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Linear, volume and hepatic texture measurements in correlation with biochemical markers -A Computed tomography based study

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Abstract: *The aims of this study were to evaluate the linear, volume and texture (CT Hounsfield) of the liver measured on CT scan and to test their reflection in interpretation of the pattern of liver enzyme abnormality.*
*The study was conducted at Antalia Hospital during the period extended from 2014-2017. Total 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 Linear, volume and hepatic texture measurements The sample included 100 patients in both genders with tested liver function; the sample included 59(59%) females and 41(41%) males .Their ages ranged between 25->65years. The linear hepatic measurements were evaluated including :Midhepatic point craniocaudad (MHP CC),Maximum CC to liver tip (Max CC),Maximum transverse dimension ,MHP anteroposterior (AP) dimension of the liver. Hepatic volume measurements were performed depended on linear hepatic measurements. : (MHP AP * Max LL * Max CC * 0.31) and the texture was evaluated for both right and left hepatic lobes and was measured in (Hounsfield) .The current study showed no significant relation between the changing in hepatic measurements done by CT and the biochemical markers values. The results showed that there is no significant relationship between the liver volume and the liver function test results except with the serum albumin at p value= 0.030 and have mentioned that liver volume does not necessarily reflect liver function. The evaluation of the liver density /texture by measuring the CT Hounsfield was obtained showing only significant relation with globulin results at p=0.047and total protein at p=0.017.*
From the presented study; we found that the knowledge of the radiological presentation is critical for interpreting Liver enzymes abnormalities correctly instead of measuring the liver alone linearly at different points or evaluating its volume and texture considering the CT diagnostic criteria as useful trend giving good value of diagnostic results.
Keywords *- Liver Function test, CT Hounsfield, liver measurements*

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I. Introduction

The liver is the largest organ in the human body and is found in the intra-abdominal cavity. It weighs around 1500g .Its function is to filter and store blood, metabolize carbohydrates, proteins, hormones and strange chemicals; to form bile, store vitamins and iron; and to produce clotting factors.[1-5]

The liver has two anatomical divisions, the right lobe and left lobe, separated by an imaginary line that runs from the gallbladder fossa into the inferior vena cava.[1,3] Clinically percussion is performed with the aim of determining the liver upper and lower boarder, estimating liver size [6]. The normal adult liver spans 10 to 12 cm for men and 8 to 10 cm for women [7]. Generally, it can vary between 6 and 12 cm in all subjects when percussion is performed in the midclavicular line. [8]

Estimation of liver measurements can be used as directory to observe many liver disease and response to treatment [9,10] .Midclavicular (MCL), craniocaudad (CC), or midhepatic (MHP) CC measurements have been used in ultrasound (US) to estimate liver size [11,12]. Ultrasonography is the first imaging method to assess hepatic diseases, which has a number of key advantages [13,14]as well the liver volume can be measured by various techniques including ultrasonography , radiography, scintigraphy, computed tomography (CT) and magnetic resonance imaging (MRI) [13,14]

Laboratory liver tests are tests valuable in the evaluation and treatment of patients with hepatic dysfunction. The liver carries out metabolism of carbohydrate, protein and fats. Some of the enzymes and the end products of the metabolic pathway which are very sensitive for the abnormality occurred may be considered as biochemical marker of liver dysfunction. These biochemical markers including serum bilirubin, alanine amino transferase, aspartate amino transferase, , alkaline phosphatase, gamma glutamyl transferase, 5' nucleotidase,ceruloplasmin, α-fetoprotein and others. An alteration of biochemical markers of liver damage in patients can challenge the clinicians during the diagnosis of disease related to liver directly or with some other organs. [15]

Laboratory liver tests aid to clarify the alteration of markers which reflect the liver disease. The evaluation of enzyme abnormalities assists in the diagnosis of the disease. But a single laboratory liver test is of small 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.[15]

In the current study the question to be answered : can the simple linear , volume and texture of the liver measured on CT scan including, Maximum craniocaudal (Max CC)to liver tip , Maximum transverse (Max LL) and MHP anteroposterior (AP) dimensions and the Mid hepatic point craniocaudal (MHP CC) , Volume , right and left liver lobe texture(CT Hounsfield) reflect and interpret the pattern of enzyme abnormality, and aid in directing the succeeding diagnosis.

II. Materials And Methods

The study was conducted at Antalia Hospital during the period extended from 2014-2017. Total 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 liver linear measurements, volume and CT Hounsfield. The sample included 100 patients in both genders with tested liver function; 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. Mean age was 54.98 years ±15.07, maximum age was 85.00 years and minimum age was 25.00 years old.

Patient position and instructions:

The patient is positioned supine. The patients are instructed to hold the breath during scan acquisition. Patients were asked to fast for 2 to 6 hours before the examination .1500 ml of oral contrast agent is administered 30 to 120 minutes before the exam. An additional volume of 150 to 250 ml was given before scanning for opacification of the stomach and duodenum.

Scan parameters:

Detector configuration and section width: 64-detector row .collimation is 0.5 to 0.625 mm; Section widths of 3 to 5 mm are used. WL: 40, WW: 350. Iv Contrast agent dose ranges from approximately 50 to 150 ml. Injection rates were between 2 and 5 ml/sec.

Linear hepatic measurements

The following measurements of the liver were performed:-

1- Midhepatic point craniocaudad (MHP CC)
2- Maximum CC to liver tip (Max CC)
3- Maximum transverse dimension
4- MHP anteroposterior (AP) dimension of the liver.

The plane of the horizontal component of the main portal vein was identified and used as a reference point for measurements. The MHP was defined as half way between the mid vertebra and right lateral margin of the liver at the level of main portal vein on a transverse section (Fig. 1). MHP CC was defined as a perpendicular measurement on the coronal images from the hepatic dome to the inferior margin of the liver passing through the midhepatic point (Fig. 2). The Max CC was defined as the greatest obtainable craniocaudad dimension of the liver from the hepatic dome to the liver tip on coronal reconstructed images (Fig. 2). Maximum transverse dimension was the maximum measurement from the right to left margins of the liver at the level of the portal vein (Fig. 1). MHP AP measurement was taken at the level of the midhepatic point from anterior to posterior margin of the liver (Fig. 1).

Hepatic volume measurement

Hepatic volume measurements were performed depended on linear hepatic measurements.

Volume = ***(MHP AP * Max LL * Max CC * 0.31)*** in ml as proposed by (Verma et al .2010)[16]

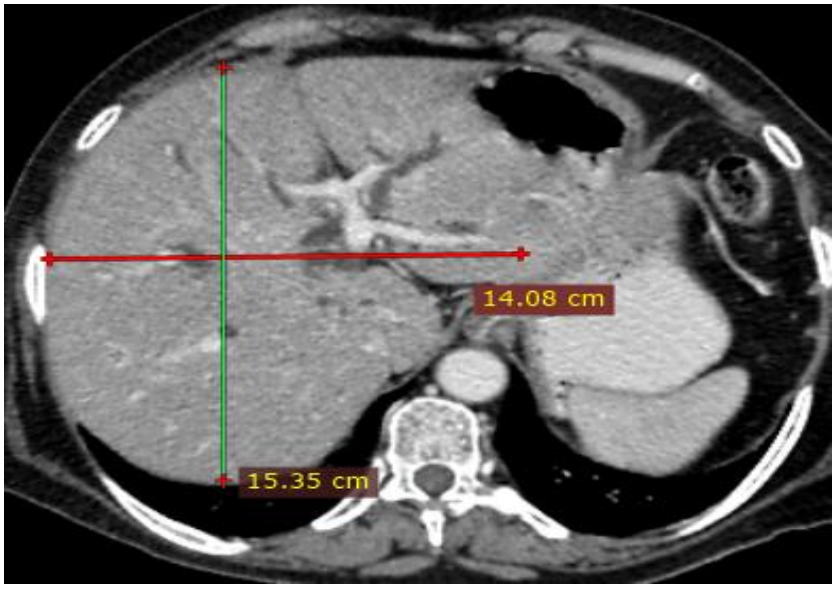

Fig 1 shows the Linear dimensions of the liver: Maximum transverse dimension (the maximum measurement from the right to left margins of the liver . Mid hepatic point AP (MHP AP) measurement was taken at the level of the midhepatic point from anterior to posterior margin of the liver

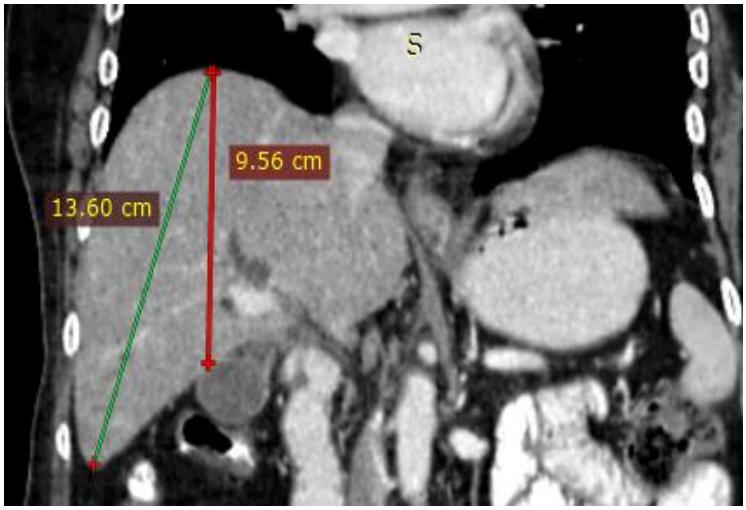

Fig 2: Linear dimensions of the liver: MHP CC was defined as a perpendicular measurement on the coronal images from the hepatic dome to the inferior margin of the liver passing through the midhepatic point. The Max CC was defined as the greatest obtainable craniocaudad dimension of the liver from the hepatic dome to the liver tip on coronal reconstructed images.

III. Results

Table 1 shows the liver measurements and CT Hounsfield

Descriptive Statistics			
Hepatic measured variables /mm	**Min**	**Max**	**Mean± STDV**
Maximum craniocaudal (Max CC)	14.80	269.50	169.15±49.46
Midhepatic point craniocaudal (MHP CC)	13.00	321.70	129.27±50.40
Maximum transverse (Max LL)	17.20	314.00	181.34±52.95
Midhepatic point anteroposterior (MHP AP)	13.70	215.70	155.98±37.29
Volume / ml	428.00	5076.00	1802.38±10.31
LT liver lobe texture (Hounsfield)	0.06	58.00	36.70±11.46
RT liver lobe texture (Hounsfield)	0.00	58.00	36.47±10.58

Table 2 shows liver findings Diagnosed by computerized Tomography(CT)

liver findings Diagnosed by CT
Abscess
Fatty Liver
Cholangiocarcinoma
Right Lobe Hemangioma
Left Lobe Hemangioma
Focal Nodular Hyperplasia
Right Liver Lobe Simple Cyst
Left Liver Lobe Simple Cyst
Klatskin Tumor
Right Liver Lobe Hepatocelluler carcinoma(HCC)
Left Liver Lobe Hepatocelluler carcinoma(HCC)
Right Lobe Metastases
Left Lobe Metastases
Cirrhosis
Other Finding

Table 3 show the liver measurements and CT Hounsfield correlated with ALP,AST,ALT Values

		ALP U/L		AST U/L		ALT U/ L	
		Mean	STDV	Mean	STDV	Mean	STDV
Maximum craniocaudal (Max CC) in mm	Normal	155.77	69.26	158.86	69.66	166.46	60.69
	High	172.09	43.99	171.56	43.64	170.53	43.017
	Total	169.15	49.46	169.15	49.46	169.15	49.46
	P-value	0.207		0.316		0.699	
Mid hepatic point craniocaudal (MHP CC) in mm	Normal	130.28	62.76	125.88	60.34	127.53	52.67
	High	129.05	47.72	130.07	48.17	130.17	49.58
	Total	129.27	50.40	129.2760	50.40	129.27	50.40
	P-value	0.926		0.746		0.806	
Maximum transverse (Max LL) in mm	Normal	180.74	60.80	190.47	59.98	180.27	65.60
	High	181.47	51.49	179.20	51.34	181.90	45.66
	Total	181.34	52.95	181.34	52.95	181.34	52.95
	P-value	0.958		0.407		0.885	
Mid hepatic point anteroposterior in mm	Normal	149.32	37.04	154.80	39.98	152.32	46.96
	High	157.44	37.41	156.26	36.89	157.87	31.42
	Total	155.98	37.29	155.98	37.29	155.98	37.29
	P-value	0.406		0.879		0.484	
Volume /ml	Normal	1695.44	1046.35	1878.94	1115.33	1982.72	1159.73
	High	1825.86	1033.20	1784.42	1017.36	1709.48	954.91
	Total	1802.38	1031.48	1802.38	1031.48	1802.38	1031.48
	P-value	0.630		0.721		0.211	
LT liver lobe texture	Normal	40.82	8.87	38.12	8.44	38.17	8.70
	High	35.80	11.80	36.37	12.07	35.95	12.64
	Total	36.70	11.46	36.70	11.46	36.70	11.46
	P-value	0.092		0.551		0.362	
RT liver lobe texture	Normal	35.16	8.31	37.68	7.27	37.05	8.91
	High	36.72	11.04	36.19	11.23	36.17	11.39
	Total	36.47	10.58	36.47	10.58	36.47	10.58
	P-value	0.565		0.582		0.695	

Normal serum ALT is 7-56 U/ L . Normal serum AST is 0 to 35 U/L .Normal serum ALP is 41 to 133 U/L[17]

Table 4 : shows the liver measurements and CT Hounsfield correlated with Total bilibrobin and Prothorombin time values

		Total Serum bilibrubin* µmol/L		Prothorombin time(PT)** Second	
		Mean	STDV	Mean	STDV
Maximum craniocaudal (Max CC) in mm	Normal	167.24	61.49	167.81	49.73
	High	169.97	43.80	182.74	47.20
	Total	169.15	49.46	169.15	49.46
	P-value	0.801		0.390	
Mid hepatic point craniocaudal (MHP CC) in mm	Normal	132.94	54.34	128.12	50.48
	High	127.70	48.94	140.86	50.95
	Total	129.27	50.40	129.27	50.40
	P-value	0.636		0.472	
Maximum transverse (Max LL) in mm	Normal	183.66	61.82	181.80	51.20
	High	180.35	49.13	176.71	72.01
	Total	181.34	52.95	181.34	52.95
	P-value	0.776		0.785	
Midhepatic point anteroposteri (MHP AP) in mm	Normal	156.76	42.84	156.29	35.75
	High	155.65	34.98	152.90	53.05
	Total	155.98	37.29	155.98	37.29
	P-value	0.892		0.796	
Volume /ml	Normal	2022.26	1220.16	1764.22	1010.75
	High	1708.15	933.16	2188.22	1220.33
	Total	1802.38	10.31	1802.38	10.31
	P-value	0.164		0.241	
LT liver lobe texture	Normal	37.77	10.63	37.22	11.35
	High	36.2496	11.83	31.48	11.91
	Total	36.7083	11.46	36.70	11.46
	P-value	0.544		0.153	
RT liver lobe texture	Normal	34.2567	10.25	36.74	10.76
	High	37.4257	10.65093	33.72	8.58
	Total	36.4750	10.58292	36.47	10.58
	P-value	0.171		0.416	

Normal serum total bilirubin varies from 2 to 21µmol/L. **Normal Prothrombin time 12-13 second
Volume = (MHP AP * Max LL * Max CC * 0.31) in ml

Table 5 : shows the liver measurements and CT Hounsfield correlated with Albumin, Globulin, and Total Protein values

	Values	Serum Albumin		Values	Globulin		Values	Total protein	
		Mean	STDV		Mean	STDV		Mean	STDV
Maximum craniocaudal (Max CC) in mm	N	162.71	52.89	N	182.43	47.32	N	165.23	52.32
	L	181.65	39.80	H	177.80	14.57	H	161.58	38.28
	p value =0.069			*p value*=0.833			L	185.28	40.81
							p value =0.241		
Midhepatic point craniocaudal (MHP CC) in mm	N	123.95	47.33	N	130.38	50.80	N	126.31	50.77
	L	139.59	55.15	H	132.36	35.47	H	118.65	38.34
	p value=0.142			*p value* =0.936			L	143.32	52.47
							p value 0.331		
Maximum transverse (Max LL) in mm	N	177.72	48.00	N	169.96	66.10	N	178.88	52.08
	L	188.37	61.61	H	178.60	37.45	H	174.46	37.18
	p value 0.343			*p value* 0.783			L	192.27	61.13
							p value 0.558		
Midhepatic point anteroposterior in mm	N	153.90	35.16	N	153.35	50.50	N	152.70	37.97
	L	160.01	41.36	H	155.22	7.10	H	160.68	16.16
	p value =0.441			*p value*= 0.936			L	165.29	40.09
							p value =0.375		
Volume/ ml	N	1642.02	891.65	N	1945.00	938.36	N	1724.37	990.02
	L	2113.67	1214.33	H	1523.80	344.85	H	1436.00	512.50
	p value= 0.030			*p value*= 0.339			L	2205.71	1223.92
							p value =0.098		
LT liver lobe texture	N	38.16	11.70	N	36.08	11.46	N	36.85	11.49
	L	33.88	10.56	H	47.52	7.85	H	46.06	6.32
	p value 0.076			*p value* =0.047			L	32.65	11.02
							p value =0.017		
RT liver lobe texture	N	37.52	10.41	N	33.12	12.65	N	37.09	10.86
	L	34.43	10.77	H	34.40	11.43	H	37.85	9.9
	p value =0.169			*p value* =0.839			L	33.84	9.8
							p value =0.436		

Serum Albumin normal values are 3.4to 5.4 gram per deciliter (gm/dL) ,Serum Globulin normal value = 2.0to3.5 gram per deciliter (gm/dL). Total blood protein is between 6 and 8.3 gram per deciliter (gm/dL)

IV. Discussion And Conclusion

Standard Liver Function Tests (LFT's) consist of the enzymes Alanine Transaminase (ALT), Aspartate Transaminase (AST), Alkaline Phosphatase (ALP) and Gamma Glutamyl Transferase (GGT), together with bilirubin, albumin, total protein and globulin; when considered together, these analyses open a diagnostic window into multiple organ systems. [18]

The current study raised an important question: can the simple linear , measured on CT scan including, Maximum craniocaudal (Max CC)to liver tip , Maximum transverse (Max LL) and MHP anteroposterior (AP) dimensions and the Mid hepatic point craniocaudal (MHP CC) , Volume , right and left liver lobe texture(CT Hounsfield) reflect and interpret the pattern of enzyme abnormality, and aid in directing the succeeding diagnosis?.All measurements were taken by CT scan .The liver measurements (linear and volume) in addition to CT Hounsfield were presented in table [1] as well the diagnostic results found by CT scan have been presented in table [2]

The current study showed no significant relation between the changing in hepatic measurements done by CT and the ALT, AST, and the ALP values. It was appreciated that the measurement of liver enzymes is widespread and frequent in primary care and asymptomatic patients may have mild elevations in alanine transaminase (ALT) and aspartate transaminase (AST) levels. The National Health and Nutrition Examination Survey found elevated liver transaminase levels in up to 8.9 percent of the survey population.[19,20]Although there are several published guidelines for the workup of asymptomatic transaminase level elevations[21-23]evidence from large prospective studies is sparse. Therefore understanding the basic disease processes that cause the elevation of liver enzymes (ALT,ALP, AST) levels may help guide the patient further diagnostic testing.

The description of changing the values between normal to high in our study is that the hepatocellular damage releases ALT and AST into the bloodstream. ALT is found primarily in the liver; AST is also found in skeletal muscles and erythrocytes. Therefore, elevations in ALT levels generally are more specific for hepatic injury. At times, those enzymes values can suggest certain disease patterns including alcoholic liver disease, or

nonalcoholic fatty liver disease or Wilson disease or even asymptomatic elevation of liver transaminase levels can be categorized into common hepatic, less common hepatic and extra hepatic causes [21-23]. As a result; hepatic measurements done does not reflect the changes in the enzymes values, therefore those linear or volume measurements should not be considered to predict the changes detected in the enzymes as presented in tables [3,4]

For that reasons studies suggested a complete blood count with platelet count, testing of prothrombin time, and measurement of albumin to be considered if there are concerns about the synthetic function of the liver. A more advance refine may proceed if there is evidence of decreased liver function.[24] This is what have been evaluated in this current study and the results of the tested values also showed no significant relation between those values prothorombin time with the linear or volume measurements done for the liver as presented in tables [4]

To better recognize the basis of various patterns, therefore each LFT component needs to be respected. The hepatocytes are rich in ALT and AST, with ALT predominant in the cytoplasm and AST mainly intramitochondrial; the typical hepatitic picture thus comprises ALT elevation, accompanied by usually lesser AST. ALP are mainly located in the bile ducts; biliary obstruction induces increased levels of ALP .Predominant elevation of ALP are thus termed the cholestatic pattern which may be due to intrahepatic obstruction where the bilirubin may be normal or raised, or less commonly extrahepatic obstruction where the bilirubin is elevated. Bilirubin, derived from the breakdown of red cell haemoglobin, is conjugated by the hepatocyte and excreted via the bile ducts into the bile. Albumin, with a biological half-life of about 3 weeks, is synthesized exclusively by the liver and levels are thus a measure of long term hepatic health. Albumin may, however, be normal early in severe acute hepatitis due to its long half-life, and only falls late in chronic liver damage due to the large hepatic functional reserve. The liver also synthesizes most other serum proteins or globulins and thus has a major effect on the serum total protein level this was mentioned clearly by Robert C. 2011[24] and justified well our results as our sample were affected with different liver findings as presented in table[2]

Liver mean volume was found to be 1802.38±10.31ml ranged from 428.00-5076.00ml which considered greater to what was mentioned in the literature. A recent study reported hepatic volumes (mean 1186 cm^3, range; 639.3-2359.4 cm^3) similar to another study [16] the mean was 1106 cm^3, range; 533-2417 cm^3 of normal healthy livers [25]. Our justification may be due that a number of cases were found to have tumors that may have a role of changing the liver measurements. The results of our study showed that there is no significant relationship between the liver volume and the LFT results except with the Serum Albumin as noticed in table [5] .However the CT volumetric measurement is currently the standard method to determine whether a patient can safely undergo liver treatment and surgery or not . [26,27,28] On the other hand studies have mentioned that liver volume does not necessarily reflect liver function, especially in patients with a compromised liver. [29,30]Therefore, it is important to reliably assess hepatic function before liver surgery in addition to CT volumetry.

The evaluation of the liver density by measuring the CT Hounsfield was obtained showing only significant relation with globulin results p=0.047 and with total protein at p=0.017 as presented in table[5]

From the results of this study, we found that interpreting LFTs would be of multifaceted because the liver is not the only source of the enzymes, in particular AST also found in muscle, red cells and etc. and ALP also bone, placenta, tumors are found elsewhere; Albumin, globulins and total protein levels may also be affected by non-hepatic pathology eg. nephrosis as may bilirubin eg haemolysis ,as well a single cause may result in multiple different patterns including medication effects. In the current study we find it helpful, on inspecting a set of LFTs to first pose the simple questions: Is this pattern likely to be due to liver pathology or not? for that point we find the answer when the CT images were taken and were diagnosed pre and post contrast showing the different diagnosis results including Abscess, Fatty Liver Cholangiocarcinoma ,Hemangioma ,Focal Nodular Hyperplasia ,simple cyst, HCC, Mets ,Klatskin Tumor and Cirrhosis as presented in table[2] showing the involved organs and enhanced characteristics of the lesions giving excellent feature for diagnostic imaging while the sectional study took place . However the linear measurements did not reflect the laboratory pattern changes.

From the presented study; we found that the knowledge of the radiological presentation is critical for interpreting LFT abnormalities correctly instead of measuring the liver alone linearly at different points or evaluating its volume and texture considering the CT diagnostic criteria as useful trend giving good value of diagnostic results.

We have categorized the laboratory patterns seen and have tried to integrate some basic diagnostic hints as measuring the liver linearly in addition to its volume trying to cast some light in a few dark corners and concentrated on the questions regarding their relationship seen in daily clinical practice

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