or identifying the hypo intense splenic lesions, these were presented in (Tables 4. 21,22,23&24).

Sickle cell clots cause ischemic vascular occlusion, which frequently affects different parts of the abdominal structures. The most commonly involved organ is the spleen, which was affected in almost all patients with SCD (Urban and Fishman,1998), (Claster and Vichinsky,1996). Studies showed that one of developing cause of splenomegaly is acute splenic sequestration. At clinical examination, patients demonstrate massive splenic enlargement and peripheral

areas of decreased attenuation with areas of increased attenuation secondary to acute hemorrhage (Manish et al, 2012).Similarly our study showed the findings of Splenomegaly in 23 cases , Splenic cyst in 5 cases Splenic Abscess in 5 cases Splenic infarction in 23cases and splenomegaly with cyst and splenomegaly with abscess in 2 and 9 cases respectively this was presented in table (1 , 6) where the patients age and SC type was considered .The literature have mentioned that repeated splenic infarctions that start within the first 18–36 months of life, in association with the dates of disappearance of protective Hb F, result in hyposplenism and asplenism. Splenic atrophy is a major etiology of compromised immune status and increased susceptibility to infections. (Urban and Fishman, 1998), (Claster and Vichinsky, 1996).

In our study the cases of splenic infarction depends on the timing of imaging and the size of the infarct. Contrast enhanced CT scan is proved to be the most sensitive tool of imaging .The typical infarct is seen as a hypo dense non- or poorly enhancing wedge, with apex pointing toward the hilum. Similar studies showed that in late period of time infarctions may resolved completely or leave a permanent scar, or liquefy with possible abscess formation. Also, multiple small infarcts or global infarct of the whole spleen are reported in the imaging findings (Emery, 1997), (Michael et al, 2004), (Morishima et al, 2008).

(Table 4.24) cross tabulated the patients' age and liver CT manifestation in SCA. Hepatic focal necrosis was found in 8 cases, hepatomegaly in 19, and hepatic abscess in 12 cases, hepatic cyst in 10 and Hepatic Infarction in 10 cases, Cholelithiasis, gall stones and dilated common bile duct and acute pancreatitis were also considered as an important manifestation of SCD and was found in 7, 15 and 5 cases in respectively and was increased by increasing of the patient age as presented in (Table 4.27), agree other study by (Jebbin and Adotey, 2011). On the other previous studies; liver infarction in SCD was reported. Acute sickle hepatic crisis affects about 10% of patients admitted for

painful crisis. It usually simulates acute cholecystitis with right upper quadrant pain, fever and leucocytosis, however unlike cholecystitis; the liver is enlarged and tender and also diagnosed by CT which is considered the most sensitive imaging tool for the diagnosis of these insults (Behrang, 2010), (Gauthier et al,1985) and (Magid et al, 2014).

Studies showed that a high incidence of gall bladder multiple pigmented gall stones is clearly demonstrated among SCD patients due to high bilirubin levels (Michael et al, 2004). (Tables 4.32) classifies the findings according to SCD types.

Table (4.26) showed the renal manifestation in SCD. It was found to be renal papillary necrosis in 15 cases ,renal abscess in 7 cases, stones with hydronephrosis in 11 cases, renal vein thrombosis in 4 cases, renal failure in 7 and renal infarction in 11 cases considering the patients age and type of SCD as presented also in (Table 4.31) .Other similar studies showed that there are multiple renal abnormalities associated with SCD including medullary renal tubular dysfunction , hematuria and papillary necrosis (Eric and Anthony, 2009) Glomerulu hypertrophy may be noted, which may account for the mild diffuse renal enlargement , focal or diffuse renal infection or infarction, nephritic syndrome is less common but may be seen with renal vein thrombosis (Morgan and Sergeant, 1981),Other studies have mentioned that sickle cell nephropathy is another debilitating complication of SCD, which develops as a result of sickling of RBCs in renal circulation. This leads to ischemia causing cortical infarctions and papillary necrosis, as well as renal tubular injury. It may be associated with complications and finally renal failure(Carly et al, 2010). Also, there is a possible bacterial infection of the scarred renal tissues and functional tubule abnormalities in conjunction with the compromised immunity, leading to abscess formation (Buckalew and Somenen, 1994),(PIatt et al, 1990).

(Table 4.25) presented the lungs CT manifestation in SCD, pleural effusion, pneumonia ,atelectasis, ground glass nodules ,consolidation ,fibrosis lung abscess which was found in different ages as well; at all types of SCD including Hb SS ,Hb SC ,Hb SB 0-thalassemia ,Hb SB+ thalassemia that are presented in (Table 4.30). Similar studies have mentioned that the acute chest syndrome is one of the most common causes of hospitalization and even death of SCA patients, pulmonary vascular obstruction (Platt et al, 1989) and pleural effusion may also be seen, (Abdulla, 2004), (Aaron et al, 2000),(Godeau et al, 1996).

Patients with SCD may develop obstructive or restrictive lung diseases, when there is a progressive decline in the pulmonary functions .This may be explained by established fibrotic lung changes from repeated episodes of pulmonary infective and vaso-occlusive events. High resolution CT scan (HRCT) shows these interstitial changes, that are of reticular or reticulonodular pattern and may be associated with traction bronchiectasis (Ademola et al, 2012).

5.2 Conclusion:

- Contrast scan computed tomography (CECT) has been shown to be an excellent modality for efficient and multisystemic evaluation of the spleen , other abdominal organs and chest in SCD patients.
- Study found that sickle cell disease results in a changes occur in spleen location, size and shape from its normal form, and also found that this disease results in decreasing in the CT attenuation number of the spleen.
- Researcher revealed that there is some lesions including cyst, abscess and infarction are found in spleen of sickle cell patients appeared in different CT phases.
- Contrast enhanced CT technique with arterial, venous and delay are of great value in the diagnosis of SCD.
- Spleen vein dilatation in patients affected with SCD is found has significant relations in patients with splenomegaly and those with enlarged lymph nodes, however similar measurements (dilated) were found equally in patients affected with cysts, abscess or infarctions.
- Regarding our findings and the study results, the SCD can cause multiple complications in the abdominal organs and chest.

5.3 Recommendation

- Researcher recommended more studies in this field should be done to provide and help the good diagnosis of this sickle cell disease and its complications.
- Also researcher advices to provide well trained and qualified radiologist and technologist, this important for well medical service management.
- To examine patients with MRI contrast phases to avoid the risk of radiation.
- Relative marriage or endogamy should be avoided as possible in southern Saudi Arabia and other areas where sickle cell disease is prevalent, to reduce the risk of disease.
- It is necessary to carry out educational campaigns to raise awareness of sickle cell anemia, how serious it is, how to detect it early, and the necessity of following up its development by conducting periodic examinations, thus increasing the life expectancy of the infected person.

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Appendices(1)

Images

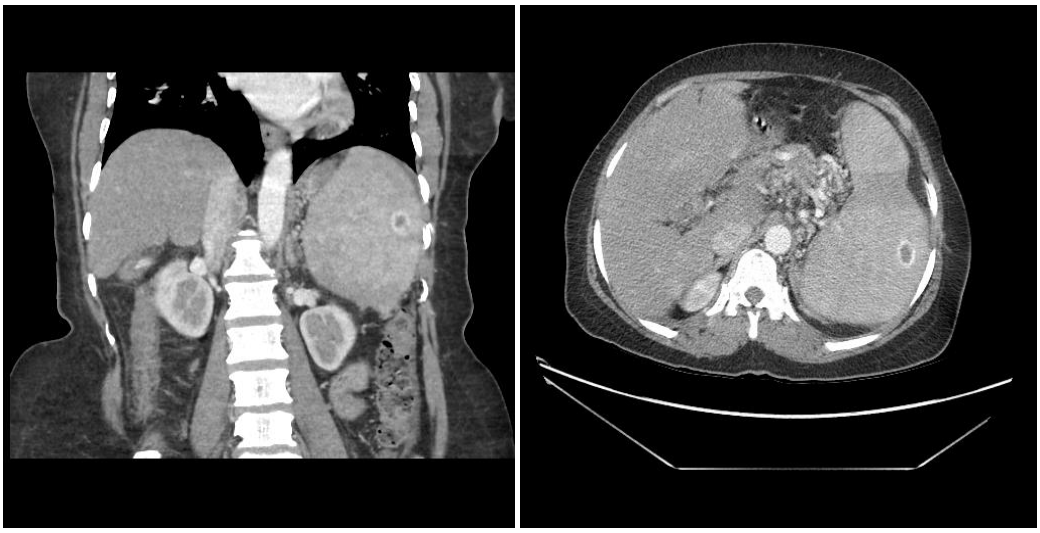

Image No.(1): Axial and coronal abdominal CT images of SCD patient show enlarged spleen and well defined hypodense lesion(abscess formation) with ring enhancement in arterial phase

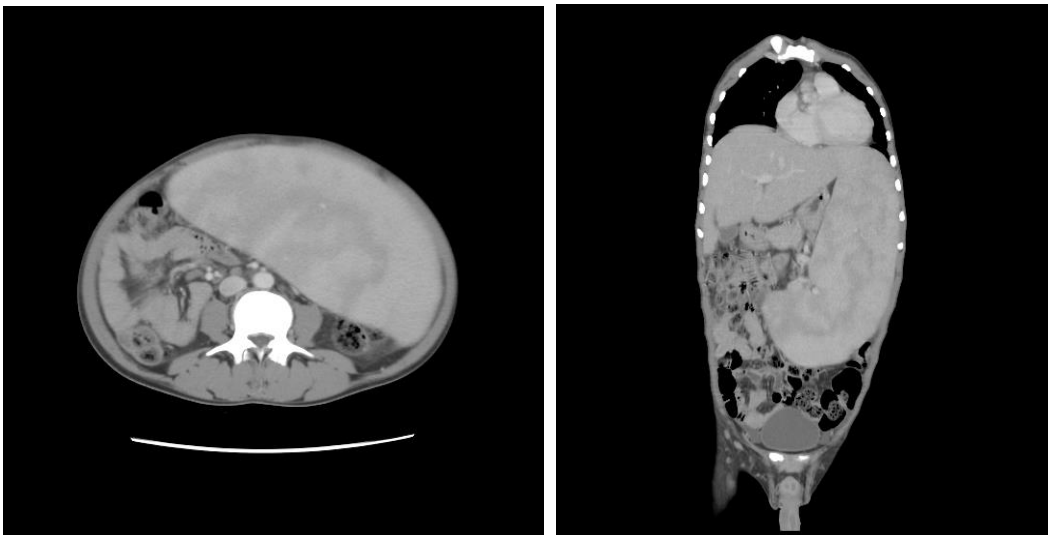

Image No.(2): Axial and coronal abdominal CT images of SCD child showing hugely enlarged spleen

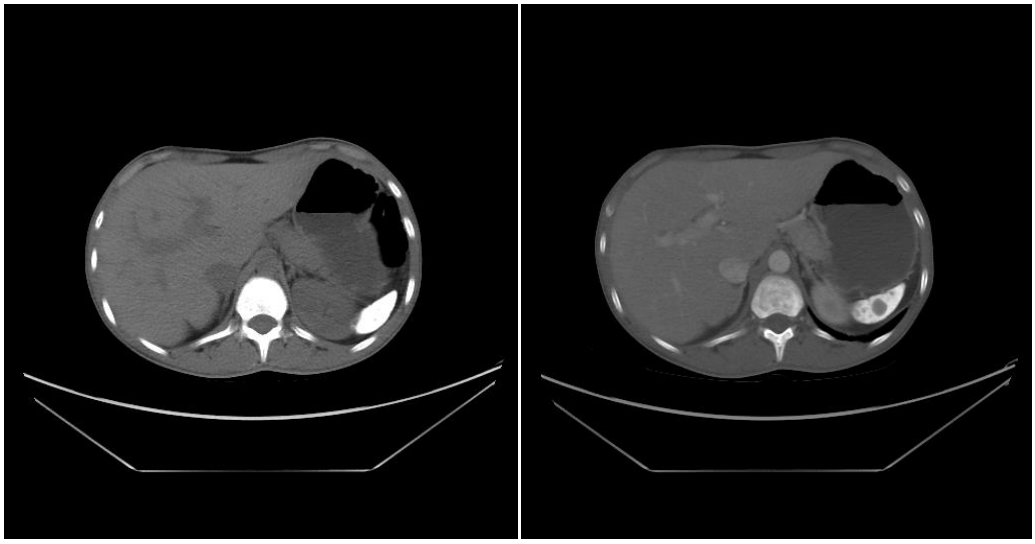

Image No.(3): Two axial abdominal CT images of SCD patient in venous (RT) and delay (LT) phases, spleen is appear shrunken and totally calcified with small hypodense lesions.

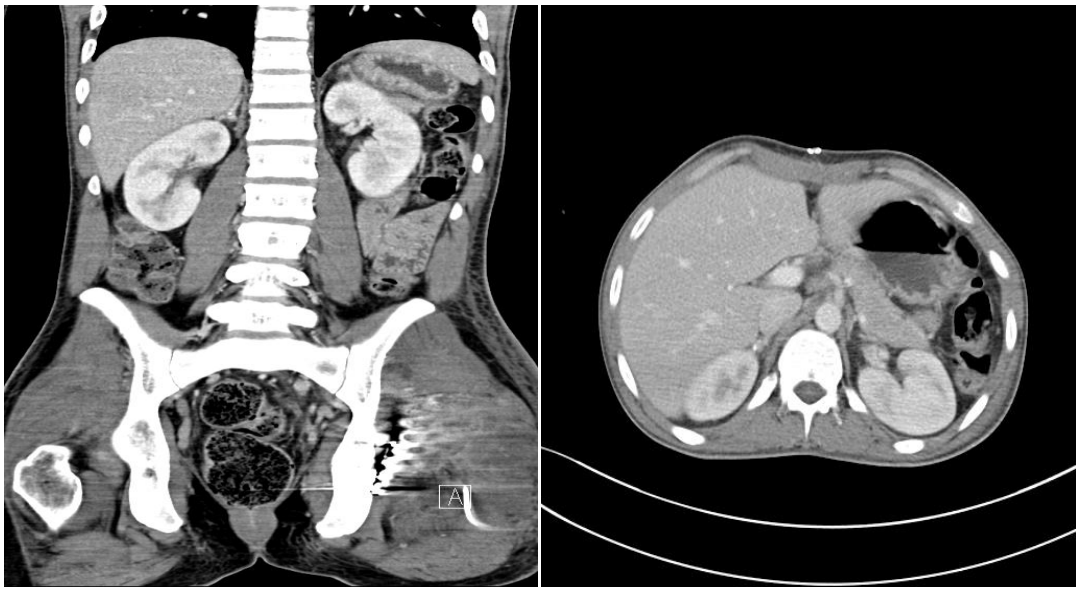

Image No.(4): Axial and coronal abdominal CT images of SCD patient, Spleen is not visualized which is surgically removed .

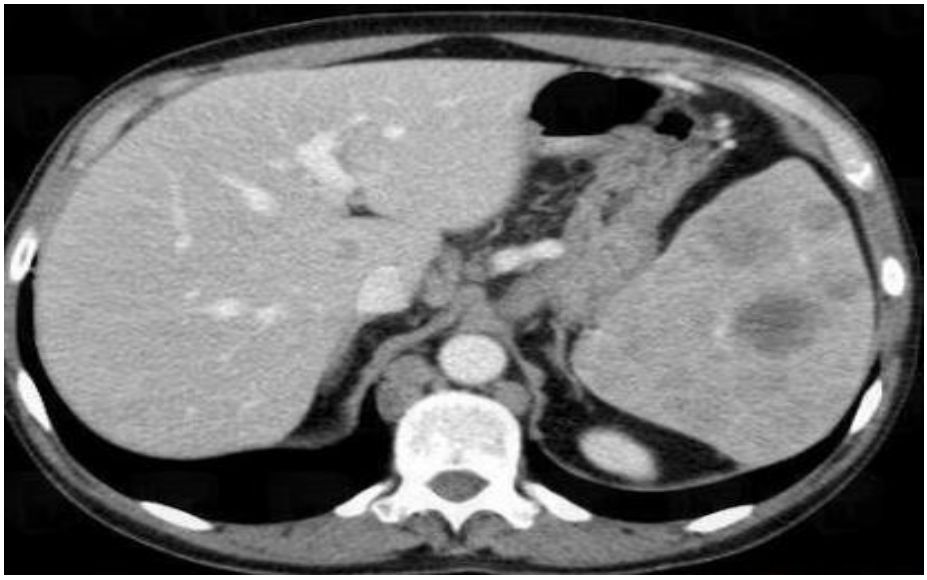

Image No.(5): Axial abdominal CT images of SCD patient showing multiple spleen abscess are well defined in a venous phase

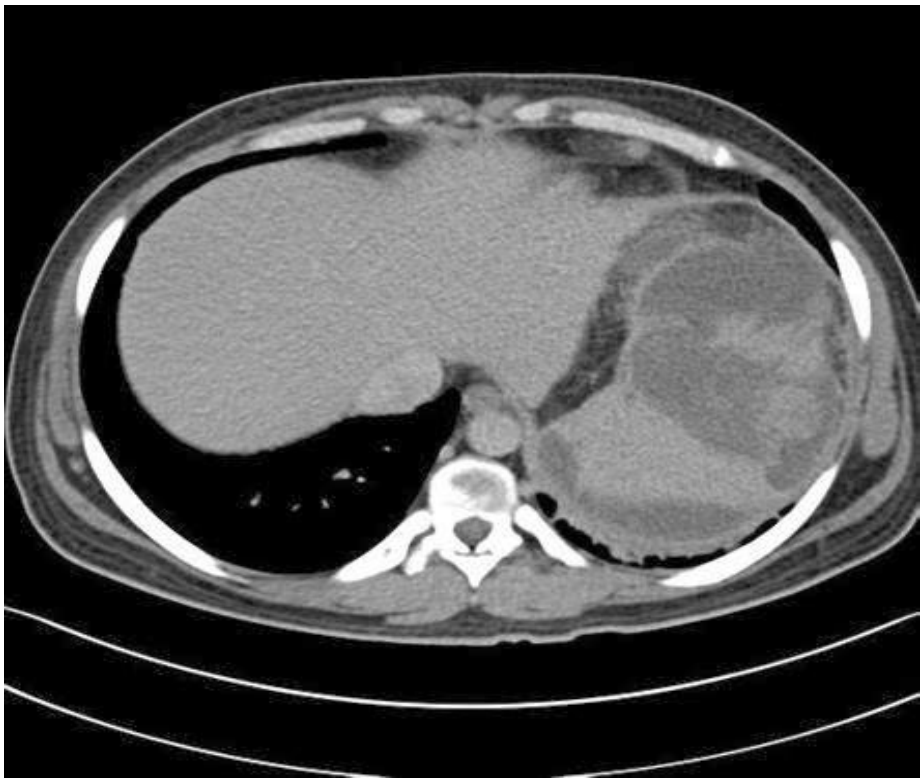

Image No.(6): Axial abdominal CT image of SCD patient show Spleen infarction performed during portal venous phase

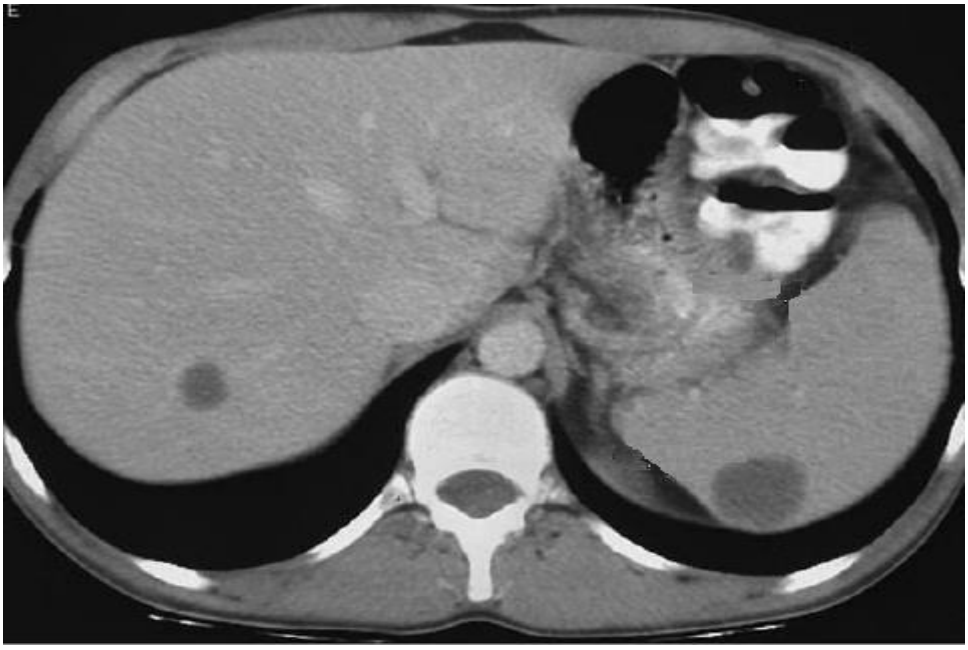

Image No.(7): Axial abdominal CT scan of SCD patient shows multiple hypodense cystic lesions in the liver and spleen

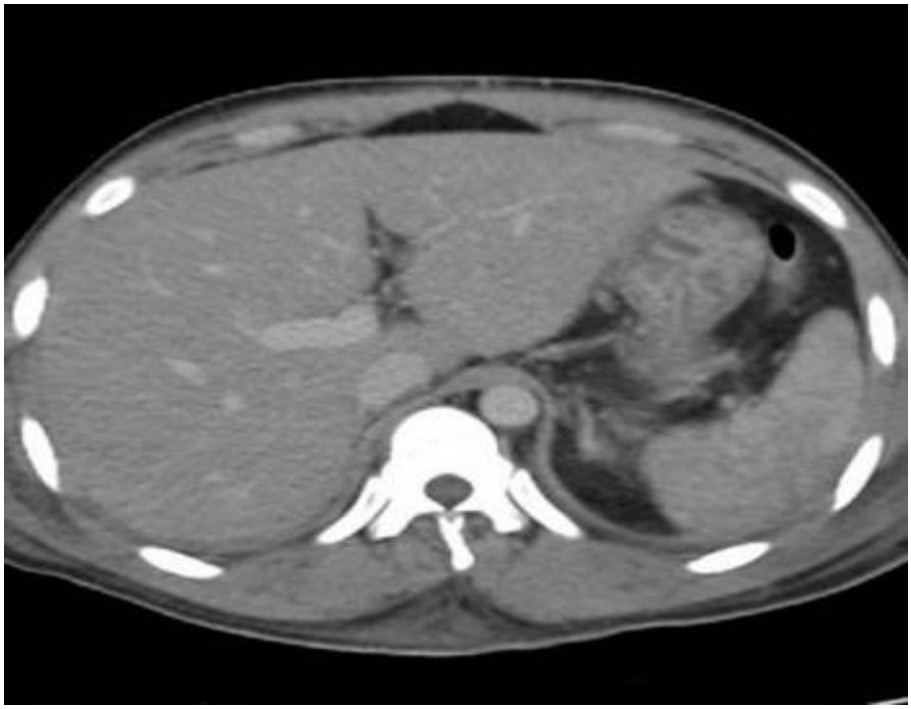

Image No.(8): Axial abdominal CT scan of SCD patient shows hepatomegaly with homogeneous contrast enhancement is seen in the portal venous phase.

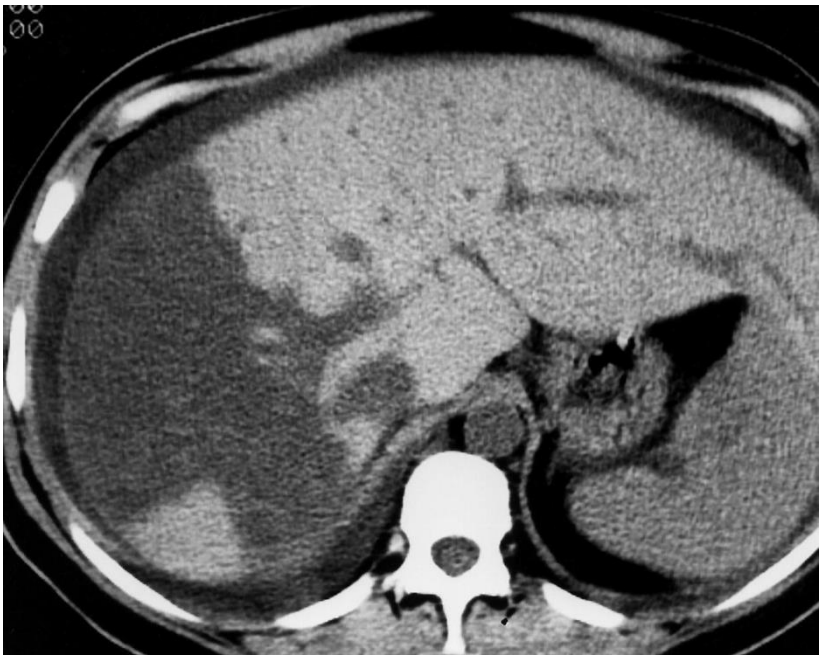

Image No.(9): Axial abdominal CT scan of SCD patient shows well defined hepatic infarction in portal venous phase

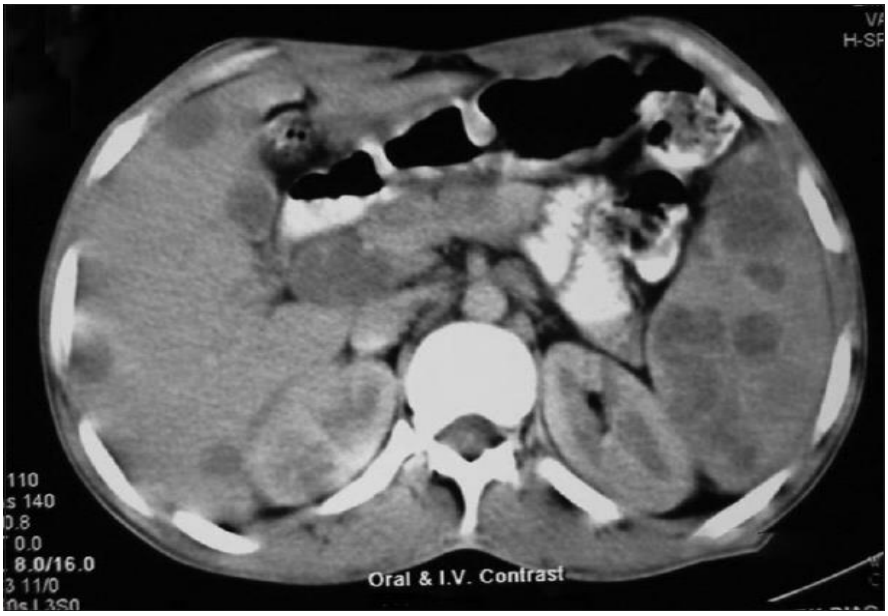

Image No.(10): Axial abdominal CT scan of SCD patient showing hepatosplenomegaly with multiple, well-defined, rounded, nonenhancing, hypodense lesions suggestive of abscesses in both the liver and spleen

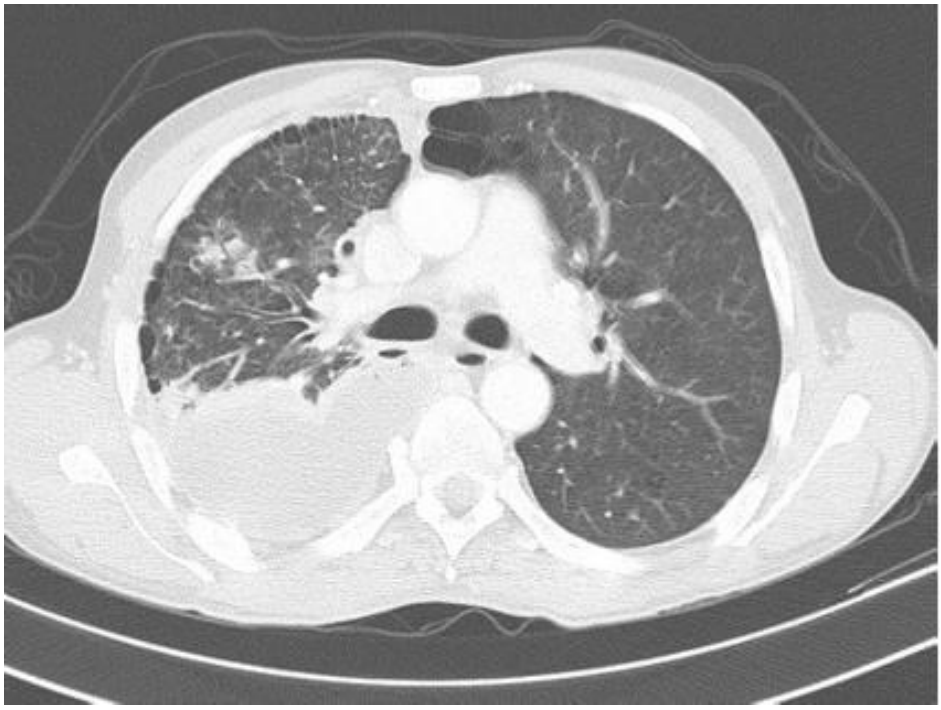

Image No.(11): Axial chest CT scan of SCD patient showing pleural effusion with parenchymal involvement (sub-segmental consolidation)

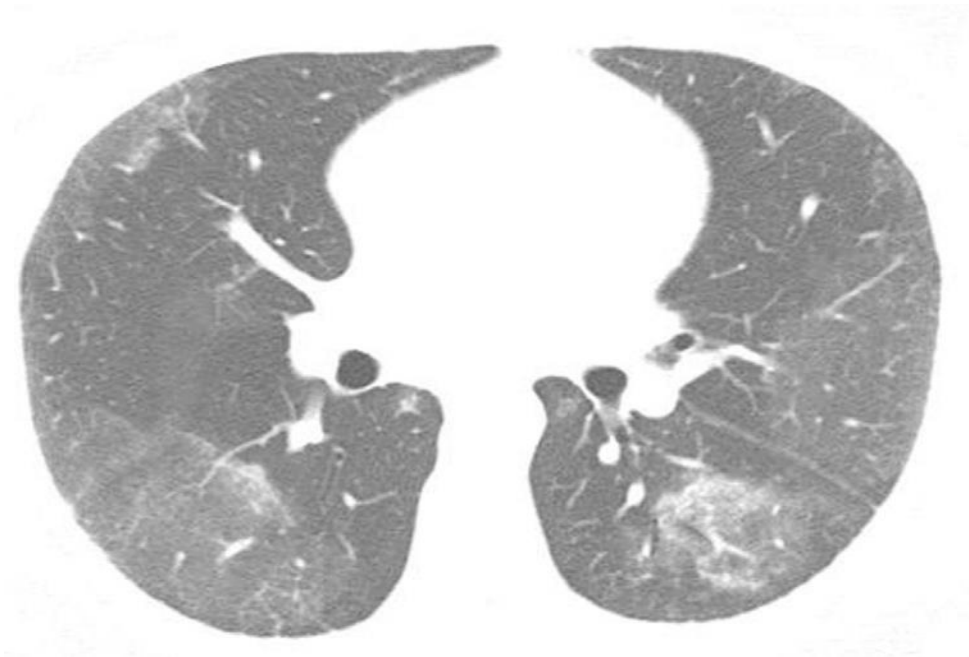

Image No.(12): Axial chest HRCT scan of SCD patient (lung window) at the level of the middle lung field, showing ground-glass opacities predominantly in the lung periphery.

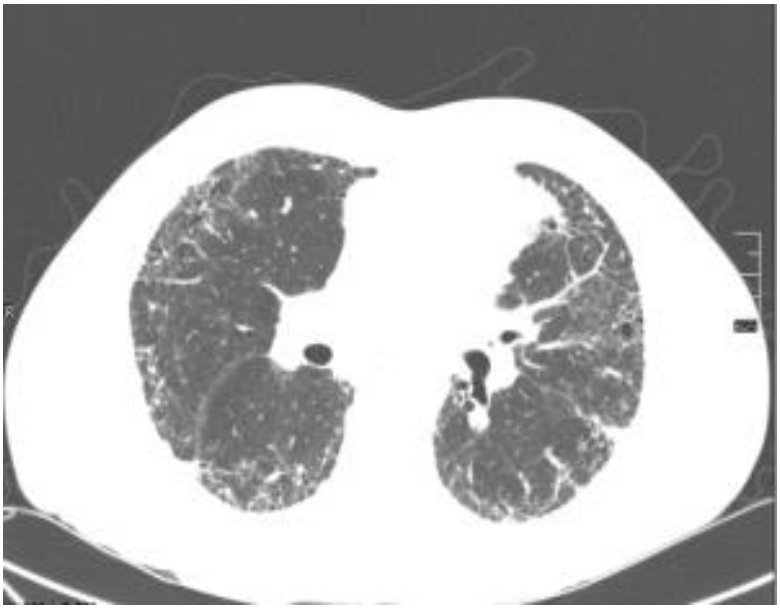

Image No.(13): Axial chest HRCT scan of SCD patient showing pulmonary fibrosis

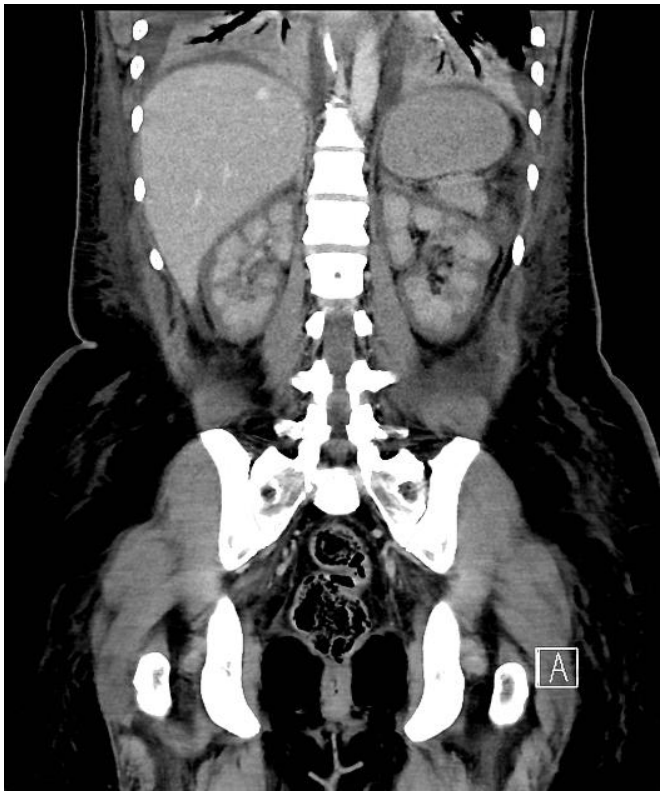

Image No.(14): Coronal abdominal CT scan of SCD patient showing renal cortical necrosis

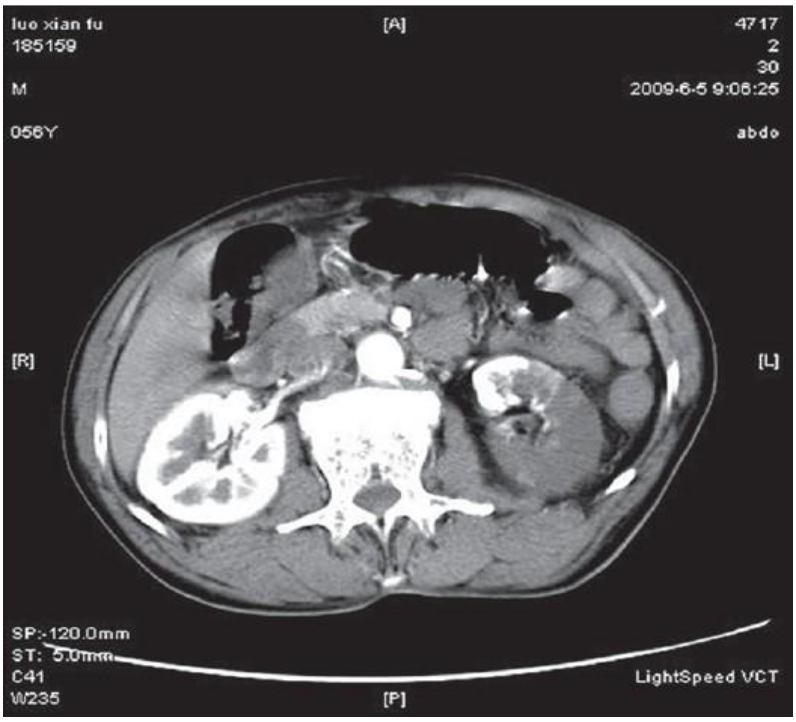

Image No.(15): Axial enhanced abdominopelvic CT scan of SCD patient showing renal infarction

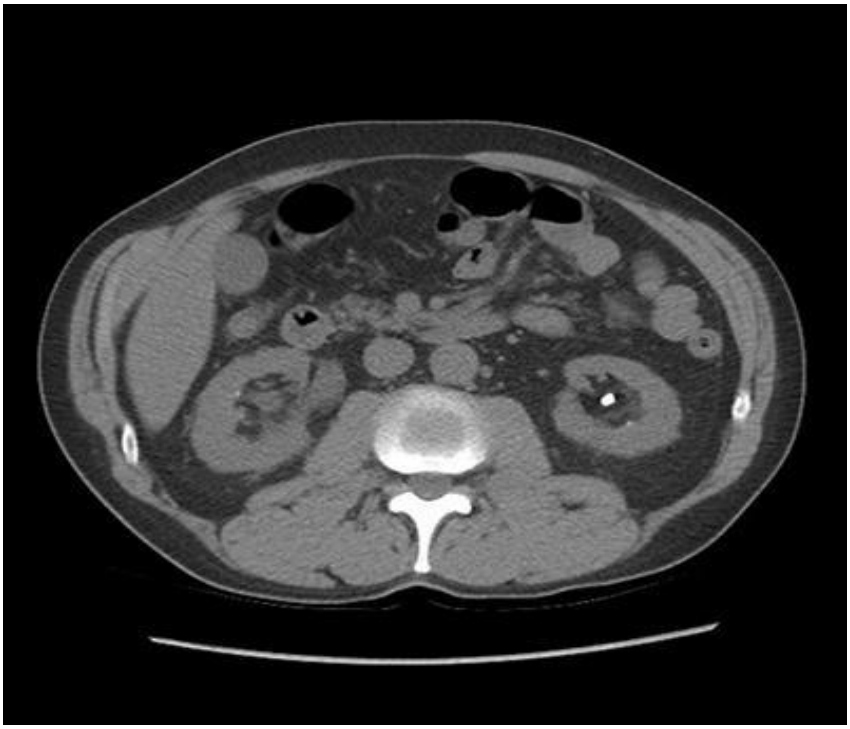

Image No.(16): Axial nonenhancing abdominopelvic CT scan of SCD patient showing CT scans showing left kidney and right ureteral stones

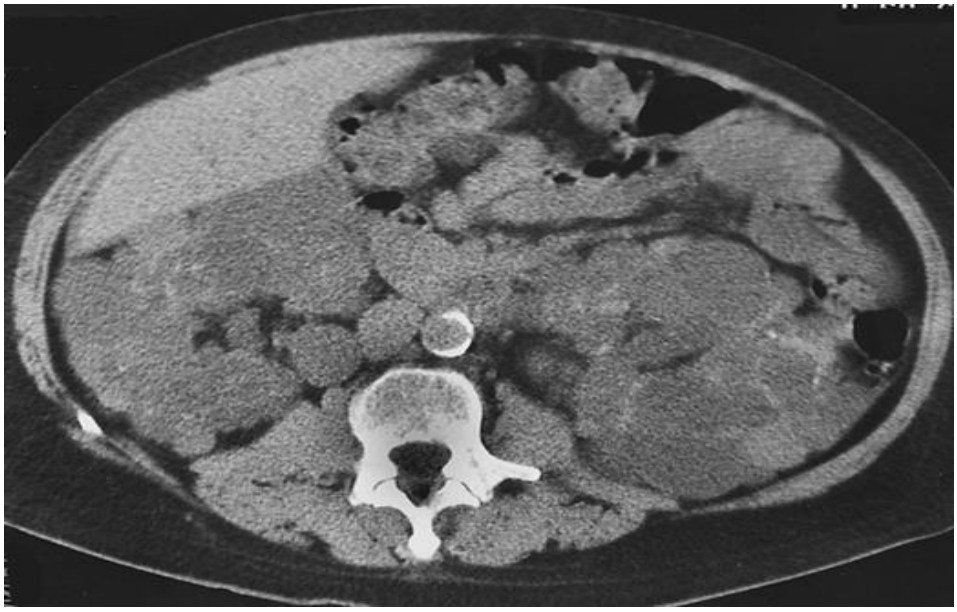

Image No.(17): Axial contrast enhanced pelvic CT scan of SCD patient showing Polycystic kidney disease with renal failure, and also shows multiple renal cysts.

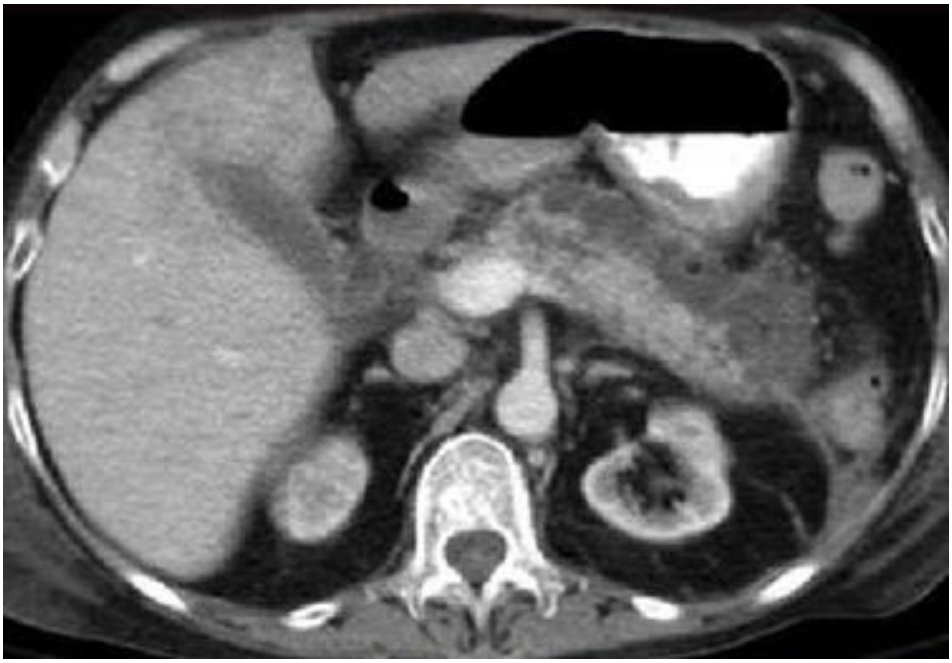

Image No.(18): Axial contrast enhanced abdominal CT scan of SCD patient shows one fluid collection in anterior pararenal space and minimal necrosis.

Appendices(2)

Data sheet of paper (1)

Pt ID number	Age	Sex	Area	Type of Sickle cell disease	CT spleen findings				Presence of Splenomegaly	CT spleen lesions appearance in each CT phase				Dilatation of spleen vein	Enlargement of spleen lymph nodes
					length	CT number	Shape	location		Before CM	Arterial phase	Venous phase	Delay		

Data sheet of paper (2)

ID Pt number	Age	Type of SCD	Comment spleen	Spleen CT number (HU)	Liver CT number (HU)	Liver Length (cm)	Comment Liver	Comment kidney	Comment lung	Comment pancreas	Comment gallbladder

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The Spleen and Sickle Cell Anemia: A Contrast Enhanced Computerized Tomography Based Study

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Abstract

The spleen is one of the most frequently affected organs in sickle cell anemia (SCA). This study aims to characterize the spleen in sickle cell anemia patients using contrast enhanced computerized tomography scanning (CECT). 67 patients with SCA from different Saudi Arabian areas were enrolled; ages are ranged from 10 months to 28 years old. The spleen was assessed with CT for abdominal pain and/or unexplained fever. The evaluation was done at different contrast enhancement scanning phases. The study showed that the least number of affected patients was from Eastern Saudi Arabia (1.5%) followed by Asseer (16.4%) then Gazan representing 82.1%. The most common type of SCA affected the Saudi children is Hemoglobin SS Disease (Hb SS) constituting 41 (61.2%). The spleen size, lymph nodes size, spleen Hounsfield (HU), splenic vein diameter and the correlation with the associated findings were evaluated for all of the patients. In children affected with SCA: 26 (38.8%) have splenomegaly, 18 (26.9%) have atrophied spleen and 2 (3.0%) are with very small tissue like structure. Lesions found in the spleen were abscess, infarction, cyst, and calcifications. At the spleen hilum region; dilated splenic vein, presence of multiple collaterals, and thrombus were also been detected. Significantly correlations were noticed between lesions type, child age, enlargement of spleen and splenic lymph nodes at $P \leq 0.033$, $P \leq 0.010$ and $P \leq 0.012$ respectively and showed an evidence that the reduction of the HU and advanced age have significant relation with changing of the spleen size at $P \leq 0.004$ and $P \leq 0.000$ respectively. Spleen lesions' enhancement pattern is well emerged in both venous and delay phase and it was significantly related with the scanning phase at $P \leq 0.000$ and with different types of SCA at $P \leq 0.037$, and $P \leq 0.055$ in venous and delay phase in respectively. CECT offers a number of morphological criteria that can be applied to differentiate hypodense lesions of the spleen in SCA. CT characterization criteria of hypodense splenic lesions are acknowledged to aid interpretation during evaluation of abdominal CT images of the spleen in symptomatic patients with sickle cell anemia.

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Keywords

Spleen, Sickle Cell Disease, Computerized Tomography

1. Introduction

Sickle cell disease (SCD) is a common genetic condition that causes ischemic vascular occlusion [1]. SCD affected different organs of the abdominal structures; the most commonly involved organ is the spleen, which is affected in almost all patients with Sickle Cell Anemia (SCA). The natural history is splenomegaly during the first decade of life and then autosplenectomy as a result of vaso-occlusion and infarction. Sometimes splenomegaly persists into an older age group or even adulthood [2]-[4]. Children with SCD are repeatedly exposed to diagnostic radiation. Plain radiographs are frequently ordered for pain, and chest radiographs are often ordered for fever and respiratory symptoms [5]. Computed tomography (CT) and nuclear medicine scans are ordered for other suspected complications [5], [6]. Direct visualization of suspected splenic disease with various imaging modalities has always been a challenge [7]. Ultrasonography (US) is frequently the first imaging modality used to evaluate the spleen. Color Doppler is useful in the evaluation of vascular pathology in the splenic hilum. Splenic focal lesions are frequently subtle and often nonspecific, appearing as hypoechoic lesions [8]. Therefore, focal heterogeneity detected on US should be further evaluated by computerized tomography (CT) or magnetic resonance imaging (MRI) [9]. Splenic lesions tend to be small or infiltrating, and without use of an organ-specific contrast agent, they tend to be difficult to detect [7]. The widespread use of CT represents probably the single most important advance in diagnostic radiology. However, CT involves much higher doses of radiation. Despite the fact that most diagnostic CT scans are associated with very favorable ratios of benefit to risk, many CT studies are being performed in the United States [10] [11], questioning the use of CT scans, in a variety of contexts, including blunt trauma [12] [13], seizures [14], and chronic headaches [15], and particularly its use as a primary diagnostic tool for children [16]. Expressively, pediatric radiologists suggested that perhaps one third of CT studies could be replaced by alternative approaches or not performed at all due to cancer risks associated with CT Scans [10]. On the other hand, on the unenhanced CT, the normal spleen is homogeneous with attenuation values ranging between 40 and 60 Hounsfield units (HU) [17]. On non-enhanced CT, infarcts are poorly visualized. After intravenous iodine contrast administration, the typical imaging findings are peripheral, wedge-shaped non-enhancing defects. However, this typical appearance is only present in less than half of all acute splenic infarcts [9]. In less typical cases, infarcts may mimic other splenic lesions, including abscesses or tumors, requiring clinical correlation, or if necessary, percutaneous fine-needle aspiration biopsy [17]. The enhancement pattern is caused by variable flow rates; this inhomogeneous enhancement pattern should not be confused with splenic disease. After intravenous contrast injection, the normal spleen enhances in a mottled pattern during the arterial and early portal venous phases giving the examination great value [18]. Splenic injury is generally silent and progressive. It can be clinically overt with acute splenic sequestration of red cells and an unpredictable complication in infants [19]. Knowledge about the CT imaging findings' characteristics of spleen in children with sickle cell anemia is important to avoid diagnostic pitfalls and misinterpretations of the early heterogeneity for focal hypointense splenic lesions; this was organized for early and proper diagnosis without need of unnecessary biopsy or unnecessary radiation exposure. In this study, we characterize the spleen abnormalities associated with SCD in all CT protocols of contrast media injection (arterial, venous phase) in order to explain the criteria in proper diagnosis for SCD done for children with SCA.

2. Materials and Methods

2.1. Place and Duration of the Study

This study was done in Ballasmar General Hospital and Fahad King Hospital CT departments, in Aseer and Gizan states (South of Saudi Arabia). Data were collected in the period spanned from June 2014 up to June 2015. The present study was approved by the Ethics Committee of the Research council, College of Medical Radiological Science as well as the Approval of the Radiology Departments. Verbal consent was obtained from all potential participants. The aims, benefits of the present study were explained to all participants in details. Medi-

cal history of all study subjects were thoroughly reviewed directly from participants themselves or from their parents and those with conditions that may in any way, alter the findings of the current study were excluded.

2.2. Study Population

A sample of 67 patients who were investigating as sickle cell anemia disease, undergo for abdomen CT examination complain of abdominal pain and/or unexplained fever. Patient's data were registered (age, gender, area, presence of family history, type of sickle cell anemia. 28 patients were females, while the 39 were males and their ages are ranged from 10 months to 28 years old. The patients who were affected with sickle cell anemia were from different Saudi Arabian areas; from Eastern Saudi Arabia 1 patient (1.5%) was affected, from Asseer 11 patients were affected and constituting (16.4%) and from Gaizan 55 patients were affected and representing (82.1%) of the total sample 67 (100%).

2.3. Machine Used

General Electric (GE) Hi-speed 60 multidetector CT scanner was used, made by GE Healthcare Manufacturer (2009). With the following specifications, Tube 2.0 MHU MX 135, 3.9 million mAs, Software level 6.03, Fast scan 1.0 sec, Helical plus, 3D max, Power 200 mA, Max 1 mm thickness, Acquisition, Helical 60 Max, Smart pre, DICOM MOD. It has voltage from 70 - 150 Kvp and four options of mA, High (110), medium (77), low (55), and extra low (22). And has three options of slice thickness: 1 mm, 3 mm and 5 mm. Similar scan interspaces, has scan time of 4.8 sec, and construction algorithm of normal option (soft tissue), high frequency (bony) and HRCT (for lungs) Images given in CD drive and store in special packs system of the hospital.

2.4. Technique Used

Two types of scanning techniques were used, for adults and other for pediatrics. CT scans typically obtained for visualizing all abdominal organs and included axial, coronal and/or sagittal cuts.

2.4.1. Technique Used in Pediatric: From 0 - 12 Years

Sedation was used for patient between ages of 6 months and 5 years. They are given IV pentobarbital sodium, 5 mg/kg to a maximum dose of 200 mg. For patient under 5 years old; a comfortable device for immobilization was used that secures patient's arms beside the head with adhesive straps. For larger children, we used adhesive straps putted under the mattress and over the patient. Scanning protocols were obtain with patient supine, feet first, patient centered with gantry and scan taken from lower chest to symphsis pubic. Thinner slices of 5 mm used for children 2 years and under 10 mm slice for children 3 years and older. A 120 kvp with mA ranged from 150 - 230 mA was used. Higher pitch of 1 to 2 was used to reduce patient dose, and window of soft tissue was chosen. A plain axial sections (sections before contrast) was taken firstly. The non sedated patients were given dilute Hypaque Sodium which has concentration of 40% to drink immediately before examination. The amount of oral contrast needed per patients was determining by ages as follow: from 6 months to 1 year given 175 ml, from 1 - 5 years 250 ml and from 6 - 12 years given 500 - 700 ml were given. IV contrast agent was also given: 1 - 2 ml/sec Omnipaque through automatic injector just before examination and three stages of scanning were taken. Early arterial phase, venous phase and delayed venous phase.

2.4.2. Techniques Which Used in Adults: Over 12 Years

Scans was obtained with patient supine, feet first, patient centered and instructed to be hold his/her breath at end of inspiration. Scan ranged from lower of the chest to iliac crest, and thinner slices of 1.2 to 4 mm collimation with 1.2 to 4 mm intervals are used. Rotation time was 0.5 sec with pitch of 1.37 and kv of 120 with auto mA range 100 - 400 and the table feed interval was 27.5 mm. Window setting which used to display images was for evaluation of soft tissue, window width (ww) of 350 - 400 Hounsfield unit (HU) and window level (Wl) of 35 - 50 HU. Images are reconstructed in coronal and/or sagittal planes. Used very thin slice (1 mm) to be reconstructed to serve as source images for coronal and/or sagittal reformatted images. A plain axial sections (sections before contrast) was taken firstly. Dilute Barium Sulfate solution (350 - 500) ml of contrast media was given to drink immediately before examination. Intravenous contrast agent was obtained, (2 to 6 ml) of Omnipaque per second with concentration of 60% was given to the patient just before examination by automatic injector, and

three stages of scanning were obtained. The early one was arterial phase scan with typical scan delays of 20 - 30 sec. The later venous phase scans with delays of 60 - 80 sec and the last one is delayed scans 1 to 4 hours.

2.5. Images Evaluation

All images were evaluated by two radiologist and three technologist, and all patients were evaluated to identify any changes occurred within abdominal organ and lower chest as a complication of sickle cell anemia. The study characterize the changes of spleen size and its correlation with the associated findings including the lesion type, spleen lymph nodes size, spleen CT number spleen, splenic vein diameter. All spleen lesions were characterized in all enhancement phases in order to put good criteria in diagnosis of spleen lesions in patients affected with Sickle cell Anemia. The readings were considered normal as follows length of spleen: In infants, children and adults: (from 1 month to 20 years) in ages ranged between 1 - 3 months (Spleen length = 4.6 cm), Ages between 10 - 12 years (Spleen length = 9.7 cm) Ages between 12 - 15 years (Spleen length = 10.1 cm) Ages between 15 - 20 years (Spleen length = 11.2 cm) as mentioned by Henrietta *et al*. (1991) [20]. Up to 13 cm length and 7 cm width in adults consider splenomegaly according to previous studies [21] [22]. Splenic length and width were measured at the level of lower third of T9 which is the highest point of the spleen, We measured both length and width of the spleen according to previous study [23]. The spleen length was measured from the tip of the spleen along the long axis, at the points where spleen gets retrocostal: from dome to tip through the hilum (craniocaudal direction). Measurement of the width of the spleen was made at the hilum. Shape and location: were also been evaluated normal shape commonly has medial concavity and normal location in: LT hypochondria, between funds of stomach and diaphragm.-Normal CT number of spleen: from (40 - 60 HU) after Thomas Van Cauwenberghe, *et al*. (2015) [17]. Splenic vein was measured at the level of L1, posterior to neck of pancreas, normal diameter of splenic vein in CT 0 < mm, after Unsal NH *et al*., 2006 [24].

2.6. Data Analyses

Data were analyzed using Statistical Package of Social Sciences (SPSS) (Inc., Chicago, Illinois version 16). The data obtained were analyzed statistically and data were presented as frequency and percentages. Paired t-test was used for testing the differences between the variables. The difference at value of $P < 0.05$ will be considered significant.

3. Results

Sickle cell types were classified and the description of spleen size, shape and location was obtained for all of the patients. The relation between lesions affected the children spleens and their ages has found to be significantly correlated at $P \leq 0.033$. In patients aged between 3 month - 10.5 years; 4 were affected with infarction, 7 with cyst 2 with abscess and ages 11 years - 20 years: 4 have infarction, 5 cyst and 3 have abscess, ages ranged between 21 years - 30 years; only 4 were affected with abscess with no children were affected with neither Infarction nor cysts. The present study showed an evidence that the advanced age has significant relation with changing of the spleen size at $P \leq 0.000$. In patients age ranged: 3 month - 10.5 y, 28 have splenomegaly, at ages between 11 y - 20 y 2 were affected and ages ranged between 21 y - 30 years old one patient have splenomegally. The study showed that the relation between lesions that affected the spleen (Infarction, Cyst, and abscess) have significantly related with and enlargement of splenic lymph nodes: $P \leq 0.012$. Children with enlarged lymph nodes 5 were affected with infarction, 2 with cyst and 7 with abscess.

4. Discussion

Sickle cell anemia is one of the most common hereditary blood disorders in Saudi Arabia and it occurs in two different forms, one form in South West of the country is similar to the African type and the other type in the Eastern province is considered to be less severe [25]. In the Eastern province of Saudi Arabia SCA is common with sickle cell trait [26]. The current study showed that the patients who were affected with sickle cell anemia were from different Saudi Arabia areas; Eastern Saudi Arabia is the least number of affected patients (1.5%) followed by Asseer; affected patients constituting (16.4%) and from Gaizan representing (82.1%) of the total sample 67 (100%). In our study the most common type of SCA affected the Saudi Children is Hemoglobin SS Disease (Hb SS) representing 41 (61.2%). This was presented in (**Figure 1**).

4.1. Characterization of Spleen in Patients with SCA

Our study characterize the spleen locations in children affected with SCA; 26 (38.8%) have splenomegally where 18 (26.9%) have atrophied spleen this was presented in (Table 1). Characterization of spleen size and shape were done in all of the affected sample with SCA the shape can be changed to be an oval, irregular, blurred out line, pyramidal, loss it's medial concavity. The changes in size may become atrophied or very small like tissue or shrunken, totally calcified or autosplenectomy; the changes occur were found to be of wide-range of variation, this was presented in (Table 2). Studies mentioned that in SCD, the spleen size changes were due

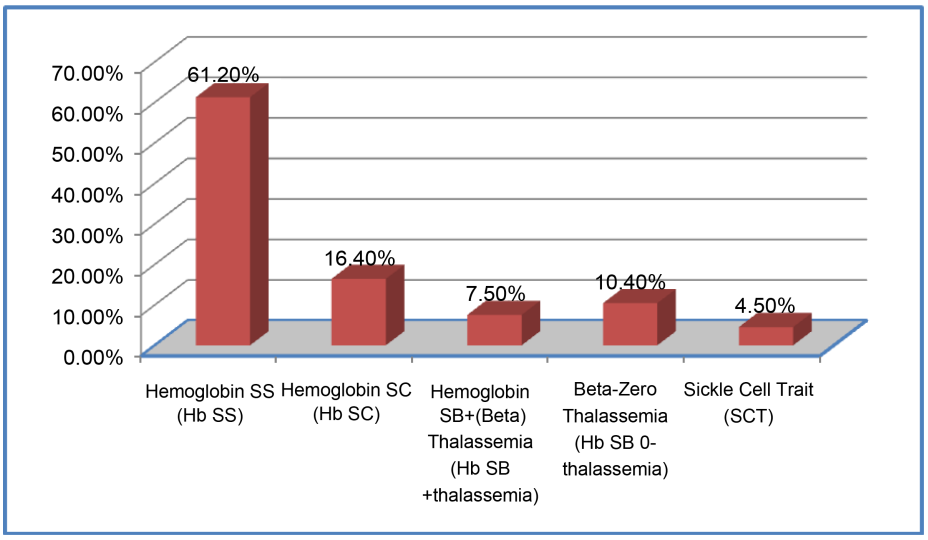

Figure 1. Distribution of Sickle Cell Anemia (SCA) types in the study sample in percentages (%).

Table 1. Characterize the spleen locations in children affected with Sickle Cell Anemia (SCA), frequency and percentages.

Spleen Location	Frequency	Percentages (%)
Normal (Left Hypochondria, between Funds and Diaphragm)	21	31.3
Extend to Left Kidney	16	23.9
Extend Below Lower Third of the Left Kidney	10	14.9
Atrophy	18	26.9
Spleen Is Not Seen	2	3.0
Total	67	100.0

Table 2. Characterization of spleen size and shape in children affected with Sickle Cell Anemia (SCA), frequency and percentages.

Spleen Size/Shape	Frequency	Percentages (%)
Normal size and shape	21	31.3
Enlarged/normal shape	5	7.4
Enlarged, oval shape	7	10.4
Enlarged, irregular line	4	6.0
Enlarged, pyramidal shape	6	9.0
Enlarged & loss it's medial concavity	4	6.0
Atrophied	18	26.9
Very small tissue like & totally calcified or autosplenectomy	2	3.0
Total	67	100.0

to repeated attacks of vaso-occlusion and infarction, however sometimes splenomegaly may occur [17], this justify our findings of the presence of various spleen features.

The spleen hilur region was evaluated and the splenic vein was measured 12 (17.9%) have dilated splenic vein, the presence of multiple vein collaterals, thrombus (filling defect) were also been detected in children with SCD. This was presented in **Figure 2**.

We characterize such cases in the contrast enhanced CT that show a total absence of or heterogeneous enhancement pattern within the spleen related to partial or total infarction. Findings of infarction on unenhanced CT are low attenuation of the spleen relative to the liver, a hyperdense intraluminal filling defect in the splenic vessels indicating an acute thrombus, and high density of the splenic capsule compared with the parenchyma. Immune-deficiency states due to disease or during immune suppression have emerged as a new, common predisposing cause of splenic abscess [27]. Persistence of splenomegaly in SCA patients predisposes them to the development of complications [28].

The classification of spleen size according to the lesion type in patients affected with sickle cell anemia was done. The infarction affected 9 children where cysts were found in 8, and abscess in 12 children with significant relations between the type of the complications and the changes in the spleen measurements at $P \leq 0.010$. In the current study; splenomegaly was observed in 10 patients (70%) with splenic abscess, other findings were observed significantly associated with enlarged spleen in patients with SCD including infarctions and cysts (**Table 3**).

Table 4 demonstrates the classification of spleen size and the normality of spleen CT number in patients affected with SCA it was found that 12 patients with splenomegally have abnormal attenuation values less than 36 HU and those with shrunken spleen were 19 patients, this may be due to the affection with cysts and abscess, infarction and inflammation that reduced the attenuation of the spleen, the reduction of the HU was significantly correlated with the changes of the spleen size at $P \leq 0.004$. Enlargement of spleen lymph nodes in patients affected with SCA were seen in 22 of patients with Splenomegaly with significant relation at $P \leq 0.000$ between the spleen size changes and the enlargement of lymph nodes, this was presented in (**Table 5**). Spleen vein dilatation in

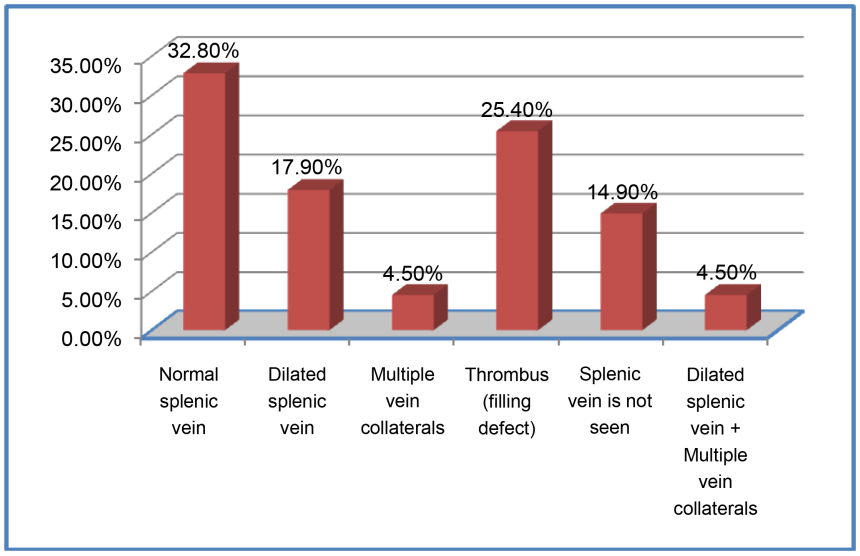

Figure 2. Findings in the spleen hilum region and splenic vein condition in children affected with Sickle Cell Anemia (SCA).

Table 3. Shows the classification of spleen size according to the lesion type in patients affected with Sickle Cell Anemia (SCA).

Size of Spleen	Infarction	Cyst	Abscess	Calcification
Splenomegaly	2	1	7	-
Shrunken Spleen	5	2	0	3
Normal Spleen Size	2	5	5	-

$P \leq 0.010$

patients affected with SCA has significant relations in patients with splenomegaly and those with enlarged lymph nodes, however similar measurements (dilated) were found equally in children affected with cysts, abscess or infarctions, these were noticed in **Table 6**.

4.2. Characterization Spleen Lesions in All of the Enhancement Phase in Patients Affected with Sickle Cell Anemia (SCA)

CT scan pre and post contrast enhancement showed well characteristics of these lesions and differentiated the

Table 4. Shows the classification of spleen size and the normality of spleen CT number in patients affected with Sickle Cell Anemia (SCA).

Size of Spleen	Less than 36 HU (Abnormal)	40 - 60 HU (Normal)	Spleen Doesn't Seen
Splenomegaly	12	19	-
Shrunken Spleen	19	3	2
Normal Spleen Size	1	11	-
	P ≤ 0.004		

Table 5. Shows the classification of spleen size and enlargement of spleen lymph nodes in patients affected with Sickle Cell Anemia (SCA).

Size of Spleen	Enlarge Lymph Nodes	Normal	Not Seen
Splenomegaly	22	9	-
Shrunken Spleen	1	1	22
Normal Spleen Size	6	6	-
	P≤0.000		

Table 6. Shows the cross tabulation between spleen and lymph nodes characteristics and spleen vein diameter in patients affected with Sickle Cell Anemia (SCA).

	Dilated Spleen Vein Diameter	Normal Spleen Vein Diameter	Not Seen
Size of Spleen			
Splenomegaly	23	8	-
Shrunken Spleen	9	-	15
Normal Spleen Size	2	10	-
	P ≤ 0.000		
Lymph Nodes Condition			
Normal Lymph Nodes	9	9	0
Enlarged Lymph Nodes	20	12	2
Lymph Nodes Not Seen	0	0	15
	P ≤ 0.000		
Lesions Affected the Spleen			
Infarction	5	1	3
Cyst	5	6	0
Abscess	5	7	0
	P ≤ 0.024		

infarction from the cysts and abscesses. Previous studies mentioned that these patients should be evaluated substantially by ultrasound and if in doubt by CT scan of the abdomen. Although ultrasound and CT scan are the best methods for the diagnosis of splenic abscess [29] [30]. We used CT scan because it allows more accurate anatomical localization of the abscess because of the presence of the contrast enhancement techniques. Similarly Nelken *et al*. reported a 96% accuracy using CT-scan for the diagnosis of splenic abscess [30].

In our study we characterize the spleen hypo attenuation lesions (abscess, cyst and infarction) in all of the CT procedures pre contrast, arterial phase, venus phase and delay phase. The diagnostic difficulty in patients with SCD is the differentiation between splenic abscess and large splenic infarct, which can also present with a large spleen. The importance of characterization of the lesion type is to reach to early diagnosis of the spleen complications because if not recognized splenic abscess may rupture locally into the peritoneal cavity, into the adjacent bowel, or into the pleural space, leading to increased mortality, these points also were recommended in other previous studies [31].

The CT appearance of the spleen depends on the timing of intravenous bolus administration of contrast material [31]. It may be heterogeneous with variable in appearance patterns include arciform, focal, and diffuse heterogeneity [32]. **Table 7** showed that the well enhanced lesions appears well in both venous and delay phase and the difference in enhancement characteristics were significantly related with the scanning phase $P \leq 0.000$. Studies mentioned that in most of pediatric CT examinations, splenic heterogeneity is resolved within 70 seconds of the beginning of contrast material injection; hence, low-attenuation lesions that are seen after this time should raise suspicion for a disease process. Helical CT scans obtained during the portal venous phase usually demonstrate homogeneous attenuation throughout the spleen [32]. Spleen Abscess in all of the enhancement phase in patients affected with Sickle cell Anemia: is well enhanced in both venus and delay phase, where most of the abscess were ill enhanced in the arterial phase, the current study showed the significant correlations at $P \leq 0.000$ between degree of abscess enhancement and timing of contrast administration. Cysts are well enhanced in the arterial phase, Spleen Infarction showed well enhancement in the delay phase and were correlated significantly $P \leq 0.000$ and 0.000 respectively. This was presented in (**Tables 8-10**).

The absence of wall-thickening, intralesional solid components or contrast-enhancement is in favor of benign lesions [17]. At CT, cysts manifest as rounded, well-demarcated no enhancing lesions with near water attenuation similar description was mentioned previously [33]. These characterizations of cyst in contrast enhancement protocol help us in distinguishing a benign cystic lesion from a malignant lesion. The presence of the infarction in our patients with sickle cell disease was justified that erythrocytes are rigid and frequently occlude the small

Table 7. Characterization spleen lesions in all of the enhancement phase in patients affected with Sickle Cell Anemia (SCA).

Degree of Lesions Enhancement	Before CM	Arterial Phase	Venous Phase	Delay
Well Enhanced	0	8	15	19
Mild Enhanced	0	1	8	1
Ill Enhanced	11	15	6	2
Not Appear	18	5	0	7
	$P \leq 0.000$			

*Note: The 3 cases (3/32) were of calcification in an atrophied spleen.

Table 8. Characterization spleen abscess in all of the enhancement phase in patients affected with Sickle Cell Anemia (SCA).

Degree of Abscess Enhancement	Before CM	Arterial Phase	Venous Phase	Delay
Well Enhanced	0	1	8	9
Mild Enhanced	0	0	4	1
Ill Enhanced	2	9	0	2
Not Appear	10	2	0	0
	$P \leq 0.000$			

sinuses of the red pulp. This leads to micro infarctions and micro-hemorrhage [34]. When we apply the contrast material, it becomes visible as small, disseminated hypodense, ill-defined lesions. It was present in early and late course of the disease, within enlarged spleen however in some cases the spleen shrinks and become calcified (**Tables 11-14**). Therefore, in patients with sickle cell disease, the presence of multiple small hypodense splenic lesions, is strongly suggestive of sickle cell-induced splenic infarctions. When we characterize children with splenic infarction, The CT appearance of infarcts was found to be reliant on the time elapsed since the insult. On non-enhanced CT, infarcts are poorly visualized. In the hyper acute phase, the spleen demonstrates a mottled texture secondary to hemorrhagic infarction with intravenous administration of contrast material. When the entire spleen is infarcted, it results in diffuse splenic hypodensity, leaving a residual rim of enhancing capsule. This appearance was described in the study done by Taylor *et al*. (1991) as known as the rim sign [34]. Over time, the lesions become better defined. Infarctions are peripheral and wedge-shaped non-enhancing defects; however some cases have an irregular margin, at delay phase the lesions were resolved (wash out), leaving the cortical defect, calcification and the rim of enhancing capsule. The diagnosis and characterization of infarction is very critical because some infarcts may mimic other splenic lesions, including abscesses or tumours, requiring clinical correlation, or percutaneous fine-needle aspiration biopsy [34].

Table 9. Characterization spleen cyst in all of the enhancement phase in patients affected with Sickle Cell Anemia (SCA).

Degree of Cyst Enhancement	Before CM	Arterial Phase	Venous Phase	Delay
Well Enhanced	0	7	3	1
Mild Enhanced	0	1	0	0
Ill Enhanced	7	0	5	0
Not Appear	1	0	0	7
	$P \leq 0.000$			

Table 10. Characterization spleen infarction in all of the enhancement phase in patients affected with Sickle Cell Anemia (SCA).

Degree of Infarction Enhancement	Before CM	Arterial Phase	Venous Phase	Delay
Well Enhanced	0	0	4	9
Mild Enhanced	0	0	4	0
Ill Enhanced	2	6	1	0
Not Appear	7	3	0	0
	$P \leq 0.000$			

Table 11. Characterization spleen lesions before CM in patients affected with different type Sickle Cell Anemia types (Hb SB + thalassemia, Hb SB 0-thalassemia, Hb SC, Hb SS and SCT).

		Type of Sickle					Total
		Hb SB + thalassemia	Hb SB 0-thalassemia	Hb SC	Hb SS	SCT	
Before CM	Not appear	-	3 (9.4%)	5 (15.6%)	13 (40.6%)	-	21 (65.6%)
	Ill defined lesions	-	1 (3.1%)	-	4 (12.5%)	1(3.1%)	6 (18.8%)
	Well defined calcifications	1 (3.1%)	1 (3.1%)	-	1 (3.1%)	-	3 (9.4%)
	Well defined nodules	1 (3.1%)	-	1 (3.1%)	-	-	2 (6.3%)
	Total	2 (6.3%)	5 (15.6%)	6 (18.8%)	18 (56.3%)	1 (3.1%)	32 (100.0%)
		P-value = 0.047					

Table 12. Characterization spleen lesions in arterial phase in patients affected with different type Sickle Cell Anemia (Hb SB + thalassemia, Hb SB 0-thalassemia, Hb SC, Hb SS, SCT).

		Type of Sickle					Total
		Hb SB + thalassemia	Hb SB 0-thalassemia	Hb SC	Hb SS	SCT	
Arterial phase	Well Enhanced Lesion& Calcifications	1 (3.1%)	3 (9.4%)	-	1 (3.1%)	-	5 (15.6%)
	Well Enhanced Nodules	1 (3.1%)	-	-	1 (3.1%)	-	2 (6.3%)
	Well Enhanced Cysts	-	-	1 (3.1%)	-	-	1 (3.1%)
	Heterogeneous Enhancement	-	-	-	2 (6.3%)	1 (3.1%)	3 (9.4%)
	Ring Enhancement	-	-	-	1 (3.1%)	-	1 (3.1%)
	Peripheral Enhancement with Ill Enhanced Lesion	-	-	-	3 (9.4%)	-	3 (9.4%)
	Ill Enhanced Lesion	-	2 (6.3%)	4 (12.5%)	6 (18.8%)	-	12 (37.5%)
	Not Enhanced	-	-	1 (3.1%)	4 (12.5%)	-	5 (15.6%)
	Total	2 (6.3%)	5 (15.6%)	6 (18.8%)	18 (56.3%)	1 (3.1%)	32 (100.0%)
	P-value = 0.085						

Table 13. Characterization spleen lesions venous phase in patients affected with different type Sickle cell Anemia Hb SB + thalassemia, Hb SB 0-thalassemia, Hb SC, Hb SS, SCT.

		Type of Sickle					Total
		Hb SB + thalassemia	Hb SB 0-thalassemia	Hb SC	Hb SS	SCT	
Venous phase	Well defined enhanced lesion	-	-	1 (3.1%)	2 (6.3%)	1 (3.1%)	4 (12.5%)
	Well defined non enhanced lesion (hypo dense)	-	2 (6.3%)	3 (9.4%)	10 (31.3%)	0 (0.0%)	15 (46.9%)
	Multiple well defined non enhance lesions	-	-	-	2 (6.3%)	-	2 (6.3%)
	Peripheral hypo dense enhanced lesion	-	-	-	1 (3.1%)	-	1 (3.1%)
	Hypo dense lesion surround by enhancing calcification	-	1 (3.1%)	-	-	-	1 (3.1%)
	Homogenous hypo dense with well defined peripheral enhancement	-	-	-	2 (6.3%)	-	2 (6.3%)
	Heterogeneous pattern	-	-	1 (3.1%)	-	-	1 (3.1%)
	Ill defined non enhanced lesion (hypo dense)	2 (6.3%)	2 (6.3%)	1 (3.1%)	1 (3.1%)	-	6 (18.8%)
	Total	2 (6.3%)	5 (15.6%)	6 (18.8%)	18 (56.3%)	1 (3.1%)	32 (100.0%)
	P-value = 0.037						

The current study characterized 3 cases of atrophied spleen with calcifications; in the noncontract films CT represented this dense splenic calcification. The current study justify this finding as it thought to be secondary to a combination of hemosiderin deposition, fibrosis as mentioned by Lieven *et al*. [35]. splenic abscess formation was also been detected At CT, abscesses typically manifest irregularly marginated lesions with low attenuation. Rim enhancement was seen on contrast-enhanced scans, this is also described by Urrutia M *et al*. (1996) [36]. The enhancement pattern in different type of SCD were seen in all of the CT scanning phase, in arterial, venus and delay phase as well as scanning before contrast, the results showed a significant relation between the character of the lesions and degree of enhancement with the scanning technique used (pre contrast, venous and delay phase) in different SCA types that means it may have an impact on the lesions enhancement however the correlation in characterizing or defining lesion is found to be frail at $p \leq 0.085$ in the arterial phase, that means we have to consider the other phases in confirmation or identifying the hypo intense splenic lesions, these were presented in (**Tables 11-14**).

Table 14. Characterization spleen lesions in delay phase in patients affected with different type Sickle Cell Anemia Hb SB + thalassemia, Hb SB 0-thalassemia, Hb SC, Hb SS, SCT.

		Type of Sickle					Total
		Hb SB + thalassemia	Hb SB 0-thalassemia	Hb SC	Hb SS	SCT	
Delay Phase	Well defined enhanced lesion	-	-	1 (3.1%)	1 (3.1%)	1 (3.1%)	3 (9.4%)
	Well defined hypo dense lesion	-	3 (9.4%)	3 (9.4%)	12 (37.5%)	-	18 (56.3%)
	Well defined peripheral enhance with unenhanced hypo dense lesion	-	-	-	2 (6.3%)	-	2 (6.3%)
	Ill defined unenhanced lesion	1 (3.1%)	-	2 (6.3%)	1 (3.1%)	-	4 (12.5%)
	Washout CM (not seen)	1 (3.1%)	2 (6.3%)	-	2 (6.3%)	-	5 (15.6%)
	Total	2 (6.3%)	5 (15.6%)	6 (18.8%)	18 (56.3%)	1 (3.1%)	32 (100.0%)
		P-value = 0.055					

5. Conclusions

In sickle cell anemia hypodense splenic lesions are frequently encountered on abdominal CT images. Although most hypodense lesions of the spleen can be considered benign, some findings necessitate closer attention to the lesion. CT offers a number of morphological criteria that can be applied to characterize the spleen and to differentiate hypodense lesions of the spleen, such as the appearance of a lesion's borders, its attenuation, SCA types as well as the presence of calcifications or solid components.

Children with SCD are frequently exposed to diagnostic radiation so a justifiable indication and proper practice is necessary for all CT selected procedures. The selection of CT sequences and contrast examination phase in diagnosis of SCA should be minimized in order to limit judiciously the exposure of children with SCD to unnecessarily diagnostic radiation. This characterization and the elucidation of imaging findings of hypodense splenic lesions are an attempt to highlight the best phase to interpret the splenic lesion in symptomatic patients with sickle cell disease.

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Sickle cell disease: chest and abdominal manifestation-A CT based study

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Abstract : *Patients with sickle cell disease (SCD) may have frequent episodes of abdominal pain and/or fever of uncertain cause. While many of these episodes represent the possibility of complications; Computed tomography (CT) was used to evaluate 67 Saudi Arabian patients with SCD .In 67 of the patients; the liver was affected in 59 patients, lungs in 56 patients, kidneys in 55 and gall bladder in 22 patients and pancreas in 5 cases. Spleen abnormalities were found to be Splenomegaly, cyst, abscess, infarction, Splenomegaly with cyst and Splenomegaly with abscess where the patient's age and SC type were considered. Hepatic abnormalities including focal necrosis, Hepatomegaly, abscess, cyst; infarction as well; Cholelithiasis, gall stones and dilated common bile duct and acute pancreatitis were also considered as an important manifestation of SCD. Renal abnormalities were found to be papillary necrosis, renal abscess, Stones with hydronephrosis, renal vein thrombosis, renal failure and renal infarction. Lungs CT manifestations were found to be pleural effusion, pneumonia, atelectasis, ground glass nodules, consolidation, fibrosis, Lung abscess. The episodes were increased by increasing of the children age at different SCD.*
Computed tomography (CT) has been shown to be an excellent modality for efficient and multisystemic evaluation of the abdomen and chest in these patients.

Keywords : *Sickle cell disease, Computerizes Tomography ,Saudi Arabia, manifestation.*

I. INTRODUCTION

Sickle cell disease (SCD) is perhaps the most common of human hereditary disorders. Patients with (SCD) are frequently experience acute painful vasoocclusive crises or fever of unknown origin .Sickle cell patients are at high risk for many serious and multi systems problems causing similar signs and symptoms. [1,2]

Computed tomography (CT) has been shown to be an excellent modality for efficient and multisystemic evaluation of the abdomen. Studies using CT scan was obtained to define hepatic and splenic abnormalities associated with abdominal pain / fever [3]. CT has proved equally useful in identifying previously undiagnosed or unconfirmed retained intrahepatic calculi, interstitial nephritis, acute focal pyelonephritis, visceral perforations with intraabdominal abscesses, and other complications of SCD.

SCD is caused by mutation in the b-globin chain, causing the hydrophilic glutamic acid to be replaced with the hydrophobic amino acid Valine. The association of two a-globin subunits with two mutant b-globin subunits forms hemoglobin S (Hb S). Under environmental low oxygen concentrations, this mutant hemoglobin will cause aggregation of hemoglobin molecules. These will distort RBCs into a sickle shaped .Consequently, these deformed RBCs fail to pass smoothly through the narrow capillaries, leading to vessel occlusion and ischemia [4,5]

There are different forms of the disease: In homozygous pattern (Hb SS), the blood will have no normal hemoglobin particles and phenotypically termed sickle cell anemia (SCA). Heterozygous genotype, in which the patient inherits a sickle cell gene from one parent and a normal gene from the other parent forming Hb SA, is phenotypically expressed as sickle cell trait. Also, other heterozygous types of Hb S may form due to combination with another different abnormal gene, such as sickle-hemoglobin C disease (Hb SC) or Hb S-beta thalassemia (Hb S-tha).[6] In Hb SS patients, severe anemia is caused by excessive destruction of the red cells. The bone marrow rate of hematopoiesis is significantly increased, but does not match the rate of destruction. In sickle trait patients with Hb SA, there is no severe hemolytic crisis as SCA patients. They may have symptoms only if they are severely deprived of oxygen [7]

The statistics of SCD in the open literature showed that (SCA) affects millions throughout the world. It is particularly common among sub-Saharan Africa population as well; Saudi Arabia; India; and Mediterranean countries. In the Unites States, it affects around 72,000 people, most of whose ancestors come from Africa. The disease occurs in 1 in 12 African Americans; carry the sickle cell trait [8]. SCD in Saudi Arabia is considered one of the major public health problems in the Eastern province. [9,10]

This research study tries to cover most of the radiological manifestations, in different systems affected by the disease, as organ-based approach in Saudi Arabian patients. Systems are arranged as according to the frequency: including spleen changes which occur in 67 of the patients, liver was affected in 59 patients, lungs in 56

patients, pancreas in 5, kidneys in 55 and gall bladder in 22 patients, and were presented and evaluated according to age of the patients and type of SCA as we encountered in practice.

II. MATERIALS AND METHODS

2.1Place and duration of the study:

This study was done at Ballasmar General Hospital and Fahad King Hospital CT departments, in Aseer and Gizan states (South Of Saudi Arabia).Data were collected in the period spanned from June2014 up to June2016.The present study was approved by the Ethics Committee of the Research council, College Of Medical Radiological Science as well as the approval Of the Radiology Departments. Verbal consent was obtained from all potential participants. The aims, benefits of the present study were explained to all participants in details. Medical history of all study subjects were thoroughly reviewed directly from participants themselves or from their parents and those with conditions that may in any way, alter the findings of the current study were excluded.

2.2Study population:

A sample of (67) patients who were investigating as sickle cell anemia disease, undergo for abdomen CT examination complain of abdominal pain and/or unexplained fever. Patient's data were registered .28 patients were females, while the 39 were males and their ages are ranged from 10 months to 28 years old. The patients who were affected with sickle cell anemia were from different Saudi Arabian areas.

2.3Machine used:

General Electric (GE) Hi-speed 60 multidetector CT scanner was used, made by GE Healthcare Manufacturer(2009).With the following specifications, Tube 2.0 MHU MX 135, 3.9 million mAs, Software level 6.03, Fast scan 1.0 sec, Helical plus, 3D max, Power 200 mA, Max 1mm thickness, Acquisition, Helical 60 Max, Smart pre, DICOM MOD. It has voltage from 70- 150 Kvp and four options of mA, High (110), medium (77), low (55), and extra low (22).And has three options of slice thickness: 1 mm, 3mm and 5 mm. Similar scan interspaces, has scan time of 4.8 sec, and construction algorithm of normal option (soft tissue), high frequency (bony)and HRCT (for lungs)Images given in CD drive and store in special packs system of the hospital.

2.4Technique used

Two types of scanning techniques were used, for adults and other for pediatrics. CT scans typically obtained for visualizing all abdominal organs and included axial, coronal and/or sagittal cuts.As well the chest was also been scanned .

2.4.1. Technique used in pediatric: (from 0-12 years)

Sedation was used for patient between ages of 6 months and 5 years .They are given IV pentobarbital sodium, 5mg/kg to a maximum dose of 200mg.For patient under 5 years old; a comfortable device for immobilization was used that secures patient's arms beside the head with adhesive straps. For larger children, we used adhesive straps putted under the mattress and over the patient.

Scanning protocols were obtain with patient supine, feet first, patient centered with gantry and scan taken from lower chest to symphsis pubic. The chest was scanned from sternal notch to lower costal margin. Thinner slices of 5mm used for children 2 years and under 10mm slice for children 3 years and older. A 120 kvp with mA ranged from 150-230 mA was used. Higher pitch of 1 to 2 was used to reduce patient dose, and window of soft tissue was chosen. A plain axial sections (sections before contrast) was taken firstly. The non sedated patients were given dilute Hypaque Sodium which has concentration of 40% to drink immediately before examination. The amount of oral contrast needed per patients was determining by ages as follow: From 6 months to 1 year given 175ml, from 1-5 years 250ml and from 6- 12 years given 500-700ml were given. IV contrast agent was also given: 1-2ml/sec Omnipaque through automatic injector just before examination and three stages of scanning were taken. Early arterial phase, venous phase and delayed venous phase

2.4.2. Techniques which used in adults: (over 12years)

Scans were obtained with patient supine, feet first, patient centered and instructed to be hold his/her breathe at end of inspiration. Scan ranged from lower of the chest to iliac crest, The chest was scanned from sterna notch to lower costal margin and thinner slices of 1,2 to 4mm collimation with 1,2 to 4mm intervals are used.Rotation time was 0.5sec with pitch of 1.37 and kv of 120 with auto mA range 100-400 and the table feed interval was 27.5mm. Window setting which used to display images was for evaluation of soft tissue, window width (ww) of 350-400 Hounsfield unit (HU) and window level (Wl) of 35-50 HU. Images are reconstructed in coronal and/or sagittal planes. Used very thin slice (1mm) to be reconstructed to serve as source images for coronal and/or sagittal reformatted images. A plain axial sections (sections before contrast) was taken firstly. Dilute Barium Sulfate solution (350-500)ml of contrast media was given to drink immediately before examination. Intravenous contrast agent was obtained, (2 to 6 ml) of Omnipaque per second with concentration of 60% was given to the patient just before examination by automatic injector, and three stages of scanning were obtained .The early one was arterial phase scan with typical scan delays of 20-30sec, The later venous phase scans with delays of 60-80sec and the last one is delayed scans 1 to 4 hours.

2.5. Images evaluation:

All images were evaluated by two radiologist and three technologist, and all patients were evaluated to identify any changes occurred within abdominal organ and lower chest as a complication of sickle cell anemia. The study classified the changes on some abdominopelvic organs .Changes were found in the spleen of 67 patients , liver was affected in 59 patients, lungs in 56 patients, pancreas in 5, kidneys in 55 and gall bladder in 22 patients

2.6 .Data Analyses:

Data were analyzed using Excel programme .The data obtained were analyzed statistically and data were presented as frequencies.

III. RESULTS

Abdomen and Chest manifestation was evaluated spleen changes occur in 67 of the patients, liver was affected in 59 patients, lungs in 56 patients, kidneys in 55 and gall bladder in 22 patients, pancreas in 5 cases.

Table1 cross tabulation between patients' age and spleen CT manifestation in SCA

Age classes	Splenomegaly	Splenic cyst	Splenic Abscess	Splenic infarction	Splenomegal with cyst	Splenomegaly with abscess
3 mon – 7y	15	3	-	3	1	6
8 y – 17 y	6	2	4	9	1	1
18y – 28y	2	0	1	11	0	2
	23	5	5	23	2	9

Table 2cross tabulation between patients' age and liver CT manifestation in SCA

Age classes	Normal	Focal Necrosis	Hepatomegaly	Hepatic Abscess	Hepatic Cyst	Hepatic Infarction
3 mon – 7y	4	3	12	3	5	1
8 y – 17 y	4	2	5	5	4	3
18y – 28y	0	3	2	4	1	6
Total	8	8	19	12	10	10

Table3 cross tabulation between patients' age and lungs CT manifestation in SCA

Age classes	Normal	Pleural effusion	Pneumonia	Atelec-tasis	Ground glass nodules	Consolid-ation	fibrosis	Lung abscess
3 mon – 7y	8	9	5	3	1	2	0	0
8 y – 17 y	3	3	1	1	4	5	2	4
18y – 28y	0	4	0	0	0	1	8	3
	11	16	6	4	5	8	10	7

Table4 cross tabulation between patients' age and kidney CT manifestation in SCA

Age classes	Normal	Papillary necrosis	Renal abscess	Stones &hydronephrosis	Renal vein thrombosis	Renal failure	Renal infarction
3 mon – 7y	8	9	2	8	1	0	0
8 y – 17 y	4	4	5	2	2	1	5
18y – 28y	0	2	0	1	1	6	6
	12	15	7	11	4	7	11

Table5 cross tabulation between patients' age , gall bladder and pancreas CT manifestation in SCA

Age classes	Cholelithiasis	Gall stones and dilated common bile duct	Acute pancreatitis
3 mon – 7y	0	3	0
8 y – 17 y	3	5	2
18y – 28y	4	7	3
	7	15	5

Table6 Relation between spleen CT manifestation in SCA and type of SCA

Type of SCA	Splenomegaly	Splenic cyst	Splenic Abscess	Splenic infarction	Splenomegaly with cyst	Splenomegaly with abscess
Hb SS	21	3	3	13	2	8
Hb SC	0	2	1	5	0	0
Hb SB 0-thalassemia	0	0	0	4	0	1
Hb SB+ thalassemia	2	0	1	1	0	0
	23	5	5	23	2	9

Table7 Relation between liver CT manifestation in SCA and type of SCA

Type of SCA	Normal	Focal necrosis	hepatomegaly	Hepatic abscess	Hepatic cyst	Hepatic infarction
Hb SS	7	4	17	5	7	5
Hb SC	1	1	0	4	2	3
Hb SB 0-thalassemia	0	3	1	1	1	1
Hb SB+ thalassemia	0	0	1	2	0	1
	8	8	19	12	10	10

Table8 Relation between lung CT manifestation in SCA and type of SCA

Type of SCA	Normal	Pleural effusion	Pneumonia	Atelectasis	Ground glass nodules	Consolidation	fibrosis	Lung abscess
Hb SS	9	13	6	4	3	6	5	3
Hb SC	1	2	0	0	1	1	2	2
Hb SB0-thalassemia	1	1	0	0	0	0	2	1
Hb SB+ thalassemia	0	0	0	0	1	1	1	1
	11	16	6	4	5	8	10	7

Table9 Relation between kidney CT manifestation in SCA and type of SCA:

Type of SCA	Normal	Papillary necrosis	Renal abscess	Stones &hydro nephrosis	Renal vein thrombosis	Renal failure	Renal infarction
Hb SS	10	13	5	8	3	4	6
Hb SC	1	1	1	1	1	2	2
Hb SB 0-thalassemia	1	0	0	1	0	1	2
Hb SB+ thalassemia	0	1	1	1	0	0	1
	12	15	7	11	4	7	11

Table10 Relation between gall bladder CT manifestation in SCA and type of SCA

Type of SCA	Cholelithiasis	Gall stones and dilated common bile duct	Acute pancreatitis
Hb SS	5	13	4
Hb SC	1	1	1
Hb SB 0-thalassemia	0	1	0
Hb SB+ thalassemia	1	0	0
	7	15	5

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IV. DISCUSSION

Splenomegaly is the commonest changes that may occur in the Saudi children sample followed by spleen infarction as seen in table (1). It should be considered that the CT appearance of the spleen largely depends on the timing of intravenous bolus administration of contrast material. The spleen may demonstrate heterogeneous enhancement during the first minute after initiation of intravenous administration of contrast material because of the different rates of flow through the cords of the red and white pulp. [11-14] This heterogeneity is itself variable in appearance; patterns include arciform , focal , and diffuse heterogeneity. [11] Therefore familiarity with these enhancement characteristics minimizes the chance that artifacts will be mistaken for disease. This is what was considered in our study during examining the patients.

Sickle cell clots cause ischemic vascular occlusion, which frequently affects different parts of the abdominal structures. The most commonly involved organ is the spleen, which was affected in almost all patients with SCA.[15,16] Studies showed that one of developing cause of splenomegaly is acute splenic sequestration. At clinical examination, patients demonstrate massive splenic enlargement and peripheral areas of decreased attenuation with areas of increased attenuation secondary to acute hemorrhage. [17]Similarly our study showed the findings of Splenomegaly in 23 cases , Splenic cyst in 5 cases Splenic Abscess in 5 cases Splenic infarction in 23cases and splenomegaly with cyst and splenomegaly with abscess in 2 and 9 cases respectively this was presented in table (1 , 6) where the patients age and SC type was considered .The literature have mentioned that repeated splenic infarctions that start within the first 18–36 months of life, in association with the dates of disappearance of protective Hb F, result in hyposplenism and asplenism. Splenic atrophy is a major etiology of compromised immune status and increased susceptibility to infections. [15,16]

In our study the cases of splenic infarction depends on the timing of imaging and the size of the infarct. Contrast enhanced CT scan is proved to be the most sensitive tool of imaging .The typical infarct is seen as a hypo dense non- or poorly enhancing wedge, with apex pointing toward the hilum. Similar studies showed that in late period of time infarctions may resolved completely or leave a permanent scar, or liquefy with possible abscess formation. Also, multiple small infarcts or global infarct of the whole spleen are reported in the imaging findings [18,19,20]

Table (2) cross tabulated the patients' age and liver CT manifestation in SCA. Focal necrosis was found in 8 cases, hepatomegaly in 19, and hepatic abscess in 12 cases, hepatic cyst in 10 and Hepatic Infarction in 10 cases. Cholelithiasis, gall stones and dilated common bile duct and acute pancreatitis were also considered as an important manifestation of SCD and was found in 7, 15 and 5 cases in respectively and was increased by increasing of the children age as presented in table 5.On the other hand in previous studies; liver infarction in SCD was reported. Acute sickle hepatic crisis affects about 10% of patients admitted for painful crisis. It usually simulates acute cholecystitis with right upper quadrant pain, fever and leucocytosis, however unlike cholecystitis; the liver is enlarged and tender and also diagnosed by CT which is considered the most sensitive imaging tool for the diagnosis of these insults [21,22]

Studies showed that a high incidence of gall bladder multiple pigmented gall stones is clearly demonstrated among SCA patients due to high bilirubin levels. [23] .Table (10) classifies the findings according to SCD types.

Table (4) showed the renal manifestation in SCA. It was found to be papillary necrosis in 15 cases ,renal abscess in 7 cases, stones with hydronephrosis in 11 cases, renal vein thrombosis in 4 cases, renal failure in 7 and renal infarction in 11 cases considering the patients age and type of SCD as presented also in table (9) .Other similar studies showed that there are multiple renal abnormalities associated with SCD including medullary renal tubular dysfunction , hematuria and papillary necrosis .[24] Glomerulu hypertrophy may be noted, which may account for the mild diffuse renal enlargement , focal or diffuse renal infection or infarction, nephrotic syndrome is less common but may be seen with renal vein thrombosis [25].Other studies have mentioned that Sickle cell nephropathy is another debilitating complication of SCA, which develops as a result of sickling of RBCs in renal circulation. This leads to ischemia causing cortical infarctions and papillary necrosis, as well as renal tubular injury. It may be associated with complications and finally renal failure. Also, there is a possible bacterial infection of the scarred renal tissues and functional tubule abnormalities in conjunction with the compromised immunity, leading to abscess formation [26,27]

Table(3) presented the lungs CT manifestation in SCA : pleural effusion, pneumonia ,atelectasis, ground glass nodules ,consolidation ,fibrosis lung abscess which was found in different ages as well; at all types of SCD including Hb SS ,Hb SC ,Hb SB 0-thalassemia ,Hb SB+ thalassemia that are presented in table(8)

Similar studies have mentioned that the acute chest syndrome is one of the most common causes of hospitalization and even death of SCA patients, pulmonary vascular obstruction. [28]and pleural effusion may also be seen, [29,30] Patients with SCA may develop obstructive or restrictive lung diseases, when there is a progressive decline in the pulmonary functions .This may be explained by established fibrotic lung changes from repeated episodes of pulmonary infective and vaso-occlusive events. High resolution CT scan (HRCT) shows these interstitial changes, that are of reticular or reticulonodular pattern and may be associated with traction bronchiectasis [31]

V. CONCLUSION

Regarding our findings and the study results, the SCD can cause multiple manifestations in the chest and abdomen; Computed tomography (CT) has been shown to be an excellent modality for efficient and multisystemic evaluation of the abdomen and chest in these patients.

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