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RESEARCH ARTICLE

HEPATOBILIAY SCINTIGRAPHY STUDIES IN IRAQ

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ABSTRACT

Introduction: Hepatobiliary (HB) scintigraphy is a radionuclide scintigraphic method frequently used in evaluation of various liver and biliary tracts disorders. **Objective:** To evaluate the usefulness of this method in diagnosis of various HB disorder; to clarify the scintigraphic patterns of each disorder, to establish the final diagnosis using this technique; to find out the sensitivity, specificity and accuracy of this technique. **Patients and Method:** 71 cases with different HB diseases who had a conventional radionuclide HB imaging in Teaching hospital nuclear medicine unit in Baghdad were reviewed retrospectively. **Results:** 33 patients were females, 38 patients were males. Their ages ranged between (1 month - 70 yr). The study showed that only two peaks of age groups:(1 month,- 6 month) (39.4 %) and 41 - 65 yr. (38%). The final scintigraphic diagnosis demonstrated that 27 cases (38 %) had biliary atresia: 7 cases (9.85 %) had acute cholecystitis; 3 cases (4.2 % had chronic cholecystitis; 8 cases (11.26%) had partial biliary obstruction: 7 cases (9.85) had complete biliary obstruction and 6 cases (8.45 %) had parenchymal liver disease. While the rest of our series showed normal scintigraphic studies (18.3%). **Conclusion:** Biliary atresia was the most common disease found in our series. This, statistically, doesn't reflect the prevalence of all HB disorders because of the limited number of patients. The overall sensitivity and specificity and accuracy for various HD disorders can be calculated. Thus, this study revealed that this technique had statistically high sensitivity 95%; excellent specificity 100 % and very high accuracy 97 %. Therefore we recommend the clinical application of HB scintigraphic technique in assessment of patients with suspected liver and biliary system disorders and we emphasize that HB scintigraphy is mandatory in urgent cases such as biliary atresia and acute cholecystitis.

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INTRODUCTION

Anatomy and physiology: The liver is the largest solid organ in the body, it occupies the right hypochondrium of the abdomen. It weighs 1.5 Kg in the adult (Gross C.M., 1966). It has two equal halves; the right lobe forms the right halfand the left half include the left lobe, caudate and quadrate lobes (Last, 1984). The blood supply ofthe liver by a dual afferents vessels consisting ofhepatic artery and portal vein which enter the liver through the porta hepatis (the gate of the liver), from which the right and the left hepatic bile ducts are perforated and leave the liver. The venous drainage by the right, left and middle hepatic veins which drain to inferior vena cava (IVC) (Last, 1984). The hepatic lobule is the anatomical unit of the liver formed of a polygonal mass of tissues about 0.7 x 2 mm in size (Carlos, 1989).

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The centre of hepatic lobule is a central vein, the periphery of each lobule formed of several Portal triads and their interlobular connective tissue portal canals. The portal triads are containing a venule, an arteriole and a tributary of the bile duct and lymph vessels. The parenchymal liver cells (hepatocytes) radiate from the central vein towards periphery; between these plates run the liver sinusoids which arise in the periphery from the portal triad and run to the centre where they drain into the central vein. These sinusoids contain the endothelial lining cells and the phagocytic (kupffer cells). The hepatocytes are a polygonal cells, The surface of each liver cell is in contact with the wall of sinusoid through the space of Disse, and with the surface of other hepatocyte (Carlos, 1989). Whenever two hepatocytes adjacent, they delineate the tubular space between them known as bile canaliculus, the canaliculi are the first portions of the biliary duct tract. The canaliculi anastomose along the plates of the hepatocytes and terminating in the region of the portal canals, where the bile enters the bile ductules, or Hering canals, these are end in the bile ducts in the portal triads.

The bile flow, therefore, progress in direction opposite to that of blood i.e. from the centre of the classical lobule to it is periphery (Carlos, 1989). The smallest interlobular ducts joins to form septal bile ducts, and these finally unite to form the right and left hepatic duct (the intra hepatic biliary tract), till it reach the porta hepatis where the extra hepatic biliary tract start. The right and left hepatic bile ducts join to form the common hepatic duct (CHD 2.5 cm length) which is soon joined by the cystic duct (CD 2.5cm length) from the gall bladder and hence the common bile duct (CBD 7-8 cm length) is formed. It opens in common with the main pancreatic duct into the ampulla of vater, this in turn open in the posterior medial wall of the second part of the duodenum. The common opening of these two ducts is surrounded by a circular muscle the sphincter of Oddi.

The gall bladder (GB) is a pear shaped organ (7.5 – 12.5 cm length) with a normal capacity of about 50 ml. It lies against the under surface of the right lobe of the liver, and it is formed of three parts: The fundus (the blind end), the body of the GB (narrower than the fundus), then the neck which is narrower than the body and at a higher level than the fundus from which the CD lies against the porta hepatis, the GB receives sympathetic nerves from the coeliac ganglia and Para sympathetic nerves from the left vagal trunk (last, 1984).

Bile Synthesis: Bile is manufactured by liver cells. It is composed of water, bile salts, bile pigments, cholesterol, fatty acids, and electrolytes (Na, K, Ca, Cl). The colour of bile is related to the presence of bile pigment (bilirubin diglucuronide, which is the metabolic product of break down of haemoglobin) and is secreted in bile in concentration 100 times greater than that present in plasma (Schwartz, 1989).

Bile Secretion and storage: The secretion of bile takes place in liver cells. All hepatocytes, continually, secrete bile in small amount. The secretion of bile is responsive to neurogenic, humoral, and chemical control. Vagal stimulation some time can double or more the secretion. Secretin hormone via the blood stimulate ductal secretion, it can increase bile Secretion as much as 80 % mainly by increase secretion of bicarbonate solution which helps to keep bile salts in solution in bile. The presence of large amount of bile salts in the blood increases the rate of liver secretion proportionately, this acts directly on the parenchymal cells to augment bile secretion. Also the greater liver blood flow increases bile secretion (Guyton, 1987 (The hepatocyte provides the driving force for bile flow by creating osmotic gradients of bile acids which forms micelles (bile acid dependant bile flow) and sodium (bile acid independent bile flow) (MacL EOD *et al.* , 1991). The bile flow through the intra hepatic biliary tract till it reach's the CBD from which the bile empties directly into the duodenum or is directed to the GB (Guyton, 1987). The GB mucosa has the greatest absorptive power per unit area of any structure in the body, this rapid absorption prevents arise in pressure within the biliary tract under normal conditions (Schwartz, 1989). The bile after concentrated, is normally stored in the GB (during fast) until it is needed in the duodenum (after meal).The CBD pressure is maintained by rhythmic contraction and relaxation of the sphincter of Oddi, during fasting this pressure exceeds the GB pressure so that the bile normally flows into the GB. After meal particularly (fatty meal) the GB contracts and empties it's store of concentrated bile mainly in response to the hormone cholecystokinin from the upper intestinal mucosa which cause specific contraction of the GB muscle. Also vagal stimulation cause an additional weak contraction of the GB. This contraction provides the pressure that forces the bile towards the CBD to the sphincter of Oddi which open in response to GB contraction, also relaxation of the sphincter of Oddi may be a direct effect of cholecystokinin. The presence of food in the duodenum produces a degree of peristaltic wave travel towards the sphincter so the sphincter with the adjacent intestinal wall momentarily relaxes and open and the bile reach the duodenum. when there is no fat in meal the GB empties poorly, but when adequate quantities of fat are present the GB empties completely in about 1 hr. (Guyton, 1987).

Bile Functions: The importance of bile for digestion only because of the presence of bile salts (cholic acid, deoxy cholic acid and chenodeoxycholic acid) in concentration of 10-20 meq/l. Bile salts emulsify the fat globule so that they can be digested by intestinal lipases, also they transport the end products of fat digestion to intestinal villi so that they can be absorbed into lymphatic, this function performed by forming a minute complexes micelles. Without the presence of bile salts in the intestinal tract up to 40% of lipids lost in stool leading to steatorrhea (fatty stool) and deficiency of fat soluble vitamins (A,D,E and k) (Guyton, 1987). Bile also provides the excretory mode for various substances some endogenous as bilirubin and hormones others are exogenous substances such as drugs, alcohol and copper (MacLEOD *et al.*, 1991). Bile also excrete variety of dyes foreign to the body such as sulfobromophthalein (BSP), rose Bengal, indocyanin green, which can be used for testing liver function)Schwartz, 1989). The N- substituted iminodiacetic acid (IDA) also concentrated and excreted in the bile which permits the visualization of the biliary tracts after labeling with radioisotope (Walker, 1984).

Hepatobiliary Scintigraphy: Definition: HB Scintigraphy is a radionuclide diagnostic imaging study including(planar imaging, SPECT, or hybrid imaging such as SPECT/ CT) that evaluate hepato cellular function and biliary system by tracing the production and flow of bile from formative phase in the liver, and its passage through the biliary system into the small intestine. Sequential (or dynamic) images of the liver, biliary tree, and gut are obtained. Computer acquisition and analysis, including pharmacologic interventions, are used according to varying indications and individual patient's needs (Mark Tulchinsky, 2010). HB Sintigraphy has been used in the last four decades, Tc 99m HB radiopharmaceuticals began to be widely used by the early 1980s. Tc 99m cholescintigraphy still a very useful study. It's strength lies in the fact that the diagnostic information provided defines pathophysiology rather than anatomy.(Ziessman HA. 2014)

HIDA: (hepato imino diacetic acid) has long been used as a generic term for cholescintigraphy. HIDA (lidofenen) is the proto type of this group of agents (Chilton, 1984). The IDA-type radiopharmaceuticals are called bi functional because they possess both hydrophilic group necessary for binding Tc 99m and lipophilic component that provides hepatocellular specificity (Chilton, 1984). It was a major advance, but image quality and diagnostic utility were sub optimal in patients with serum bilirubin levels above 5 mg/dl. It's no longer available. Perhaps the most widely used IDA compound is diisopropyl IDA(DIS IDA; disofenin or Hepatolite) which with its longer substituted chain allows for increased biliary excretion and visualization of HB system at serum bilirubin levels approaching 20 mg /dl. (Mettler, FredA., 2006).

Mebrofenin (Trimethyl-bromo IDA or Choletec) was approved in 1993, it had higher liver extraction 98% vs. 90% and more rapid biliary clearance than Tc 99m disofenin. The halftime of liver clearance for both agents is 15 to 20 minutes (Mettler, Fred, 2006). After intravenous injection, Tc 99m HIDA radiopharmaceuticals are transported in the blood bound to serum albumin. They dissociate from albumin in the hepatic peri sinusoidal space and are extracted by hepatocytes by receptor-mediated endocytosis similar to bile salts, free fatty acids, and bilirubin, except that they are secreted into biliary canaliculi unchanged, without undergoing conjugation (ziessman 2014).

Common clinical indications for HB Scintigraphy Congenital abnormalities:

- **Biliary Atresia:** It is present in 1 per 10,000 live births. The cause is unknown, possibly viral in origin rather than failure of embryogenesis. Variable length of biliary tree are occluded. 10% are correctable, 90% are non correctable. Jaundice is present by the end of the first week and deepens progressively. Later on features of obstructive jaundice and complications are common and biochemically clear. Diagnosis is confirmed by biliary scintigrphy which shows non visualization of the biliary tree and failure of radio tracer to reach intestine(Harding Rains, 1990)

- **Choledocal cysts:** It is caused by a specific weakness in a part or the whole of the CBD, it is a rare condition affecting females four times than males. It is seldom manifested before the age of six months, (only half of the cases present before the age of twenty). The patient presented by attacks of obstructive jaundice accompanied by upper abdominal pain and pyrexia, in most of cases a swelling is detected in the upper abdomen and the ultrasound shows it's cystic nature. If un treated ultimately the condition fatal, due to ascending cholangitis and biliary cirrhosis or diffuse peritonitis following rupture of the cyst, carcinoma may develops in choledochal cyst.(Harding Rains, 1990). Can be confirmed by demonstration of radio tracer within it (Sutton David, 1998).

- **Caroli's Syndrome:** It is a congenital dilatation of the intra hepatic bile ducts. Biliary stasis leads to stone formation and cholangitis. This condition appears in childhood or in early adult life. (Harding Rains, 1990). HB scintigraphy show dilatation of multiple intra hepatic bile ducts. multiple cold defects seen in early liver images; later fill in and retain Tc 99m IDA, showing multiple hot spots while remainder of liver clears. (Specht NT., Russo RD., 1998)

Neonatal and childhood jaundice: The causes of persistent conjugated hyper bilirubinemia in infants are many, biliary atresia and neonatal hepatitis(secondary to CMV, HAV, HBV, Rubella and Toxoplasma infection) account for 70-80%. (Col SS Anand, Lt Col RK Handa, 2006). HB excretion scintigraphy has an important role in neonatal jaundice in defining surgically correctable disorders as biliary atresia, this condition can be excluded if the radio tracer enters the small intestine (Sutton David, 1998).

Acute Cholecystitis: The condition is almost always caused by obstruction of the gall bladder neck or CD by a gall stone, occasionally, obstruction may be by mucous, worm or a tumor. The patient present with sever upper abdominal pain either in the right upper quadrant, radiating to the right scapular region, or occasionally, with epigastric or left upper quadrant or retrosternal pain. It lasts more than one hour and is associated with restlessness and sweating, nausea and vomiting, fever, rigor may occur. Physical signs including fever, tachycardia, right hypochondrium tenderness and rigidity worse on inspiration (Murphy's sign) may occur too. Leucocytosis is common except in elderly patient. The inflammation resolve even if not treated but it recur, on the other hand it may progress to empyema or perforation and peritonitis. The mortality rate in elderly may reach about 10%. Biliary scintigraphy has a high sensitivity in the diagnosis of acute cholecystitis. Persistent non visualization of the gall bladder is an indicator of CD obstruction. Other positive finding of acute cholecystitis include the "rim sign" and "cystic duct sign" where increased tracer up take is present within the adjacent liver and CD proximal to obstructing calculus.(Sutton David, 1998).

Chronic Cholecystitis: Chronic inflammation of the GB is almost invariably associated with gallstones. The patient suffers from recurrent episodes of constant right upper quadrant pain, often at night and some time precipitated by a heavy meal. If untreated the episodes last 1-6 hours. but it recur. Cholecystectomy is advisable. Delayed GB visualization correlate well with chronic GB disease, it may be excluded when stimulation with CCK (Cholecystokinin) analog allows passage of bile with delayed visualization of GB. (Sutton David, 1998)

Biliary obstruction

Complete Biliary Obstruction: It is a surgical emergency. There are two types that caused by tumor and that caused by cholilithiasis. Those caused by tumor; present with painless hyperbilrubinemia anatomic (Ultrasound) imaging will detect dilated biliary ducts and often the tumor causing the obstruction. Obstruction by cholelithiasis; presents as acute sever biliary colic. The obstruction causes an increase in intra biliary duct pressure. Bile flow is reduced, followed by ductal dilatation. However, dilatation of biliary ducts may not be seen on anatomic imaging until 24 – 72 h after the obstructive event. Thus, ultrasonography may be negative when a patient presents in the emergency room with acute pain. Here cholescintigraphy can play an important diagnostic role, because the pathophysiologic scintigraphic finding are seen promptly after the obstructive event. If the patient has good hepatic function, high grade complete biliary obstruction can be diagnosed within the first hour of imaging after injection of Tc99m–HIDA radiopharmaceutical. The referring physician should be promptly notified. (Ziessman, HA. 2014). Lack of visualization of the biliary tree with good visualization of the liver (liver scan sign) is typical with complete obstruction of the CBD. (Mettler, Fred A., 2006). Also there is no visualization of intestinal activity, in late cases differentiation of obstruction from hepatitis can be difficult or impossible with out the use of ultrasound.

Partial Biliary Obstruction: Patients complain of recurrent biliary colic. Liver function test results are normal. The bile ducts are not dilated. With partial bile duct obstruction the biliary tree is visualized to the level of obstruction, and occasionally a filling defect is identified at that point. Partial duct obstruction is suggested by persistent visualization of the CBD or delayed clearance of activity from the duct. Poor clearance from biliary ducts is diagnostic. (Ziessman, HA.

2014) Delayed appearance of activity (> 60 minutes) in the duodenum and small bowel is not specific and can occur in 20% - 25% of normal people. Partial obstruction can be caused by a CBD stone, benign or malignant stricture, or sphincter of Oddi dysfunction with elevated sphincter pressure.

Biliary leaks: post traumatic and post surgical biliary scans, bile leaks may occur following surgery or trauma. Loculated or free radio tracer may then be demonstrable in the peritoneal cavity. Less common indications: Evaluation of biliary dyskinesia and sphincter of Oddi dysfunction.

Biliary Dyskinesia: The condition presents with upper quadrant discomfort in the absence of gall stones. The cause is related to disorders of motility of the GB either excessive contraction or hypo functioning of the GB. It also may be related to dysfunction of the sphincter of Oddi or stenosis of the ampulla of Vater. Diagnosis is made by excluding gall stones. Hepatobiliary scintigraphy may be helpful by doing the test with fatty meal or cholecystokinin to demonstrate that the contraction of the GB is associated with pain or the papilla is stenosed. Endoscopic sphincterotomy is used to assess the condition often result in treatment of many of these patients (MacLEOD *et al*., 1991).

Post Cholecystectomy Syndrome :HB scintigraphy may be helpful

Purpose of the study: A retrospective study for conventional HB scintigraphic studies in nuclear medicine unit were reviewed in order to evaluate :

- The usefulness of this study in diagnosis of various HB disorders.
- To estimate the most common ages examined. To clarify the scintigraphic patterns of each disorder to establish the final diagnosis using this technique.
- To find out the sensitivity, specificity and accuracy of this technique.

MATERIALS AND METHODS

Patients: Of many cases with different liver and biliary system disorders who had radionuclide HB imaging in Teaching Hospital-Nuclear Medicine Unit - in Baghdad during the period 1988-1990, only 71 cases were reviewed 33 patients were females, 38 were males. The age ranged between (8 days - 70 years). The mean age was 25.8 years.

Technique Preparation of Radiopharmaceutical: (Tc 99m) pertechnetate was prepared from (Mo-99 Tc- 99m)generator elution, while the labeling substance (the HB agent EHIDA) was supplied in special kits. Each vial of 10 ml size EHIDA contains a freeze-dried mixture of 42.7mg Etifenin sodium and 0.4 mg Stannous chloride dihydrate, sealed under an inert atmosphere with a rubber closure. (This agent used in our study was supplied by the Amersham International PLC company, Amersham UK). Tc-99m-2,6-diethylphenyl-carbamoyl methyl imino diacetic acid (EHIDA), was prepared by complexation of reduced Tc-99m with HB agent EHIDA, using tin chloride (sncl 2) as a reductant at room temperature. The tin is not a part of the complex and technetium is in +3 oxidation state. Thus, the overall charge of complex was – 1 This complex is quite stable.

For preparation of Tc - 99m - EHIDA we apply (aseptic technique) throughout following this procedure:

- Place one of the vials in a suitable shielding container and Swab the rubber closure with the sterile Swab provided.
- Using 10 ml sterile syringe , inject a suitable volume between 3-8 m1 of the eluate from a Tc-99m sterile generator into the shielded vial , with draw an equal volume of the gas from the space above the solution to normalize the pressure in the vial, shake the shielded vial for 10 seconds to ensure complete dissolution of the powder.
- Assay the total activity.
- Incubate at room temperature for 15 minute.

The preparation is now ready for intravenous injection of the calculated dose.

Setting of the Gamma Camera: A large field of view gamma camera (General electric GE, Maxi Camera 11), fitted with a general purpose or high sensitivity collimator was used. Tc -99m window 140 + minus 20 was opened. The intensity adjusted according to each case. The camera set on 300 K count per image, computer was used to accomplished this study, as follows: we choice static comments, so we need to determine the count number as mentioned above, then each 5 minute take one image till 30 minute then every15 minute ti11 one hour. Other information also introduced to computer in order to obtain complete study according to each case.

Procedure of the Technique: Each patient was prepared for the study by fasting for at least 3 hours no more than 6 hours. Also the patient should be well hydrated to diminish any interference from the kidneys. The patient then was placed in a supine position with a gamma camera detector fitted with a general purpose or high sensitivity collimator were placed over the patient anterior abdomen. The study was performed in one view, only the anterior view. Then 2-5mci Tc-99m-EHIDA according to the age was administered to the patient intravenously rapidly as a bolus dose in the anti cubital vein. Then serial images were obtained on 5, 10, 15, 20 , 30 ,45 minutes,1 hour, and if the (GB) or bowel activity are not visualized by 1 hour, delayed images at 1.5 hr, 3 hr 5hr, and probably 24 hours in jaundiced patient should be obtained. Fatty meal were used in some cases to induce GB emptying and then re-examined.

Description and Interpretation of the studies: Analysis and interpretation of the obtained images using special protocol done by us. This protocol depends on the following scintigraphic criteria: Radiotracer extraction by the liver; radiotracer distribution through out the liver any liver space occupying lesion; 1iver size; visualization of the extra hepatic biliary tracts; visualization of the GB and CD; Bowel visualization. The results were classified according to this protocol and then the final diagnosis scintigraphically was established. Additional clinical and scintigraphic information obtained from this study were discussed.

RESULTS

The results of 71 HB scintigraphic studies were analyzed.The distribution of our series according to the age demonstrated in (table.1) Most of the cases referred for HB scintigraphy were during the period of life ranging between less than one month and 6 months (39.4%), and 41 to 65years (38 %). Thus about more than two thirds (77.4 %) of the referred cases were in these age ranges. The protocol was applied in this study to assess the anatomy and pathophyisology of the study and the relation ship of these findings with the clinical information's of the presented cases. The study disclosed that 27 cases (38%) had biliary atresia (B.A) which represented the most common HB disorder encountered in our series. The abnormal scintigraphic findings for those 27 cases were found as follows: 23 cases(85%) demonstrated good extraction of radiotracer by the liver; 26 cases(96 %) showed uniform distribution of radiotracer throughout the liver, while only 12 cases (44.4%) revealed hepatomegaly versus 15 cases (55.5 %) with normal liver size. Non visualization of extra hepatic biliary tracts as noted in 27 cases (100%), non-visualization of the GB and bowel activity were observed in 27 cases (100%) (Fig.1) showed the scintigraphic findings in a case with biliary atresia.

The study showed the scintigraphic findings for 7 cases (9.85%) who having acute cholecystitis: 5 cases (71.4%) with good extraction of radiotracer by the liver; 4 cases (57%) with uniform distribution of radioactivity in the liver versus 3 cases (42.8%) with non uniform distribution of radioactivity; the liver is enlarged in 3 cases (42.8%) versus 4 cases(57%) with normal liver size.The extra hepatic biliary system was visualized in 6 cases (85.7 %) versus one case (14.2 %) non visualized. All cases (100%) was showing non visualization of the GB. Bowel activity was detected in 7 cases (100%) in different periods of time. (Fig.2) showed the scintigraphic finding in a case of acute cholecystitis. The study revealed the scintigraphic finding for 3 patients (4.2%) with chronic cholecystitis.

Two cases (66.6%) showed good extraction of radiotracer by the liver versus one case (33.3%) with fair extraction; 2 cases (66.6%) showed non uniform distribution of radioactivity within the liver versus one Case (33.3 %) with uniform distribution. Only one case (33.3 %) presented with space occupying 1esion which was single and well defined. The liver was enlarged in 2 cases (66.6 %) versus one case (33.3%) with normal liver size. A11 the three cases (100%) the extra hepatic visualization and bowel activity were noted in different times, also the 3 cases (100%) showed delayed visualization of the GB (90 min-180 min). (Fig.3) showed the scintigraphic findings in a case with chronic cholecystitis.

The study was illustrated the scintigraphic findings in 6 cases (8.45%) with parenchymal liver diseases. Four cases (66.66%) revealed good radiotracer extraction by the liver versus 2 cases (33.3 %) with fair extraction; 5 cases (83.3%) were showed non uniform distribution of radioactivity versus one case (16.6%) with uniform distribution of radioactivity; 2 cases (33.3%) demonstrated a single S.O.L which was well defined in one case and ill-defined in the other; other case presented with multiple S.O.L which were ill defined. The size of the liver was enlarged in 6 cases (100%); visualization of extra hepatic biliary system, GB and bowel activity was seen in all cases in various times. (Fig.4) showed the scintigraphic findings in a case with parenchymal liver disease. The study was showed the scintigraphic findings in 8 cases (11.26%) with partial extra hepatic biliary obstruction; 7 cases (87.5%) showed good radiotracer extraction versus one case (12.5%) with fair extraction; 6 cases (75%) demonstrated uniform distribution of radiotracer in the liver versus two (25%) with non-uniform distribution; the liver was enlarged in 4 cases (50%) versus 4 cases (50%) with normal size; 5 cases (62.5 %) showed non visualization of the extra hepatic biliary System versus 3 cases (37.5 %) with visualization in various times; 4 cases (50 %) with non visualization of GB , while other 4 cases (50 %) were showed visualization of GB in various time too; all 8 cases (100%) demonstrated delayed visualization of the bowel activity. (Fig. 5) showed the scintigraphic findings in a case with partial extra hepatic biliary obstruction.

The study was demonstrated the scintigraphic findings in 7cases (9.8%) with complete extra hepatic biliary obstructions as follows: 4 cases (57%) with fair uptake of radiotracer by the liver, 2 cases (28.5%) with poor uptake versus one case (14.3%) with good uptake of radiotracer by the liver; 3 cases (42.8%) with uniform distribution of radioactivity in the liver versus 4 cases (57%) with non-uniform distribution of radioactivity within the liver; liver enlargement was noted in all cases (100%); the extra hepatic, GB and bowel activity were not seen in all cases (100%). (Fig.6) showed the scintigraphic findings in a case with complete extra hepatic biliary obstruction.

The study was disclosed the normal scintigraphic findings in 13 individuals (18.3%). All the cases (100%) were showed a good radiotracer extraction by the liver, with a uniform distribution of radioactivity within the liver; also normal liver size was noted in all cases (100%); extra hepatic biliary tract visualization and bowel activity were noted in all cases (100 %), GB was visualized in 12 cases (92.3%)versus one case (7.69 %) with non-visualization of the GB due to a known previous cholecystectomy. (Fig.7) showed the scintigraphic findings in a normal individual. (Table.2) was summarized the distribution of the final scintigraphic diagnosis for 71 cases with various HB system disorders in our series. 27 cases (38%) which were represented the most common HB disease encountered and diagnosed scintigraphically in our study were biliary atresia. While other HB disorders were as follows: CD obstruction and acute cholecystitis represent (9.85%) versus 3 cases with chronic cholecystitis (4.2%(; and partial biliary obstruction 8 cases (11.26%); while Complete biliary obstruction was seen in 7 cases (9.85%); parenchymal liver disease was noted in 6 cases (8.45%); Normal studies were obtained in 13 individual (18.3%). (Table.3) was showed the overall sensitivity, specificity, and accuracy of HB scintigraphic studies for various HB disorders.

DISCUSSION

It was found that the most common age ranges were at two different periods of life, which were the first 6 months of life and the second period at the 5th and 6th decade. The first peak is probably due to increased incidence of neonatal jaundice during this age group. It was published that radionuclide imaging with Tc 99m labeled HB agents appears promising for the non invasive diagnosis of biliary atresia(Gerhold JP., *et al*., 1983) (Ziessman HA., 2014). Also it is important to diagnose infant with extra hepatic biliary atresia as early as possible, as the success of the kasai's procedure (hepatoportoenterostomy).

Table 1. Showing Age Distribution

Age (year)	No. of patients	Percentage %
Less than 1month – 6month	28	39.4 %
7 month – 1 year	4	5.6 %
1 yr – 5yr	2	2.8 %
6 – 10 yr	1	1.4 %
11 – 15 yr	--	----
16 – 20 yr	--	----
21 – 25	1	1.4 %
26 – 30	--	- –-
31 – 35	3	4.2 %
36 – 40	1	1.4 %
41 – 45	6	8.4 %
46 – 50	8	11.3 %
51 – 55	2	2. 8 %
56 – 60	6	8.4 %
61 – 65	5	7 %
66 – 70	4	5.6 %
Total	71	100 %

Female = 33*;Male = 38*

Table 2. Showing the distribution of the final scintigraphic diagnosis for 71 cases*

Scintigraphic diagnosis	No. of Pts.	%
Biliary Atresia	27	38 %
Cystic duct obstruction & Acute Cholecystitis	7	9.85%
Chronic cholecystitis	3	4.2%
Partial extra hepatic biliary obstruction	8	11.26 %
Complete extra hepatic biliary obstruction	7	9.85 %
Parenchymal liver disease	6	8.45 %
Normal	13	18.3 %
Total	71	100 %

Classification according to final nuclear diagnosis *

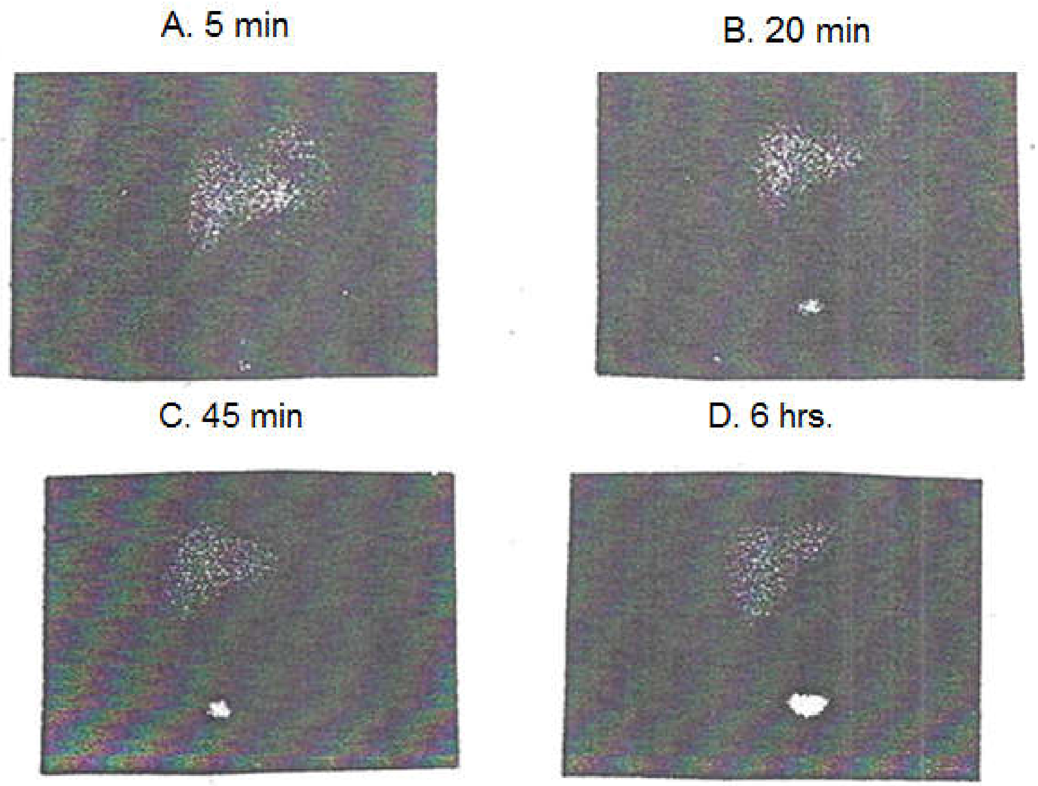


Fig 1. Showing the hepatobiliary scintigraphy in a 2 months male infant patient with biliary atresia

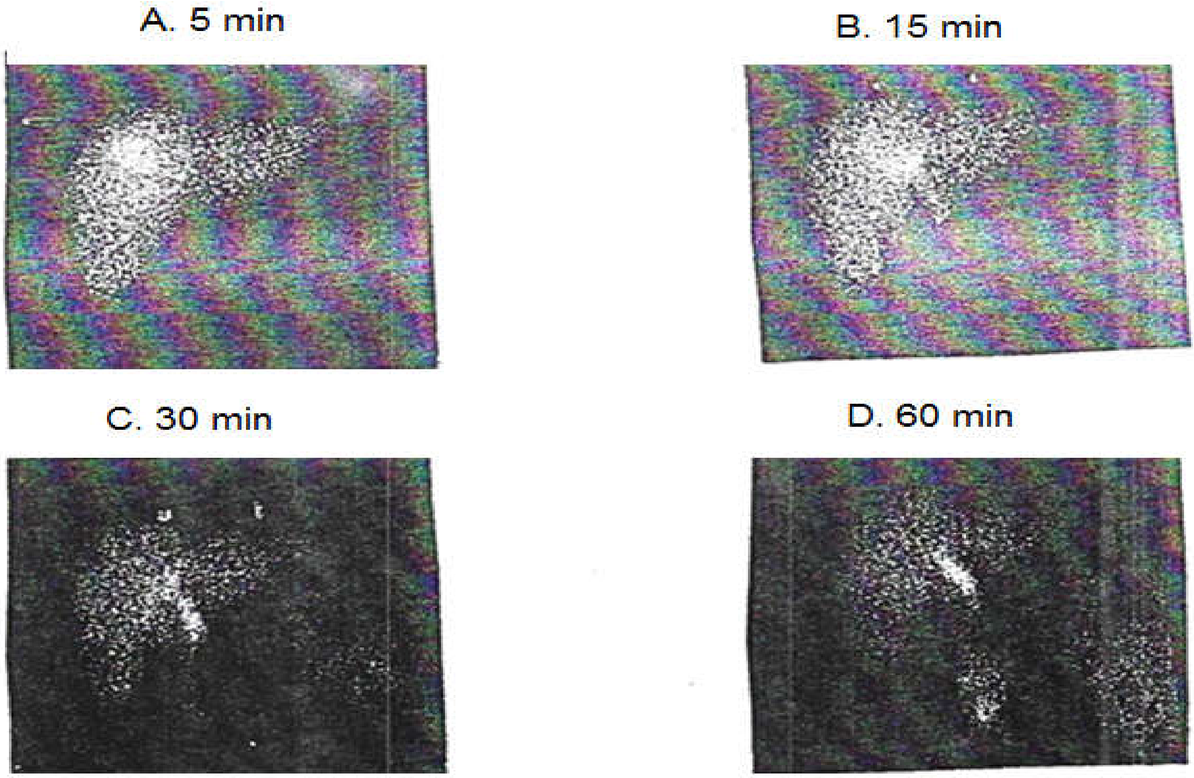


Fig 2. Showing the hepatobiliary scintigraphy in Female patient with a cute cholecystitis

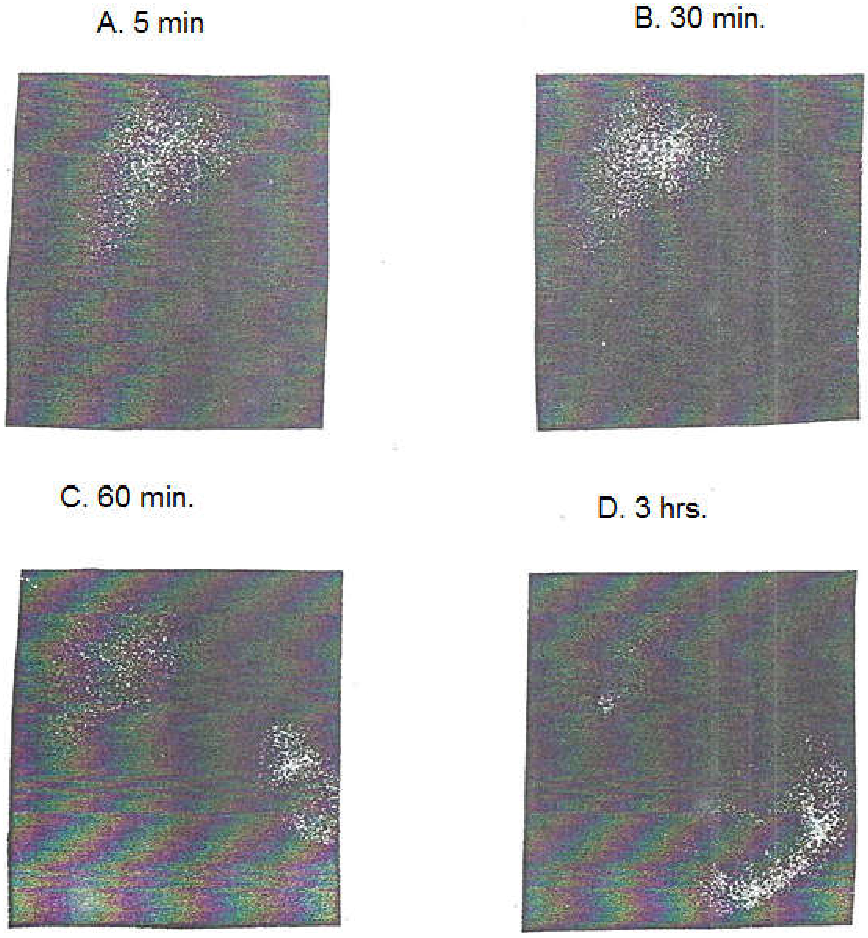


Fig .3. Showing the hepatobiliary scintigraphy in patient with chronic cholecystitis

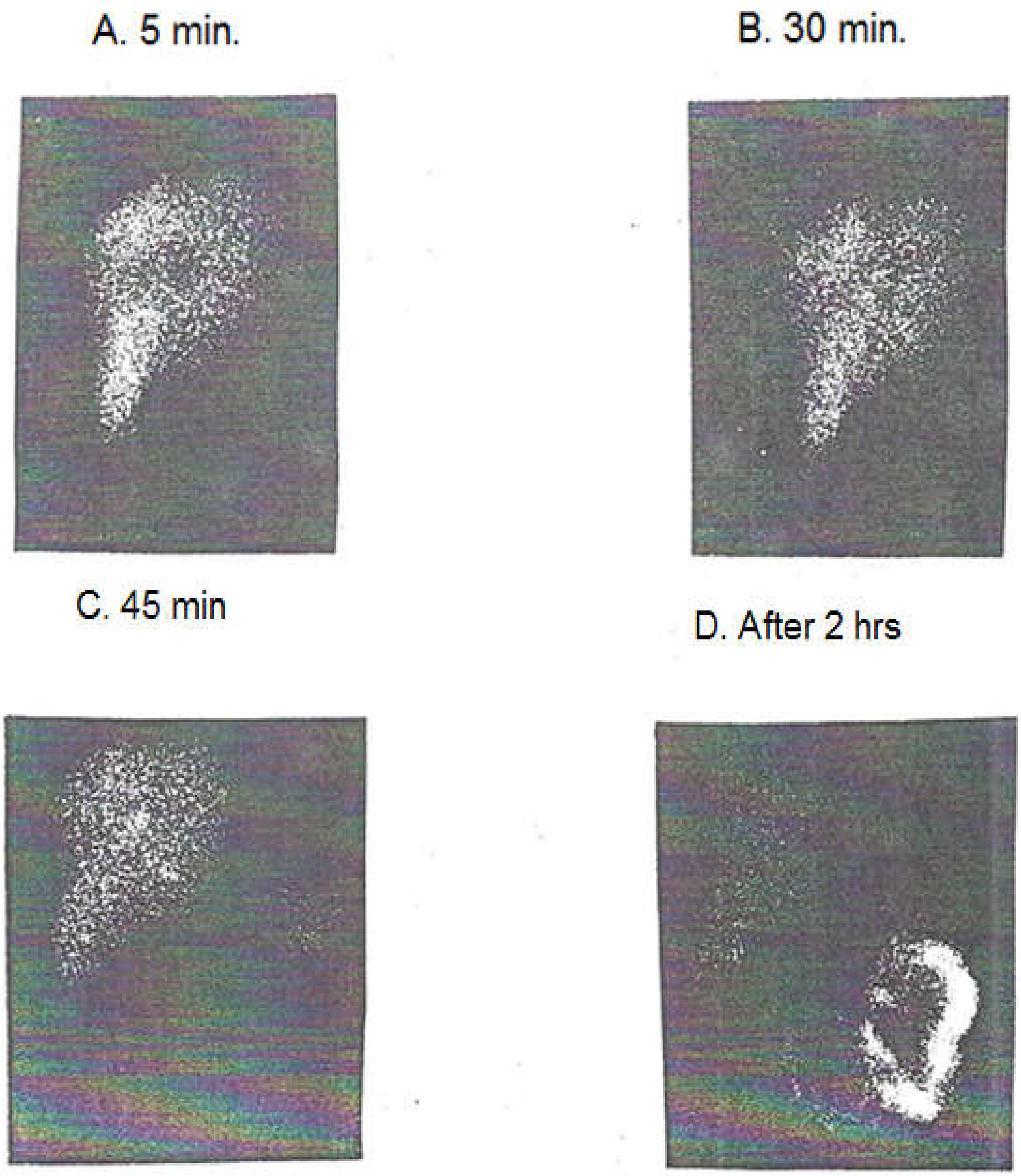
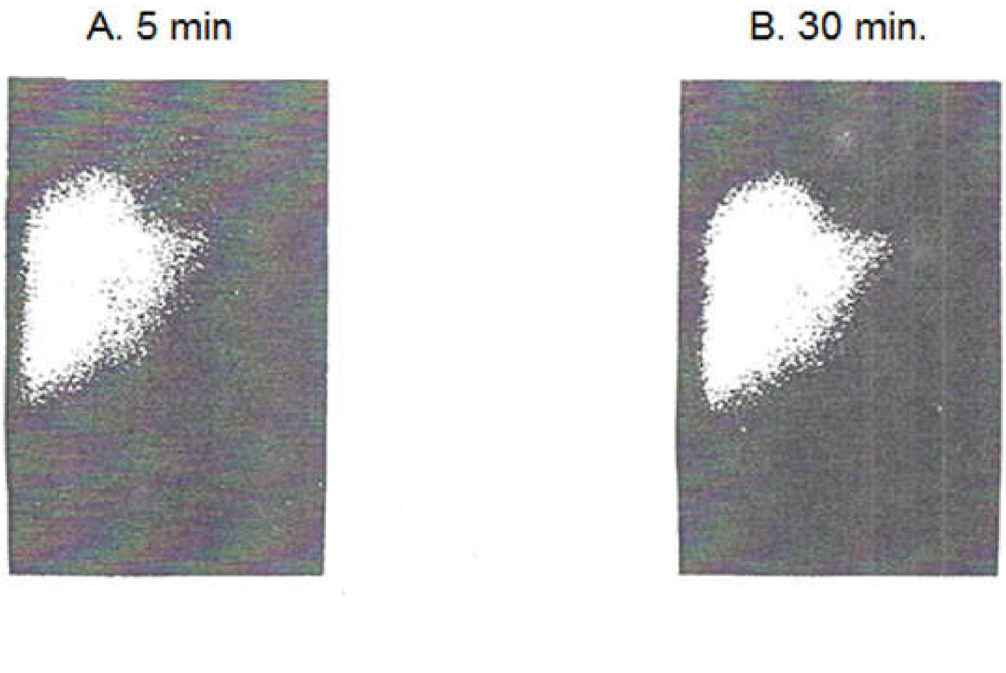


Fig 4. Showing the hepatobiliary scintigraphy in Female patient with paranchymal liver disease



Continue …

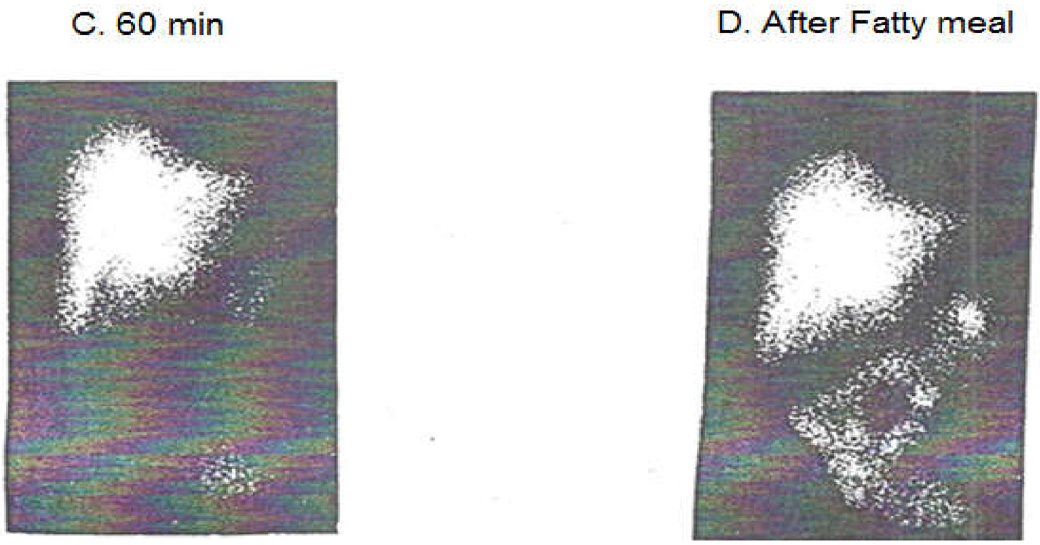


Fig 5. Showing the hepatobiliary scintigraphy in male patient with partial hepatic biliary obstruction

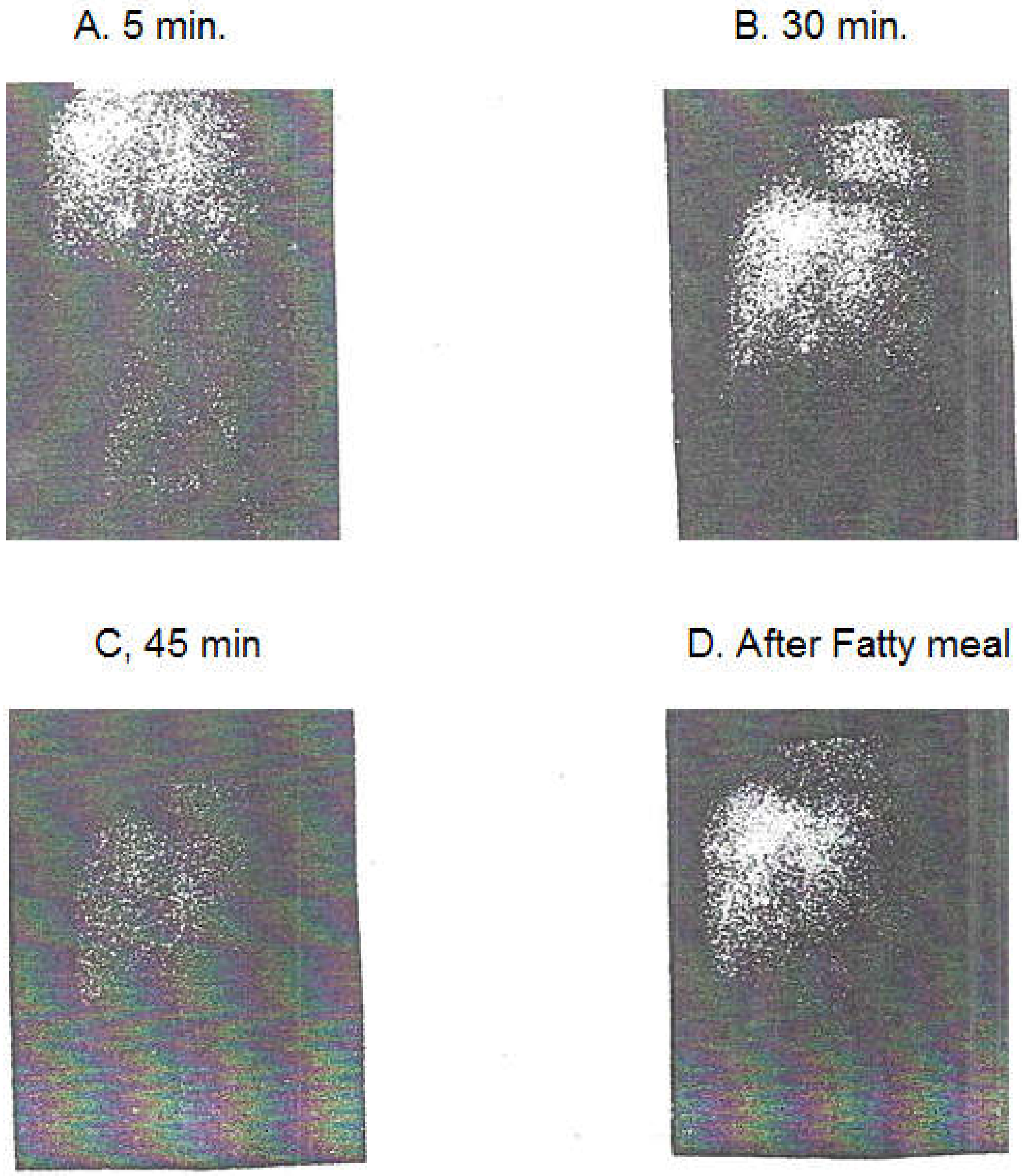


Fig 6. Showing the hepatobiliary scintigraphy in female patient with completed biliary obstruction

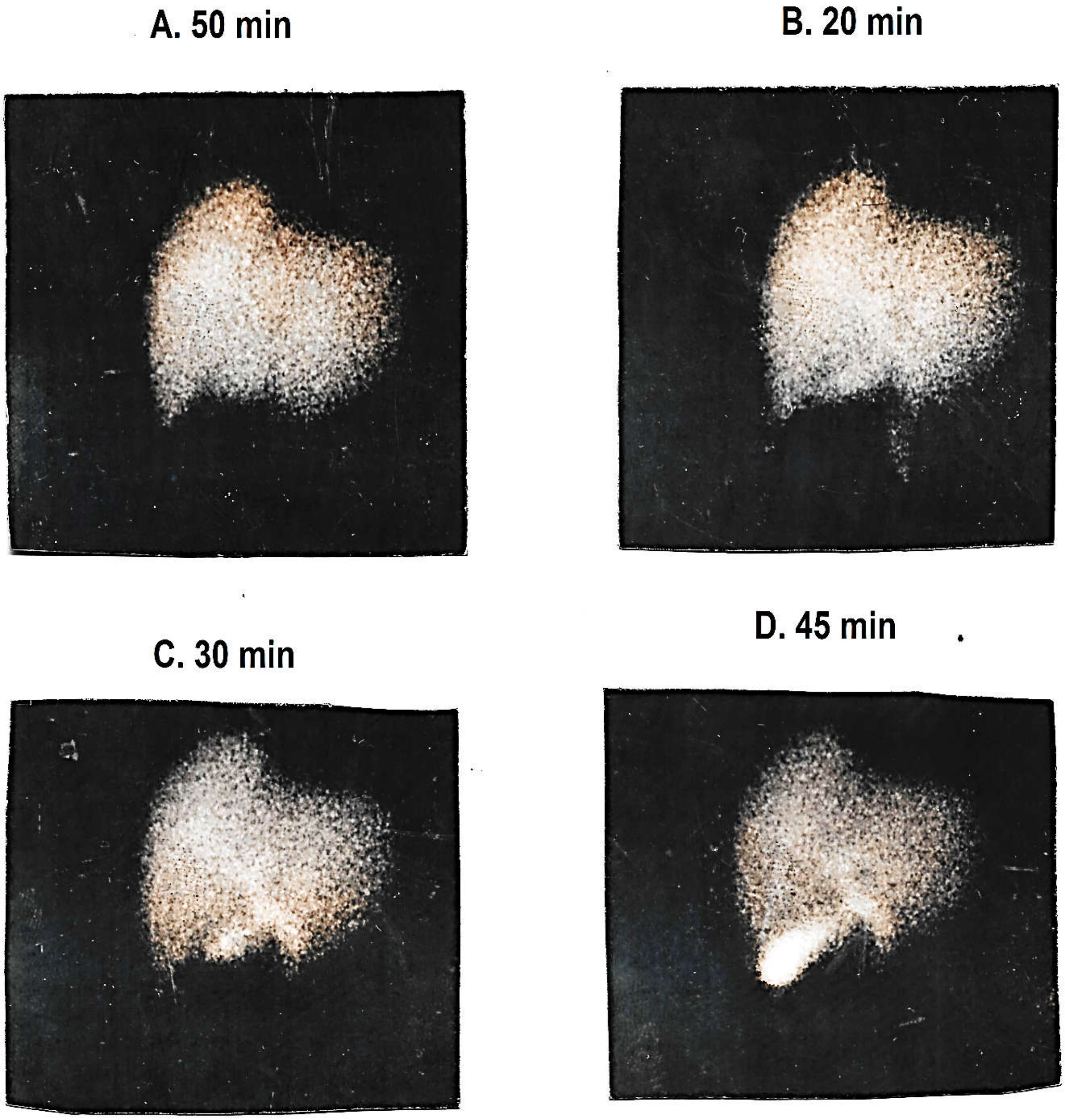


Fig 6. Showing the hepatobiliary scintigraphy in a 50 year old lady

is inversely related to the age and is greatest if performed during the first 2-3 months of life (Gerhold JP., *et al*., 1983 and Coller B.D, *et al*., 1980) (Ziessman HA.2014). Contrary, the infant with intra hepatic cholestasis from other causes e.g. neonatal hepatitis, should not be subjected to laprotomy (Gerhold, *et al*., 1983). Therefore, this technique is important to distinguish the line of treatment of jaundiced patients (whether surgical or medical) particularly, in the surgical method, since in vitro laboratory studies and closed needle biopsy are often unable to differentiate between biliary atresia and neonatal hepatitis (Coller B.D, *et al*., 1980).While, the second peak of the increasing number was probably due to the prevalence of liver diseases and gall stones and their complications during this age range (James, 1986 and Bouchier, 1986). Biliary atresia was the most common disease found in our series (38 %) which was the only cause of neonatal jaundice encountered in this study (Table. 2). This may be probably due to the majority of the referred cases were during this age group as shown in (table.1). However, this statistically, doesn't reflect the real prevalence of HB disorders because of the limited number of patients. The scintigraphic findings in these cases are studied as follows:

The radiotracer extraction was good in most cases (85%) with uniform distribution of radioactivity within the liver (96%) these findings are possibly due to early referring the cases with sign and symptom of neonatal jaundice to confirm the diagnosis of biliary Atresia as early as possible. Early diagnosis is critical and must be made within the first 60 days of life to prevent irreversible liver failure(Ziessman HA. 2014) , since the results of the Kasai procedure at this age has a 90% success rate whereas beyond 3 months success rate drops to 20%.(Col SS Anand, Lt Col RK Handa, 2006), so results are poor beyond the age of 10-12 weeks, as irreversible liver damage have occurred (Shepherd , 1986). Hepatomegaly versus normal size was (44.5) and (55.5%) respectively which is in significant. The extra hepatic biliary tracts, GB, and bowel were not visualized in all cases. Non visualization of bowel activity even throughout the 24 hour was the most useful diagnostic criterion reported previously (Gerhold., *et al*., 1983).Also non visualization of the GB in our study was in agreement with report of B. David (Coller B.D, *et al*., 1980). Early diagnosis of acute cholecystitis is very important since it is one of the most common surgical emergency. Prompt diagnosis of acute cholecystitis is highly indicated to decrease the morbidity and mortality associated with this condition (Weissmann, *et al.*, 1979). Cholescintigraphic technique has proved to be the most sensitive method available for documenting CD patency or obstruction and has become the procedure of choice in evaluation of patients with suspected acute cholecystitis (A1-Eid MA., *et al.*, 1988 and Freitas, 1982). This technique does not have the limitations which are present with other imaging procedure such as oral cholecystography, ultrasound and computerized tomography (Al-Eid MA.,. *et al.*, 1988 and Weissmann, *et al.*, 1979). The incidence of acute cholecystitis in our series was 9.85 %. The scintigraphic findings demonstrate the following criteria. The extra hepatic biliary system was visualized in 85.7% only one case show non visualization of extra hepatic biliary System. A11 cases (100%) revealed non visualization ofGB within 60 minutes which is the major diagnostic criteria of acute cholecystitis

which indicate CD obstruction (Freitas, 1982;Weissmann, *et al.*, 1981), bowel activity was detected in all cases (100%). In case No. 3 the extra hepatic biliary tract non visualization in addition to non visualization ofGB and normal visualization of bowel within 60 minutes, since the GB was not visualized and normal biliary to bowel transit within 60 minutes the diagnosis of acute cholecystitis can be presumed even if the CBD is not visualized (Weissman, *et al.*, 1981). Although the main finding encountered in acute cholecystitis was non visualization of the gall bladder, other parameters such as the degree and rate of liver uptake, visualization and caliber of CBD and the presence of intestinal activity as well as rapidity of biliary tract to bowel transit of the radiotracer forms secondary findings for acute cholecystitis, so our study appear to be confined to this spectrum of cholescintigraphic patterns (Weissmann, *et al.*, 1981) (ZiessmanHA,2003). In our series chronic cholecystitis forms only 4.2%.The scintigraphic patterns for chronic cholecystitis were variable in our study because of the nature of this chronic disease. The most common diagnostic finding of chronic cholecystitis in this method is the delayed visualization of the GB, ranging between 90-180 minutes post injection of radiotracer and after fatty meal. Normal visualization of extra hepatic biliary tracts and bowel were seen in all cases (100%). However, only one case was presented with liver S.O.L which was single and well defined, this case is probably has another pathology in the liver. It was reported that the delayed visualization of GB at later than 1hour after IDA injection intravenously is most commonly associated with chronic cholecystitis (Weissmann HS., *et al.*, 1981). Delayed GB visualization most probably induced by a partial functional obstruction of CD due to viscous bile, chronic mucosal oedema and luminal debris. Cholescintigraphy appears of limited value in diagnosis of chronic cholecystitis in comparison to acute cholecystitis (Freitas, 1982). Moreover, the cholyscintigraphic method assesses the patency of CD and CBD, but it does not have sufficient anatomic resolution to detect the presence of gallstones associated with chronic cholecystitis (Freitas, 1982) other wise, in minimal symptomatic patients at least 90% have normal cholescintigraphy while remaining 10 % will show either delayed GB visualization (up to 4 hours post injection) or persistent non visualization. Since the majority of patients with chronic cholecystitis demonstrated normal cholescintigram, cholescintigraphy is not a useful Screening tool in the evaluation of patient with suspected chronic cholecystitis such screening is performed by oral cholecystography or real time ultrasonography (Freitas, 1982 and Laing FC., *et al.*, 1981). This may reflect the low percentage of chronic cholecystitis in comparison to acute cholecystitis in our series) (3 cases). Parenchymal liver disease represents 8.45 % in our series. All cases (100%) demonstrated hepatomegaly with 50% of cases revealed space occupying lesion two cases with single (one well defined and the other i11 defined) and one case with multiple i11 defined; the radiotracer extraction were variable, while 83.3% of cases with non uniform distribution of radioactivity; visualization of extra hepatic biliary system, GB

Table (3) Showing the over all sensitivity, specificity, and accuracy of HB scintigraphic studies for various HB disorders

	Disease	No disease	Total	
Abnormal	45 TP	0 FN	45	Total +ve
Normal	2 FP	24 TN	26	Total -ve
Total	47	24	71	

TP : True + ve , FP : False + ve
TN : True - ve, FN : False - ve

and bowel activity were detected in all cases at various times. Our findings are supported by the characteristic features of parenchymal liver disease scintigraphically as reported in literatures as follows: A reduced rate of accumulation of TC-99m IDA by the hepatocyte, a normal or delayed appearance of radioactivity in the bowel and no evidence of stasis within the biliary tract (Rosenthal, 1982). Impaired liver uptake correlate well with hepatocellular disease since it has been observed that for a given serum bilirubin level the uptake is higher for mechanical obstruction than that it is for hepatocellular disease (Rosenthal, 1989). In jaundiced patient the interpretation depends on the level of serum bilirubin, if serum bilirubin ≤ 5mg% with no dilatation of bile ducts this goes with hepatocellular disease, and when the serum bilirubin more than 5mg% and biliary duct not visualized with appearance of gut activity at 24 h. and GB visualized the finding goes with hepatocellular disease, but if there is no gut activity at 24 hours with either GB visualization this is with hepatocellular disease or GB not visualized this suggest either hepatocelluar disease or complete biliary obstruction. Partial extra hepatic biliary obstruction form 11.26% of our series the scintigraphic findings were as follows:

(87.5 %) showed good radiotracer extraction with uniform distribution of radiotracer in the liver in (75%), this high percentage of uptake correlate well with extra hepatic biliary obstruction against paranchymal liver disease(Rosenthal, 1982). Hepatomegaly finding during cholescintigraphy was not specific (50 %). The extra hepatic biliary system was non visualized in 5 cases (62.5%) versus (37.5%) visualized with moderately delayed time between (30-60minute). The GB visualized in 50 % versus 50 % non visualization, all cases (100%) showed delayed visualization of bowel activity ranging between (60-180 minute). Therefore, the most common pathognomonic finding of partial biliary obstruction in our study was the delayed visualization of the bowel. This finding was accepted as the pathognomonic sign of partial extra hepatic biliary obstruction, also a dilated main biliary duct with pooling of radioactivity within the biliary tract was reported in previous literatures) Rosenthal *et al.*, 1978 and Pouwels S., *et al.*, 1978 and Rosenthal, 1982. Complete extra hepatic biliary obstruction constitute 9.8% of our series. The scintigraphic findings revealed:

Non visualization of the extra hepatic biliary system, GB and bowel activity in all cases (100%). These findings are corresponding with the previous studies which regard the absence of radioactivity in biliary tracts and intestine up to 24 hr after administration of Tc-99m IDAs the diagnostic criteria of complete extra hepatic biliary obstruction when the bilirubin level is 5mg% or less) Rosenthal L. *et al*., 1978 and Freitas, 1982 and weissman, 1979 and Pauwels S., *et al*., 1978). Moreover, the explanation of non-visualization of GB and extra hepatic biliary tract is due to the high intra ductal pressures prevent the transport of Tc-99m IDA from the hepatocyte to the canaliculi (Rosenthal, 1982). Only case No. 4 the non-visualization of GB was due to previous cholecystectomy. The degree of uptake should be reserved as a second order parameter and used only in questionable cases. Since the only criteria that may help to differentiate between an obstructed and a hepatocellular problem is the fact that in cases of a complete extra hepatic biliary obstruction, the liver is clearly seen early, whereas in cases of complete hepatocellular obstruction (hepatocellular disease) it is usually hard to recognize the liver, accordingly the differential diagnosis is almost impossible in cases of hepatocellular process complicating a complete mechanical obstruction. This implies that when there is a complete biliary obstruction the use of Tc-99m diethyl-IDA never permit localization of the site of obstruction, since the main bile ducts are not seen (Pauwels S., 1978). In these cases ultrasound can confirm CBD obstruction and determine it is cause. 18.3% of our series 13 cases shows normal HB scintigraphy. A11 cases, (100%) demonstrated good extraction of radiotracer by the liver, uniform distribution of radioactivity within the liver, normal 1iver size, visualization of extra hepatic biliary tract and bowel activity in all cases (100%) was observed with average times 17 minutes and 29minute respectively. The GB was visualized in 92.3 %within 28 minute in average (normal time). Only one case 7.69 %disclosed non visualization of the GB which was known to have cholecystectomy. Therefore, our findings are within normal ranges documented by previous reports as follows:

Maximum extraction of radiotracer by the liver is within 5-10 minute; the CBD, GB and bowel are usually visualized between 15-30 minute, the upper limit of normal visualization of these structures is 1 hour (Weissman, *et al*., 1979 and Rosenthal L. *et al*., 1978). (Table.2) was summarized the distribution of the final scintigraphic diagnosis for 71 cases with various HB disorders in our series. In this study we can't able to estimate the sensitivity and specificity of each HB disorder because the study was a retrospective one with randomly referred cases were included and was not designed for one specific disease. However, the overall sensitivity and specificity and accuracy for various HB disorders can be calculated. The results of our work showed that this nuclear technique has, a statistically high sensitivity (95 %), and specificity (100 %) and accuracy (97 %). We can conclude that this technique is highly useful in evaluation or assessment of patients with suspected hepatic and biliary system disorders.

Abbreviations:

HB: Hepatobiliary.

CHD: Common hepatic duct.

CD: Cystic duct

CBD: Common bile duct

GB: Gall bladder.

IDA: Imino diacetic acid

mci: Milli curie.

uci: micro curie.

REFERENCES

Al- Eid MA., Lafrance ND., Wagner HN. 1988. "Radionuclide imaging in emergencies part 2", Iraqi Medical Journal, volume 36, No. 1.

Bouchier I.AD. 1986. " Gallstones " Medicine International 29 May

Brant William E., Helms Clyde A. 2007. "Fundamental of Diagnostic Radiology". 3rd Edition copy right

Carlos L.J., Kelley R.O. "Basic Histology" 6th ed. Prentice-Hall international inc. P: 316-327 , 198.

Cheruv LR., Nunn AD., Loberg MD. 1982. "Radiopharmaceutical for Hepatobiliary Imaging". Seminars in Nuclear Medicine ,Vol. XII , No.1 (January)

Chilton HM., Witcofski RL., " Nuclear pharmacy " 1986. Lea & Febiger 600 Washington Square Philadelphial, PA 19106-4198 U.S.A. (215) 922-1330.

Cooksley G.: " Acute viral Hepatitis". Medicine international 28April, 1986, p. 1160- 1164.

Col SS Anand, LT Col RK Handa, Mr Jogender Singh, Lt Col I Sinha: " Hepatobiliary Scintigraphy in diagnosis of Biliary Atresia" MJAFI, Vol. 62, ,No.1, 2006 page 20-21..

Early P.J., Sodee D.B., "Principle And Practice of Nuclear Medicine". The C.V. Mosby company , P : 156 , 1985.

Freitas JE. 1982. " Cholescintigraphy in Acute and chronic cholecystitis". Seminar in Nuclear Medicine, vol. XII , No. 1 , (January).

Gerhold JP., Klingensmith III WC., Kunicc., *et al*." 1983. Diagnosis of Biliary Atresia with Radionuclide Hepatobiliary Imaging". Radiology 146 : 99-504 , February , 1983.

Gross C.M. 1966. " Grey's Anatomy of the Human Body". 28ed.Philadelphia, Len &Febriger.

Guyton AC. 1987. "Text Book of Medical Physiology 6thed. Philadelphia W.B. Saunders Company.

Harbert J. 1984. "Text Book of Nuclear Medicine Vol. I Basic Science (2nd ed.), Philadelphia , Lea and Febriger PP. 19, 30, 40.

Harding Rains AJ., Mann CV. *et al.* 1990. "Baily and Loves short practice of surgery " 20th ed. Chapman and Hall Ltd. 11 New Fetter Lane, London.

Harvey, John, Mekusick, *et al*. 1988. "The principle and practice fMedicine " 22 ed. Prentice-Hall International inc. U.S.A.

James O. 1986. " Assessment of Jaundice". Medicine International , 28,April

Last RJ. 1984. " Anatomy Regional and Applied " 7th ed. Churchill Livingstone, PP 207.

Mark Tulchinsky, BrianW.Ciak, Dominique Delbeke, Andrew Hilson, Kelly Anne Holes-Lewis, Michael G. Stabin and Harvey A .Ziessman. 2010. " SNM practice Guideline for Hepatobiliary Scintigraphy 4.0" Journal of Nuclear Medicine Technology. Vol.38. No. 4. December

Macintyre W.J. *et al*. 1988. "Sensitivity and Resolution In Radioisotope Scanning ". In medical radioisotope scintigraphy IAEA, vol. 1, PP. 391..

Macleod J., Edwards CE., Bouchier I. 1991. "Davidson's Principles and practice of Medicine" 16thed. Churchill Livingstone , medical division of Longman group UK Ltd.

Merrick MV. 1984. "Essential Nuclear Medicine". First published 1984. Churchill Livingstone, Edinburgh London Melbourne and new York.

Mettler Fred A. JR., Guiberteau Milton J.

"Essentials of Nuclear Medicine Imaging" 5th ed 2006

Paras P. 1980. "Performance and Quality Control of Nuclear Imaging". AEA. Vol. 1, PP. 92-89.

Pouwels S., Piret L., Beckers C. 1978. "Clinical Evaluation of Tc-99m – Diethy1 IDA in Hepatobiliary Disorders". *J Nus1 Med*., 19: 783-788.

Rollo F. D. 1974. "An Index To compare the Performance of Scintigraphic Imaging System ". J. Nucl Med 15 : 757-762.

Rosenthall L. 1982. "Cholescitigraphy in the presence of Jaundice utilizing Tc-IDA " . Seminars In Nuclear Medicine , vol. XII , No. 1(January) , 1982.

Rosenthall L., Shaffer E.A., Libona R., *et al.* 1978. "Diagnosis of Hepatobiliary Disease by Tec-99m-HIDACholescintigraphy". Radiology 126: 467-474, February , 1978.

Schwartz, Shires, Spencer, 1989. "Principles of Surgery", 5th.ed. chapter 31 page 1881, McGraw-Hill Book Company.

Shepherd R. 1986. "Hepatic and biliary disorders in infancy and Childhood". Medicine International , 29 , May.

Specht NT., Russo RD., "Practical Guide to Diagnostic Imaging" First edition copy right 1998 by Mosby- Year Book, Inc.

Sutton David, "Text Book of Radiology and Imaging " Volume 2. 6th edition 1998.

Wagner H. N., "Principles of Nuclear medicine ". W.B. Saunders Company , 1969.

Weissmann HS., Frank MS. Bernstein LH, *et al*., "Rapid and accurate diagnosis of acute cholecystitis with Tc-99m HTDA cholescintigraphy". AJR 132 : 523 - 528 , April , 1979.

Weissmann HS., Badja J., Sugarman LA. , *et al* : "Spectrum of 99m-Tc-IDA cholescintigraphic pattern in Acute Cholecystitis". Radiology 138 : 167-175 , January, 1981.

Ziessman HA., " Acute cholecystitis, Biliary Obstruction and Biliary Leakage, "Semin Nucl Med33: 279-296, 2003

Ziessman HA., " Hepatobiliary Scintigraphy in 2014" J. Nucl. Med. Technol. 2014; 42: 249-2.

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