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The Assessment of Liver Disease Utilizing a Panel of Liver Function Tests

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ABSTRACT

Liver is a vital organ in the body that perform very important functions to keephealth hemostasis. Liver function tests are a group of tests that determine the liver health in physiological and pathological conditions. The main objectives of the present study were to assess liver function using a panel of liver function tests among a sample of liver patients and to compare their levels with a sample of subjects who had no liver disease. To achieve the study objectives, we analyzed a dataset posted on Kaggle. The dataset described Indian liver patients and included 583 subjects among which 414 patients with liver disease and 167 subjects without liver disease. The results showed that demographic variables including age and gender were predictors of liver disease. On the other hand, liver function tests including bilirubin, ALT, AST, albumin, albumin globulin ratio, alkaline phosphatase were significantly associated with liver disease. The level of total proteins was not significantly associated with liver disease. Taken together, liver function tests can be used to assess liver disease. The interpretation of total proteins and AST should be considered with cautious.

KEYWORDS: Liver disease, liver function test, alkaline phosphatase, ALT, AST

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INTRODUCTION

The liver is responsible for multiple tasks, including primary detoxification of different metabolites, protein synthesis, and theproduction of digestive enzymes. It is placed in the right upper quadrant of the body, below the diaphragm. The liver is also involved in metabolism, red blood cell (RBC) control, and glucose synthesis and storage (1).

There may be no indications or symptoms of liver disease until complications such as liver failure or portal hypertension emerge. The tests of liver function—bilirubin, albumin, international normalized ratio (INR), and platelet count—may be abnormal at this late, typically pre-terminal stage (2). Liver enzymes are frequently elevated in necro-inflammatory hepatic diseases (3), whereas liver enzymes may be normal or elevated in apoptotic diseases, such as fatty liver disease (alcohol and non-alcoholrelated), but the degree of abnormality is unrelated to the stage of progression from simple fatty liver to progressive fibrosis to cirrhosis (4). Since the 1950s, when the current liver blood tests were created, they have been the gold standard for detecting liver illness, resulting in many people with liver disease being undiagnosed until they have acquired substantial liver fibrosis (4).

Liver blood or function tests (LFTs), which are thought to be inexpensive, are being evaluated increasingly frequently in both primary10 and secondary care to rule out liver illness, to monitor potential liver side effects of medications like statins, and to investigate the generally unwell patient. These tests frequently yield an aberrant result with no evident clinical significance. However, they are frequently sought in response to non-specific symptoms withminimal potential link to the possibility of liver disease, or blood tests are performedfor unrelated purposes such as chronic illness monitoring.

Alanine transaminase (ALT) and aspartate transaminase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), serum bilirubin, prothrombin time (PT), the international normalized ratio (INR), and albumin are typically discussed when evaluating LFTs. These tests can assist identify the location of hepatic damage, and the pattern of elevation can aid in the organization of a differential diagnosis. The term "liver function tests" is misleading

because many of the tests do not assess the liver's function but rather identify the source of the damage. ALT and AST levels are out of proportion to ALP and bilirubin levels. Hepatocellular disease is defined by elevated ALT and AST levels that are out of proportion to ALP and bilirubin. A cholestatic pattern would be indicated by an increase in ALP and bilirubin in proportionto ALT and AST. The ability of the liver to manufacture albumin and vitamin K- dependent clotting factors can be used to assess its real function (5 -7).

Bilirubin is mostly a by-product of the reticuloendothelial system's breakdown of the hematological component of hemoglobin (8). It can be found in two different forms: unconjugated and conjugated. Bilirubin is transported in its insoluble unconjugated form to the liver, where it is transformed to soluble conjugated bilirubin and eliminated. Hemolysis or defective conjugation are the most common causes of unconjugated hyperbilirubinemia, whereas parenchymal liver disease or biliary blockage are the most common causes of conjugated hyperbilirubinemia. Total bilirubin, which includes both unconjugated and conjugated fractions, is commonly reported by most laboratories. As a result, increases in either percentage will result in an increase in the measured bilirubin concentration. Gilbert's syndrome, a hereditary metabolic condition that results in defective conjugation due to diminished activity of the enzyme glucanosyltransferase, is the most prevalent cause of an isolated high bilirubin levels (9).

Albumin is a protein produced only in the liver that has a variety of biological functions, including maintaining oncotic pressure, binding of other substances (suchas fatty acids, bilirubin, thyroid hormone, and medicines), lipid metabolism, and antioxidant characteristics. The serum albumin content is frequently used as a metric of the liver's synthetic function because albumin is solely produced by the liver. However, misinterpreting albumin concentrations as a measure of the severity of liver disease is not always justified. Invarious clinical circumstances, such as sepsis, systemic inflammatory illnesses, nephrotic syndrome, malabsorption, and gastrointestinal protein loss, albumin concentrations are lowered (2).

Alkaline phosphatase (ALP) is mostly produced in the liver (by the biliary epithelium), although it is also abundant in bone and found in smaller amounts in the intestines, kidneys, and white blood cells.

Children's levels are higher due to bone growth, and pregnant women's levels are higher due to placental production. Pathologically elevated levels are most common in bone disease (such as metastatic bone disease and bone fractures) and cholestatic liver disease (such as primary biliary cholangitis, primary sclerosingcholangitis, common bile duct obstruction, intrahepatic duct obstruction (metastases), and drug-induced cholestasis). Furthermore, cholestasis (elevated ALP levels and/or bilirubin) might be caused by hepatic congestion caused by right-sided heart failure. When ALP is increased in isolation, - glutamyl transferase can be used to determine whether the ALP is hepatic or non-hepatic (10). While there is no data on the most prevalent causes of an isolated elevated ALP in an asymptomatic population, vitamin D deficiency or a normal increase found in children due to rapid growth is the most likely reason. Paget's disease and bone metastases are two further reasons. If there is any ambiguity, electrophoresis to separate the ALPisoenzymes can be used to distinguish between hepatic and non-hepatic causes of elevated ALP.

Hepatocytes produce AST and ALT enzymes, which are released into the bloodstream in reaction to hepatocyte injury or death (hepatitis). The most prevalentanomaly found on liver blood test profiles is elevations in either of these enzymes. Although both enzymes are found in a variety of tissues, ALT is thought to be more liver-specific because it is found in low concentrations in non-hepatic tissue and non-liver-related increases are rare.

However, because AST is plentiful in skeletal, cardiac, and smooth muscle, it may be increased in myocardial infarction or myositis patients. Although ALT is a more specific sign of liver illness, the concentration of AST in situations including alcohol-related liver disease and some types of autoimmune hepatitis may be a more sensitive predictor of liver injury (AIH) (11, 12).

A total protein is a biochemical test for determining the total amount of protein in serum (13). sometimes known as total protein (13). Albumin and globulin are two proteins found in serum. The globulin, in turn, is made up of globulins (13). Protein electrophoresis can be used to quantify these fractions; however, the total protein test is a faster and less expensive method that calculates the sum of all fractions.

Total serum proteins (TSP) are evaluated in the body to diagnose nutritional issues including protein energy waste (PEW), which is a condition in which the body's protein and energy stores are depleted. Thisis caused by a lack of protein and energy- rich foods, and it happens when people are malnourished (14).

Albumin is responsible for the transfer of chemicals such as unconjugated bilirubin and certain hormones, accounting for 65 percent of TSP in the blood. It is responsible for maintaining the blood's 80% colloid osmotic pressure and is utilized as a long- term indicator of malnutrition, resulting in nutrition-related chronic deficiencies diagnosis (15).

During normal health checks, the albumin/globulin ratio is usually tested. Atotal protein test, which uses a blood sample to evaluate the total combined amount of albumin and globulin in the blood, yields the A/G ratio (16). The total protein test, in turn, is part of a comprehensive metabolic panel (CMP), which is a collection of 14 tests that assesses how effectively your metabolism is working. CMPs are typically done at annual checkups or while in the hospital (17).

Study objectives

The main objectives of the present study were to explore the liver function tests in a sample of patients with liver disease and to investigate their relationship with normal persons.

METHODS AND SUBJECTS

Study design:

A retrospective study design was conducted to analyze data of liver patients from India.A dataset posted in Kaggle about liver disease was analyzed (18).

Study sample: Study sample included 583 patients, of whom 414 with liver disease, and 167 normal persons.

Study variables: Study variables included age, gender, total proteins, bilirubin, ALT,AST, alkaline phosphatase, albumin, and albumin/globulin ratio.

Statistical analysis: The data were analyzed using SPSS version 21. Descriptive analysis including frequency and percentage, mean and standard deviation to describe categorized and non-categorized variables. The relationship between variables were assessed using independent T test. Significance was considered if $\alpha \leq 0.05$.

RESULTS

General characteristics of studyparticipants

As illustrated in table (1), the mean age of participants was 44.75±16.19 years, males were predominant (75.6%). The mean levelof total bilirubin was 3.3±6.21 mg/dl. Themean level of direct bilirubin was 1.49±2.81 mg/dl. The mean level of alkaline phosphatase was 290.58±242.40 IU/L. the mean level of ALT was 80.71±182.62 IU/L. The mean level of AST was 109.91±288.92 IU/L. The mean level of total proteins was 6.48±1.09 g/dl. The mean level of albumin was 3.14±0.8 g/dl. The ratio of albumin/globulin was 0.974±0.32. The health status of participants was normal for about 29%, and with liver disease for 71%of persons.

Table 1: General characteristics of study participants

Variable	Description
Age (M±SD) years	**44.75 (16.19)**
Gender (N, %):	
- **Males**	**441 (75.6%)**
- **Females**	**142 (24.4%)**
Total bilirubin (M±SD) mg/dl	**3.30±6.21**
Direct bilirubin (M±SD) mg/dl	**1.49±2.81**
Alkaline phosphatase (M±SD) IU/L	**290.58±242.4**
ALT (M±SD) IU/L	**80.71±182.62**
AST (M±SD) IU/L	**109.91±288.92**
Total protein (M±SD) g/dl	**6.48±1.09**
Albumin (M±SD) g/dl	**3.14±0.80**
Albumin/globulin (%)	**0.974±0.32**
Health status (N, %):	
- **Diseased**	**416 (71.4%)**
- **Normal**	**167 (28.6%)**

The relationship between study variables for study participants using independent T test

As seen in table (2), the mean age of persons with liver disease was 46.15±15.65 years. This was significantly higher than that of persons without liver disease (41.24±16.99years, p=0.001). The level of total bilirubin was significantly higher in liver patients (4.16±7.14 mg/dl) than normal persons (1.142±1.00 mg/dl, p=0.000). The level of direct bilirubin was significantly higher inpatients with liver disease (1.92±3.2 mg/dl) than in normal persons (0.39±0.52 mg/dl, p=0.000). The level of alkaline phosphatase was 319±268.3 IU/L in liver patients, and 219.75±140.98 IU/L in normal persons. The difference in means was statistically significant (p=0.000). The level of ALT was 99.60±212.76 IU/L in liver patients, and 33.65±25.06 IU/L in normal persons. The difference in means was statistically significant (p=0.000). The level of AST in liver patients was 137.69±337.38 IU/L, and 40.68±IU/L in normal subjects. The difference in means was statistically significant (p=0.000). The level of total proteins were 6.45±1.09 g/dl in liver patients, and 6.54±1.06 g/dl in normal persons. The difference in means was not statistically significant (p=0.399). The level of albumin was 3.06±0.78 mg/dl, and 3.34±0.78 mg/dl. The difference in means was statistically significant (p=0.000). The ratio of albumin/globulin was 0.91±0.32 in liver patients, and 1.02±0.28 in normal persons. The difference in means was statistically significant (p=0.000).

Table 2: The relationship between study variables for study participants

Variable	Dataset	N	Mean	Std. Deviation	P value
Age	Disease	416	46.15	15.65	0.001
	Normal	167	41.24	16.99	
Totalbilirubin	Disease	416	4.16	7.14	0.000
	Normal	167	1.142	1.00	
Directbilirubin	Disease	416	1.92	3.20	0.000
	Normal	167	0.39	0.52	
Alkalinephosphatase	Disease	416	319.00	268.30	0.000
	Normal	167	219.75	140.98	
ALT	Disease	416	99.60	212.76	0.000
	Normal	167	33.65	25.06	
AST	Disease	416	137.69	337.38	0.000
	Normal	167	40.68	36.41	
Totalprotein	Disease	416	6.45	1.09	0.399
	Normal	167	6.54	1.06	
Albumin	Disease	416	3.06	0.78	0.000
	Normal	167	3.34	0.78	
Albumin/globulin_ratio	Disease	414	0.91	0.33	0.000
	Normal	165	1.03	0.29	

The relationship between gender andhealth status using Chi-Square

As seen in table (3), gender was significantly associated with health status. A total of 50 females (32.5%) had liver disease, while a total of 117 (26.5%) males had liver disease. The variation in developing liver disease was significant (p=0.047). this implies that females were more likely to develop liver disease.

Table 3: The relationship between gender and health status

			Health status		Total
			Normal	Disease	
Gender	Female	Count	92	50	142
		% Within gender	64.8%	35.2%	100.0%
		% Within health status	22.1%	29.9%	24.4%
		% of Total	15.8%	8.6%	24.4%
	Male	Count	324	117	441
		% Within gender	73.5%	26.5%	100.0%
		% Within health status	77.9%	70.1%	75.6%
		% of Total	55.6%	20.1%	75.6%
Total		Count	416	167	583
		% Within gender	71.4%	28.6%	100.0%
		% Within health status	100.0%	100.0%	100.0%
		% of Total	71.4%	28.6%	100.0%
P value		0.047			

DISCUSSION

The present study was conducted to evaluate the liver function tests among a group of patients with liver disease and to compare their findings with a group of patientswithout liver disease.

The results showed that gender was significantly associated with liver disease (p=0.047). Females were more likely to develop liver diseases. The result of this study confirm other studies in which females were more likely to develop liver disease ina large meta study (19).

The results of this study showed that aging was significantly associated liver disease (p=0.001). This result is in line with other studies that showed age is a predicting factor for acute liver disease. Aging is a conditionin which a person's ability

to maintain homeostasis gradually deteriorates owing to structural changes or dysfunction, leaving them vulnerable to external stress or injury (20).

The results showed that patients with liver disease had increased significant levels of bilirubin compared with normal persons (p=0.000). This is consistent with other studies in which increased levels of bilirubin reflect damage and inflammation conditions (8).

The results showed that the level of alkaline phosphatase was significantly elevated in patients with liver disease compared with normal persons. Alkaline phosphatase isbeneficial in the assessment of liver injury; but may be not specifically indicating liver disease (2, 10).

The results of this study showed that both ALT and AST levels were significantly increased in patients with liver disease compared with normal subjects (p=0.000). ALT and AST are both beneficial in the assessment of liver function alterations, although ALT is more specific (11, 12).

The results showed that the level of total proteins was not significantly associatedwith liver diseases (p=0.399). Both groups of participants had similar levels of total proteins. It implies that our results failed to prove significant inclusion of total proteins in assessing liver pathology.

The results showed that albumin level was significantly higher in liver patients compared with normal persons. However, its increased levels reflect liver pathology and malnutrition (15).

The results showed that albumin/globulin ration is significantly higher in normal subjects compared with patients who haveliver disease (p=0.000). This may indicate that liver patients had less globulins than albumins, this is usually involved in cancer cases (21).

CONCLUSION

The results of this study showed that liver function tests can be used to assess liver disease. Total proteins did not show significant assessment of liver disease.

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