

Liver function in patients with liver diseases: A CT based study

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Abstract : Prospective study of the ability of laboratory tests and liver imaging tests to detect hepatic diagnosis was performed. 100 patients with evidence of abnormal liver function (LFT) test were tested for correlation between the laboratory tests and CT imaging results. The study was conducted at Antalia Hospital during the period extended from 2014-2017. Total Bilirubin, Direct Bilirubin, Alkaline phosphatase (ALP), Aspartate amino transferase (AST), Alanine amino transferase (ALT), Albumin, Globulin, Total protein, and prothrombin time have been evaluated and were clearly correlated with the CT imaging results.

Cholangiocarcinoma was correlated significantly with AST values at $p=0.038$. Hepato cellular carcinoma (HCC) was correlated significantly with total bilirubin and with direct bilirubin at $p=0.000$. Liver metastases increased albumin level and is correlated significantly at $p=0.030$, while the prothrombin time is increased significantly with the presence of liver cirrhosis at $p=0.007$. In the presence of Klatskin tumor the increasing of globulin was correlated significantly at $p=0.003$ and with total protein at $p=0.001$ and albumin at $p=0.030$.

Results showed that there are no significant relation between the presence of the Hemangioma, Focal Nodular Hyperplasia and simple cyst with the total bilirubin, direct bilirubin, ALP, AST, ALT, Albumin, Globulin, Total protein, and prothrombin time

Many lesions can be present and diagnosed by imaging but not affected the LFT parameters on the other hand the elevation of the laboratory tests may be caused by many different causes as they were produced from many sources. On the other hand Laboratory liver tests can help to explain the alteration of markers which reflect the liver disease including (HCC), Cholangio carcinoma, Klatskin tumor, metastases and cirrhosis. The assessment of enzyme alteration, associated with CT examination in the diagnosis of the disease is important. And a single laboratory liver test is of little value in screening for liver disease as many serious liver diseases may be associated with normal levels and abnormal levels might be found in asymptomatic healthy individuals

Keywords – liver function test, HCC, CT scan, Liver enzymes

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I. Introduction

Identification of abnormal liver biochemical tests is one of the most common inventions during health examinations. Physicians of all specialties need a working knowledge of the meaning of these abnormalities, and a general sense of when urgency for evaluation is necessary. Guideline for the evaluation of \uparrow LFT's is stated. A focused evaluation of abnormal LFT's includes four areas of importance: Categorization of severity, symptoms and duration, complete medical history and complete physical examination. The pattern of the abnormal LFT's can be divided into three categories, that become branch points in the evaluation of hepatitis: patterns predominantly reflecting hepatocellular injury (\uparrow ALT/AST), patterns predominantly reflecting cholestasis (\uparrow Alk Phos +/- \uparrow Bili), Mixed hepatocellular and cholestatic (\uparrow Both ALT/AST and Alk Phos), Increases in conjugated bilirubin can be seen in each category. \downarrow Albumin suggest severe hepatitis, cirrhosis or malnutrition, \uparrow PT suggests significant cholestasis, hepatitis or vitamin K deficiency, bilirubin in the urine reflects direct or conjugated hyperbilirubemia, and unconjugated bilirubin is bound to albumin only in urine with renal disease. [1]

Laboratory and radiologic tests have three major roles including screening, diagnosis and management.[2] Although many imaging tools have been assessed in non alcohol fatty liver disease subjects, used for quantification of liver fat but the results of these imaging tests cannot be used to differentiate between the histological subtypes of simple steatosis nor can they be used to stage the degree of fibrosis [3,4]

Noninvasive diagnostic imaging is frequently used in the evaluation of patients with hepatobiliary tract diseases [5] while imaging is often very useful, patients with liver disease can be accurately diagnosed with only a history, physical examination and biochemical liver tests in an estimated 80% of cases. [6]

The primary modalities currently used for diagnostic imaging of the liver and biliary tract are ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI)[7] While radionuclide studies, are additional useful noninvasive modalities, however they are less frequently requested for the initial investigation of abnormal laboratory test results. [5]

(US) is currently the most common method for screening asymptomatic patients with elevated liver enzymes [8]. (CT). Allows for a more quantitative assessment with measurement of liver attenuation in Hounsfield units (HUs) compared to US.[9]In (MRI) a good correlation has been reported between MRI, US, and histology in patients with non alcoholic fatty liver disease. [10]Among these modalities, MRI has been shown to most accurately detect lower levels of steatosis than those detected by US and CT.

A common indication for abdominal imaging is to assist in the evaluation of abnormal liver function test (LFT) results. [6] The liver function tests commonly include the measurement of aspartate aminotransferase, alanine aminotransferase, total and direct bilirubin and alkaline phosphatase levels. While the term liver function tests is a misnomer because abnormal values for most of these tests actually reflect hepatocellular damage or dysfunction, not synthetic or metabolic function, [11] it is widely used in the clinical field.

Few data are available regarding the findings in imaging modalities done for patients with abnormal LFT results. [2]While choosing radiologic tests of a specific pathologic entity or a certain clinical presentation have been developed [11] less information is available regarding the evaluation of patients with abnormal LFT results as the primary indication for imaging requests.

Also, it has often been difficult to obtain detailed and accurate information about the indications selected by physicians who are ordering imaging tests. However, at our departments, there is no clear guidance for selection of specific imaging test regarding specific abnormal liver function test.

We used data from those patients to perform a study to assess the yield of abdominal imaging ordered for the indication of abnormal LFT results. Additional goals included reviewing literature for assessment the clinical usefulness of abdominal imaging for abnormal LFT results, categorizing the diagnoses and assessing the correlation between the liver function test results and interpreting abdominal imaging studies.

II. Materials and Methods

Sample:

The sample included 100 patients in both genders with abnormal liver function test; the sample included 59(59%) females and 41(41%) males .Their ages ranged between 25->65years. Ages ranged from 25-34 were (12), 35-44 were (14), 45-54 were (15), 55-64 were (26), and >65 constituting (33) patients.

Exam preparation:

Patients fast for 2 to 6 hours before the examination. Fasting results in an empty proximal GIT, facilitating its evaluation an oral contrast agent is administered to distend the GIT and demonstrate the intestinal lumen. 1500 ml of oral contrast agent is administered 30 to 120 minutes before the exam. Protocol for oral contrast agent administration is: 450 ml given 90 to 120 minutes before the exam for opacification of the distal intestines.300 to 450 ml given 30 minutes before the exam for opacification of the proximal intestines. An additional volume of 150 to 250 ml given just before scanning for opacification of the stomach and duodenum.

Patient position and instructions:

The patient is positioned supine with the arms placed overhead. The patients are instructed to suspend respiration (hold the breath) during scan acquisition.

Scan parameters:

Detector configuration and section width: 64-detector row .collimation is 0.5 to 0.625 mm, with images reconstructed at widths based on the anatomy or pathology in question. Section widths of 3 to 5 mm are used. Section widths of 1 to 2 mm or less are preferable during multi-phasic studies and in anticipation of 3D and MPR. The detector configuration, table speed, and pitch were optimized according to the clinical indications of the exam. The mA and KVP settings were based on patient size, yielding to the noise soft tissue of the abdomen: WL: 40, WW: 350. The administration of an iodinated IV contrast agent improves the quality of abdominal and pelvic CT imaging by: Enhancing, the CT density of abdominal organ parenchyma, increasing the detect-ability of lesions from normal structures.opacifying vascular structures, providing assessment of organ perfusion and function. Non-contrast, pre and post-contrast imaging were used for: Characterizing the enhancement pattern of a lesion, evaluation of calcifications within organ parenchyma. Assessment of unenhanced parenchymal attenuation values. Contrast agent dose ranges from approximately 50 to 150 ml. The total dose depends on the patient's condition and the clinical indication for the study. Injection rates vary between 2 and 5 ml/sec. rate selected depends on the enhancement phase(s) to be acquired and the capacity of the venous access. There are three distinct phases of hepatic contrast enhancement used:

Arterial phase: the period of peak arterial enhancement typically occurs at 25 to 35 seconds after the initiation of contrast agent administration. During this phase, hyper-vascular tumor or tumors supplied by the hepatic artery undergo maximal enhancement. The lesions are made conspicuous by the relatively unenhanced hepatic parenchyma surrounding them.

Portal venous phase: the period of peak hepatic parenchymal enhancement during which contrast material redistributes from the blood into the extra-vascular spaces. Typically occurring at 60 to 70 seconds after the initiation of contrast agent administration, this is the phase during which hypo-vascular lesions are most conspicuous owing to their density difference from the enhancing hepatic parenchyma. Equilibrium phase: usually occurs at 2 to 3 minutes after the initiation of contrast agent administration. During this phase, hepatic parenchymal enhancement dissipates and there is minimal difference in contrast enhancement between the intra-vascular and extra-vascular spaces.

III. Results

Table (1) shows the correlation between the liver CT findings with the laboratory result (liver Function tests)

	Total Bilirubin	Direct Bilirubin	ALP	AST	ALT	Albumin	Globulin	Total protein	Prothromb in time
Abscess	0.511	0.511	0.638	0.626	0.471	0.471	0.548	0.814	0.752
Fatty Liver	0.250	0.250	0.410	0.394	0.207	0.207	0.473	0.532	0.135
Cholangio carcinoma	0.125	0.125	0.638	0.038	0.161	0.161	0.267	0.814	0.752
Right Lobe Hemangioma	0.198	0.198	0.591	0.164	0.319	0.076	0.369	0.385	0.354
Left Lobe Hemangioma	0.133	0.133	0.189	0.017	0.771	0.208	0.619	0.493	0.378
Focal Nodular Hyperplasia	0.350	0.350	0.503	0.489	0.305	0.629	0.528	0.575	0.653
Right Liver Lobe Simple Cyst	0.594	0.594	0.730	0.527	0.129	0.434	0.619	0.650	0.817
Left Liver Lobe Simple Cyst	0.467	0.467	0.118	0.444	0.091	0.325	0.961	0.663	0.907
Klatskin Tumor	0.250	0.250	0.410	0.394	0.207	0.207	0.003	0.001	0.580
Right Liver Lobe HCC	0.004	0.000	0.004	0.876	0.902	0.493	0.318	0.192	0.662
Left Liver Lobe HCC	0.000	0.025	0.042	0.876	0.212	0.661	0.090	0.789	0.622
Right Lobe Mets	0.834	0.834	0.987	0.375	0.861	0.395	0.619	0.391	0.259
Left Lobe Mets	0.195	0.195	0.141	0.128	0.434	0.030	0.619	0.025	0.007
Cirrhosis	0.140	0.140	0.607	0.294	0.302	0.947	0.619	0.912	0.030
Other Finding	0.148	0.148	0.888	0.060	0.335	0.555	0.325	0.780	0.341

IV. Discussion and Conclusion

Total Bilirubin, Direct Bilirubin, ALP, AST, ALT, Albumin, Globulin, Total protein, and prothrombin time have been evaluated and were clearly correlated with the CT imaging results.

Cholangiocarcinoma was correlated significantly with AST values at $p= 0.038$ this was consigned with the literature that discuss the causes of elevation of AST.

AST is found in highest concentration in heart compared with other tissues of the body such as liver, skeletal muscle and kidney [12] Normal serum AST is 0 to 35U/L [13] Elevated AST seen in extensive tissue necrosis during myocardial infarction and also in chronic liver diseases.[14] This was consigned with our results that the AST is increased in the presence of Cholangiocarcinoma . Literature also has mentioned that the ratio of mitochondrial AST to total AST activity has diagnostic importance in identifying the liver cell necrotic type condition and alcoholic hepatitis [15]. AST elevations often predominate in patients with cirrhosis and even in liver diseases that typically have an increased ALT [16]. But in our study the ALT dose not significantly affected with the presence of choleangiocarcinoma.

Right liver lobe HCC was correlated significantly with total Bilirubin at $p= 0.00$, and with direct Bilirubin at $p=0.000$ and ALP at $p= 0.004$.As well Left liver lobe HCC was correlated significantly with total Bilirubin at $p=0.000$, direct Bilirubin at $p= 0.025$ and ALP at $p= 0.042$ Literature has stated that ALP is present in mucosal epithelia of small intestine, proximal convoluted tubule of kidney, bone, liver and placenta. The serum ALP activity is mainly from the liver with 50% contributed by bone [12]. Normal serum ALP is 41to 133U/L [13]. In acute viral hepatitis, ALP usually remains normal or moderately increased. Tumors secrete ALP into plasma and there are tumor specific isoenzymes [17].this was consigned with our result in both presence of HCC in right and left lobes.In one study done by Erdem Okay2014 [18] showed that in patients with HCC, AST is increased and ALT is normal. While in another study done by Yoshihiko Yano2003 [19] all of total Bilirubin AST,ALT ,ALP ,GGT are raised while there is reduction in albumin values.

Hepatic and bony metastasis can also cause elevated levels of ALP. While mildly elevated levels of ALP may be seen in cirrhosis, and other diseases [17]. However our study showed that in Left lobe metastases

the increased Albumin level is correlated significantly at $p=0.030$, while the prothrombin time is increased significantly with the presence of liver cirrhosis at $p=0.007$

In the presence of Klatskin Tumor the increasing of Globulin was correlated significantly at $p=0.003$ and with total protein at $p=0.001$ and albumin at $p=0.030$

Results showed that there are no significant relation between the presence of the Hemangioma, Focal Nodular Hyperplasia and Simple Cyst with the Total Bilirubin, Direct Bilirubin, ALP, AST, ALT, Albumin, Globulin, total protein, and prothrombin time that means many lesions can be present and diagnosed by imaging but not affected the LFT parameters, on the other hand The elevation of the laboratory tests may be caused by many different causes as they were produced from many sources. On the other hand laboratory liver tests can help to explain the alteration of markers which reflect the liver disease including HCC, Cholangio

Carcinoma, Klatskin Tumor, Mets and cirrhosis. But a single laboratory liver test is of little value in screening for liver disease as many serious liver diseases may be associated with normal levels and abnormal levels might be found in asymptomatic healthy individuals. The pattern of enzyme abnormality, interpreted in the context of the patient's symptoms and imaging results can aid in directing the succeeding diagnosis.

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