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# Enzymatic and Non-enzymatic Liver Function Test: A Review

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**ABSTRACT**

Since the liver performs a variety of functions like metabolic, synthetic, excretory etc. Therefore, no single test is sufficient to provide complete estimate of function of liver. Liver function tests (LFT) are a helpful screening tool, which are an effective modality to detect hepatic dysfunction. Some of the enzymes and the products of the metabolic pathway that are very sensitive for the abnormality occurred may be considered as biochemical marker of liver dysfunction. These markers are serum bilirubin, albumin, caeruloplasmin, α-fetoprotein, prothrombin time, alanine aminotransferase, aspartate aminotransferase, ratio of aminotransferases, alkaline phosphatase, γ-glutamyl transferase, and 5/- nucleotidase. An isolated or conjugated 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. Often clinicians are faced with reports that do not tally with the clinical condition of the patient and they face difficulty in interpreting the LFT.

**Key words:** Bilirubin, albumin, aminotransferases, alkaline phosphatase, γ-glutamyl transferase.

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## INTRODUCTION

Liver is a versatile organ of the body and it performs different kinds of biochemical function such as metabolic, synthetic, excretory, detoxification etc. It also helps to maintain homeostasis and host defence of the body. Mostly the defence mechanisms occur through Kupffer cells, Ito cells, endothelial cells, hepatic cells and neutrophils by directing production of tumor necrosis factor (TNF) and interleukin-1 (IL-1) [1]. The protective function of liver is because of its central location with a large number of immunological cells [2]. This is the first organ to receive substances absorbed or bacterial translocated from gastro intestinal tract (GIT) after infection / inflammation or in healthy persons [3]. Liver disease is a collection of conditions, diseases, and infections that affect the cells, tissues, structures, or functions of the liver [4]. Any abnormality or dysfunction of the liver leads major impairment of the organ function, which, in turn, influences the health of the individual. This can be assessed by biochemical tests that reflect the damage or dysfunction of the liver. However, no single biochemical test can detect the global function of liver. A series of tests employ for initial detection and management of liver diseases and these tests are usually referred as "Liver function test" (LFT) [5].

The routine laboratory testing is automated and is frequently part of an annual checkup; physicians are often faced with the problem of a patient with abnormal LFTs result on measurement of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and γ-glutamyl transferase (γ-GT). Abnormal LFTs cannot be ignored because a subgroup of these patients will have progressive and potentially life-threatening liver disease for which therapeutic interventions are often available. Even in an asymptomatic individual, a careful history may identify potential causes of abnormal LFTs. A minor elevation (less than twice the normal value) may be of no clinical importance if the disorders listed in Table-1 have been ruled out and, in fact, may not even be abnormal.

The tests discussed above are often termed 'liver function tests', but the term is a misnomer. Tests to measure the synthesis by the liver of proteins like albumin, caeruloplasmin, α-antitrypsin. α-fetoprotein, prothrombin time etc. can more accurately be termed LFTs .These biochemical tests are useful in the evaluation and management of patients with hepatic dysfunction.

Although a liver biopsy is the gold standard for assessing both aetiology and the degree of fibrosis, it is associated with some morbidity and should be undertaken only after assessing the risk benefit. The clinical setting, together with the specific pattern of LFT abnormality and appropriate additional tests, can narrow the differential diagnosis and provide a cost-effective approach to identifying those patients who need a liver biopsy.

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## ENZYMATIC TEST

**1. Alanine aminotransferase (ALT):** Alanine aminotransferase (ALT), also called Serum Glutamate Pyruvate Transaminase (SGPT) is an enzyme present in kidney, heart, muscle and greater concentration in liver compared with other tissues of the body [6]. ALT catalyze the transfer of the α-amino acids of aspartate and alanine respectively to the α-keto group of ketoglutaric acid (alanine + α-ketoglutarate = pyruvate + glutamate) [7]. ALT is a cytoplasmic enzyme and normal serum of ALT is 10-56 U/ L [8]. Any type of liver cell injury can reasonably increases ALT levels and values up to 300 U/L are considered nonspecific. Marked elevations of ALT levels (>500 U/L) observed most often in persons with diseases such as viral hepatitis, ischemic liver injury and toxin-induced liver damage [9]. Viral hepatitis like A, B, C, D and E may be responsible for a marked increase in aminotransferase levels and hepatitis C infection tends to be more than hepatitis A or B [10] . Elevation in ALT levels is greater in persons with non-alcoholic steatohepatitis than in those with uncomplicated hepatic steatosis [11]. Hepatic fat accumulation in childhood obesity and non-alcoholic fatty liver disease are also causes for serum ALT elevation. Moreover, increased ALT level was associated with reduced insulin sensitivity, adiponectin and glucose tolerance as well as increased free fatty acids and triglycerides [12]. ALT level is normally elevated during 2nd trimester in asymptomatic normal pregnancy [13]. One of the recent studies has shown that coffee and caffeine consumption reduces the risk of elevated serum ALT activity in excessive alcohol consumption, viral hepatitis, iron overload, overweight, and impaired glucose metabolism [14]. Moderate elevation (3-20 times) of ALT suggests in acute hepatitis, neonatal hepatitis, chronic hepatitis, drug induce hepatitis, alcoholic hepatitis and acute biliary tract obstruction. In uncomplicated acute viral hepatitis, the very high initial levels approach normal levels within 5 weeks of onset of illness and normal levels are obtained in weeks in 75% of cases [5]. Mild elevations (1-3 times) are usually seen in sepsis induced neonatal hepatitis, extrahepatic biliary atresia , fatty liver cirrhosis, drug toxicity , Duchenne muscular dystrophy and even after vigorous exercise [1,5].

**2. Aspartate aminotransferase (AST):** Aspartate aminotransferase (AST) also called Serum Glutamic Oxaloacetic Transaminase (SGOT). AST catalyse transamination reaction (alanine + α-ketoglutarate = oxaloacetate + glutamate). AST is present in both mitochondria and cytosol and normal serum AST level is 0 to 35 U/L [6, 8]. About 80% of AST activity in human liver is contributed by the mitochondrial isoenzymes whereas most of the circulating AST activity in normal people is derived from cytosolic isoenzymes [15]. AST is found in highest concentration in heart compared with other tissues like liver, skeletal muscle and kidney. Elevated mitochondrial AST seen in extensive tissue necrosis during myocardial infarction and in chronic liver diseases like liver tissue degeneration and necrosis [16]. However, the ratio of mitochondrial AST to total AST activity has diagnostic importance in identifying the liver cell necrotic type condition and alcoholic disease [17]. AST elevations often predominate in patients with cirrhosis and even in liver diseases that typically have an increased ALT [18]. AST levels in symptomatic pregnant patient in hyperemesis gravidarum were 73 U/L, in pre-eclampsia 66 U/L, and 81 U/L was observed in hemolysis with low platelet count and elevated liver enzymes [19] and in chronic liver disease [20]. Therefore, these assays of mitochondrial AST have been

advocated in myocardial infarction. The common cause of elevated serum transaminases is given in Table-2.

**3. AST/ALT ratio:** The ratio of AST to ALT is of use in alcoholic disease and ratio of more than two is usually observed. In viral hepatitis, the ratio is generally less than one. The ratio always rises to more than one as cirrhosis develops possibly because of reduced plasma clearance of AST secondary to impaired function of sinusoidal cells [21]. ALT exceeds AST in toxic hepatitis, viral hepatitis, chronic hepatitis and cholestatic hepatitis [7]. A coenzyme pyridoxal phosphate (PLP) deficiency may depress serum ALT activity and consequently increases the AST/ALT ratio [22]. The ratio increases in progressive liver functional impairment and found 81.3% sensitivity and 55.3% specificity in identifying cirrhotic patients [23]. Whereas mean ratio of 1.45 and 1.3 was found in alcoholic liver disease and post necrotic cirrhosis respectively [24]. The ratio greater than 1.17 was found in one-year survival among patients with cirrhosis of viral cause with 87% sensitivity and 52% specificity [25]. An elevated ratio greater than 1 shows advanced liver fibrosis and chronic hepatitis C infection [26]. A recent study differentiated non-alcoholic steatohepatitis (NASH) from alcoholic liver disease showing AST/ALT ratio of 0.9 in NASH and 2.6 in patients with alcoholic liver disease [27]. Wilson's disease can cause the ratio to exceed 4.5 and similar such altered ratio is found even in Hyperthyroidism [28, 29].

**4. Alkaline phosphatase (ALP):** Alkaline phosphatases (ALP) are a family of zinc metaloenzymes, with a serine at the active center; they release inorganic phosphate from various organic orthophosphates. ALP is present in mucosal epithelia of small intestine, proximal convoluted tubule of kidney, bone, liver and placenta. Alkaline phosphatase from the liver, bone and kidney are thought to be from the same gene but that from intestine and placenta are derived from different genes [7]. It performs lipid transportation in the intestine and calcification in bone. In healthy people most circulating alkaline phosphatase originates from liver or bone [30]. Tumours secrete ALP into plasma and there are tumour specific isoenzymes such as Regan, Nagao and Kasahara [7].

The serum ALP activity is mainly from the liver with 50% contributed by bone [6]. Normal serum ALP is 30-120 UI/L [8]. In acute viral hepatitis, ALP usually remains normal or moderately increased. Elevation of ALP with prolonged itching is related with Hepatitis A presenting cholestasis. Hepatic and bony metastasis can also cause elevated levels of ALP. Other diseases like infiltrative liver diseases, abscesses, granulomatous liver disease and amyloidosis may cause a rise in ALP. Mildly elevated levels of ALP may be seen in cirrhosis, hepatitis and congestive cardiac failure [7]. Low levels of ALP occur in hypothyroidism, pernicious anemia, zinc deficiency and congenital hypophosphatasia [19]. ALP activity was significantly higher in the third trimester of asymptomatic normal pregnancy showing extra production from placental tissue [13]. ALP levels in hyperemesis gravidarum were 21.5 U/L, in pre-eclampsia 14 U/L, and 15 U/L in hemolysis with low platelet count was seen during symptomatic pregnancy [31].

Average values of alkaline phosphatase vary with age and are relatively high in childhood, puberty and lower in middle age and higher again in old age. Males usually have higher values

as compared to females [32]. Transient hyperphosphataemia in infancy is a benign condition characterized by elevated ALP levels of several folds without evidence of liver or bone disease and it returns to normal level by 4 months [33]. Highest levels of alkaline phosphatase occur in cholestatic disorders and levels are likely to be very high in extrahepatic biliary atresia [5]. ALP has been found elevated in peripheral arterial disease, independent of other traditional cardiovascular risk factors [34]. Often clinicians are more confused in differentiating liver diseases and bony disorders when they see elevated ALP levels and in such situations measurement of gamma glutamyl transferase assists as it is raised only in cholestatic disorders and not in bone diseases [7].

The mechanism by which alkaline phosphatase reaches the circulation is uncertain; leakage from the bile canaliculi into hepatic sinusoids may result from leaky tight junction [5, 35] and the other hypothesis is that the damaged liver fails to excrete alkaline phosphatase made in bone, intestine and liver [1]. In acute viral hepatitis, alkaline phosphatase is usually either normal or moderately increased. Hepatitis A may present a cholestatic picture with marked and prolonged itching and elevation of alkaline phosphatase. Elevated serum levels of intestinal alkaline phosphatase have been found in patients with cirrhosis, particularly those with blood group type O, and may be associated specifically with intrahepatic disease as opposed to extrahepatic obstruction [36]. Wilson's disease complicated by hemolysis might be the result of replacement of cofactor zinc by copper and subsequent inactivation of alkaline phosphatase [37]. Drugs like cimetidine, frusemide, phenobarbitone and phenytoin may increase levels of alkaline phosphatase [7].

**5. γ-Glutamyl Transferase (γ-GT):** γ-Glutamyl transferase is a membrane bound glycoprotein which catalyses the transfer of γ- glutamyl group to other peptides, amino acids and water. γ-GT is a microsomal enzyme present in hepatocytes and biliary epithelial cells, renal tubules, pancreas and intestine. Serum γ-GT activity mainly attributed to hepatobiliary system even though it is found in more concentration in renal tissue [6]. The levels of γ-GT are high in neonates and infants up to 1 yr and increase after 60 yr of life. Children more than 4 yr old have serum values of normal adults. The normal range is 0-51 IU/L [1,7].

In acute viral hepatitis the levels of γ-GT will reach the peak in the second or third week of illness and in some patients remain elevated for 6 weeks [7]. In extrahepatic biliary atresia (EHBA), γ-GT is markedly elevated [7]. Increased level is seen in about 30% of patients with chronic hepatitis C infection [38]. Elevated serum γ-GT levels of more than 10 times is observed in alcoholism due to structural liver damage or pancreatic damage [39]. Other conditions like uncomplicated diabetes mellitus, acute pancreatitis, myocardial infarction, anorexia nervosa, Gullian barre syndrome, hyperthyroidism, obesity and dystrophica myotonica caused elevated levels of γ-GT [7]. Drugs like phenobarbitone, phenytoin, paracetamol, tricyclic antidepressants may increase the levels of γ-GT [7]. It can also be an early marker of oxidative stress since serum antioxidant carotenoids namely lycopene, α-carotene, β-carotene, and β-cryptoxanthin are inversely associated with alcohol-induced increase of serum γ-GT found in moderate and heavy drinkers[40].

γ-GT levels may be 2-3 times greater than 51 IU/Lin more than 50% of the patients with non-alcoholic fatty liver disease [41]. There is a significant positive correlation between serum γ-GT and triglyceride levels in diabetes and the level decreases with treatment especially when treated with insulin. Whereas serum γ-GT does not correlate with hepatomegaly in diabetes mellitus [42]. Serum γ-GT activity was significantly lowers in the second and third trimesters of normal asymptomatic pregnancy [13].

**6. $5^{/}$ - Nucleotidase (NTD):** NTD is a glycoprotein generally distributed throughout the tissues of the body localized in cytoplasmic membrane catalyzing release of inorganic phosphate from nucleoside-5-phosphates. The normal range established is 0-15 U/L [6]. The levels of NTD activity is increased in obstructive jaundice, parenchymal liver disease, hepatic metastases and bone disease [1]. Both ALP and NTD levels also increased in intra or extra hepatic obstruction due to malignancy [43]. Elevation of NTD is found high in acute hepatitis than chronic hepatitis [44].

## NON-ENZYMATIC TEST

**1. Serum Bilirubin:** Bilirubin is the catabolic product of haemoglobin produced within the reticulo endothelial (RE) system of liver and spleen, released in unconjugated form which enters into the liver, converted to conjugated forms bilirubin mono and diglucuronides by the enzyme UDP-glucuronyltransferase [6]. The classification of bilirubin into direct (conjugated) and indirect (unconjugated) bilirubin are based on the original van der Bergh method of measuring bilirubin. Normal serum total bilirubin varies from 0.2-1 mg/dl (4 -17µmol/L). The serum bilirubin levels more than 17µmol/L suggest liver diseases and levels above 24µmol/L indicate abnormal laboratory liver tests [5, 16].

Jaundice occurs when bilirubin becomes visible within the sclera, skin, and mucous membranes at a blood concentration of around 40 µmol/L [45].The occurrence of unconjugated hyperbilirubinemia due to over production of bilirubin decreased hepatic uptake, conjugation, or both due to genetic defect of UDP-glucuronyltransferase causing Gilbert's syndrome, Crigler-Najjar syndrome and reabsorption of large hematomas and ineffective erythropoiesis [46] Hyperbilirubinemia seen in viral hepatitis, hepatocellular damage, toxic or ischemic liver injury and which is directly proportional to the degree of histological injury of hepatocytes [16]. It has been observed that the decrease of conjugated serum bilirubin is a bimodal fashion when the biliary obstruction is resolved [47]. Other causes of extreme hyperbilirubinemia include severe parenchymal disease, septicemia and renal failure [7].The biochemical change for the differential diagnosis of hyperbilirubinemia is given in Table-3.

Parenchymal liver diseases or incomplete extrahepatic obstruction due to biliary canaliculi give lower serum bilirubin value than those occur with malignant obstruction of common bile duct but the level remains normal in granuloma[1]. It has been observed that marked increased serum bilirubin from 20.52-143.64µmol/L in acute inflammation of appendix[ 48]. Total bilirubin and conjugated bilirubin concentrations were significantly decreased during

second and third trimesters of pregnancy [13]. The recent study has shown that a high serum total bilirubin level may protect neurologic damage due to stroke [49].

Neonatal hyperbilirubinemia results from a predisposition to the production of bilirubin in newborn infants and their limited ability to excrete it. Infants, especially preterm infants, have higher rates of bilirubin production than adults, because they have red cells with a higher turnover and a shorter life span [50]. In newborn infants, unconjugated bilirubin is not readily excreted, and the ability to conjugate bilirubin is limited. Together, these limitations lead to physiologic jaundice in the first days of life in full-term infants, followed by a decline during the next several weeks to the values commonly found in adults. The average full-term newborn infant has a peak serum bilirubin concentration of 5- 6 mg/dl (86 -103 µmol/L). Serum bilirubin concentrations higher than 17 mg /dl (292µmol/L) in full-term infants are considered pathologic jaundice [51].

**2. Urine bilirubin:** Unconjugated bilirubin is tightly bound to albumin and not filtered by the glomerulus and thus not present in urine. Measurable amounts of conjugated bilirubin in serum and in urine are found only in hepatobiliary disease especially in early acute viral hepatitis [1]. Tests strips impregnated with diazo reagent are easy to use and detect as little as 1-2 µmol /L bilirubin [7].

**3. Urobilinogen:** An increase in the urobilinogen in urine is a sensitive indicator of hepatocellular dysfunction. It is a good indication of alcoholic liver damage, well-compensated cirrhosis or malignant disease of the liver. It is markedly increased in hemolysis and disappears in cholestatic jaundice [7]. Freshly voided urine sample gives a purple reaction to Ehrlich's aldehydes reagent. A dipstick containing this reagent allows rough and ready quantification of urobilinogen [7].

**4. Albumin:** Liver is the only site of synthesis of albumin and is a useful indicator of hepatic function [7]. Albumin synthesis is affected not only in liver disease but also by nutritional status, hormonal balance and osmotic pressure. Serum albumin level is not a reliable indicator of hepatic protein synthesis in acute liver disease because of its half-life in serum is as long as 20 days. The serum levels are typically depressed in patients with cirrhosis and ascites. In patients with or without ascites, the serum albumin level correlates with prognosis [52]. In addition the rate of albumin synthesis has been shown to correlate with the Child- Pugh score [53].

Normal serum values range from 3.5- 5.0 g/dl. The serum levels at any time reflect its rate of synthesis, degradation and volume of distribution. Corticosteroids and thyroid hormone stimulate albumin synthesis in hepatocytes [54].

The serum albumin levels tend to be normal in diseases like acute viral hepatitis, drug related hepatotoxicity and obstructive jaundice. Albumin levels below 3g/dl in hepatitis should raise the suspicion of chronic liver disease like cirrhosis, which usually reflects decreased albumin synthesis. In ascites, there may be normal synthesis but the levels may appear reduced

because of increased volume of distribution [55]. Hypoalbuminemia is not specific for liver disease and may occur in protein malnutrition, nephrotic syndrome and chronic protein losing enteropathies [1].

**5. Ceruloplasmin:** Ceruloplasmin is synthesized in the liver and is an acute phase protein. It binds with the copper and serves as a major carrier for copper in the blood [6]. Normal plasma level of Ceruloplasmin is 0.2-0.4 g/L [1]. The plasma concentration rise in infections, rheumatoid arthritis, pregnancy, non -Wilson liver disease and obstructive jaundice and low levels may also be seen in neonates, Menke's disease, kwashiorkor, marasmus, copper deficiency and aceruloplasminemia [16]. In Wilson's disease, ceruloplasmin level is depressed due to diminished rate of synthesis of the caeruloplasmin resulting copper accumulation in liver because of copper transport defect in Golgi apparatus, since ATP7B is affected [7]. Serum ceruloplasmin levels were elevated in the chronic active liver disease but lowered in the Wilson's disease. Hence, it is the most reliable routine chemical screening test to differentiate between chronic active liver disease and Wilson's disease [56].

**6.α-fetoprotein (AFP):** AFP is the major serum protein in the developing mammalian fetus produced at high levels by the fetal liver and visceral endoderm of the yolk sac and at low levels by fetal gut and kidney. AFP is required for female fertility during embryonic development by protecting the developing female brain from prenatal exposure to estrogen [57]. The AFP gene is highly activated in fetal liver but is significantly repressed shortly after birth. The normal level of AFP is 0-15µg/L [8]. It is increased in hepatocellular carcinoma (HCC) and more than 90% of such patients have raised levels about 400 -500 µg/L [58]. A high AFP concentration ≥ 400µg/L in HCC patients is associated with greater tumour size, bilober involvement, portal vein invasion and a lower median survival rate [59]. Higher serum AFP levels independently predict a lower sustained virological response (SVR) rate among patients with chronic hepatitis C [60].

**7. Prothrombin time (PT):** The liver is the major site of synthesis of all blood coagulation proteins: fibrinogen, prothrombin, labile factor, stable factor, Christmas factor, Stuart prowe factor, prekallikrein and high molecular weight kininogen [1]. Most of these are present in excess and abnormalities of coagulation only result when there is substantial impairment in the ability of the liver to synthesize these factors. The half-life of prothrombin is 6 hours only; therefore, PT is a useful indicator of liver function. The standard method to assess is the one stage prothrombin time of quick, which evaluate the extrinsic coagulation pathway [6].

Normal control usually is in the range of 14-16 seconds. A prolongation of more than 2 seconds is considered abnormal [1]. The prolonged PT is not specific for liver diseases and is seen in various deficiencies of coagulation factors and ingestion of certain drugs. In acute and chronic hepatocellular disease, the PT may serve as a prognostic indicator. In acute hepatocellular disease, deterioration of PT suggests increased chances of acute hepatic failure. Prolongation of PT is also suggestive of poor long-term outcome in chronic liver disease [5]. Vitamin K deficiency is also cause for prolonged prothrombin time. If the PT returns to normal or improves by at least 30% within 24 hr of a single parenteral injection of vitamin K (5-10 mg),

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**Table -1: The causes of abnormal liver function tests**

| | |
|---|---|
| **Hepatic causes** | **Medications** |
| Alcohol abuse | Antibiotics |
| Medication | Synthetic penicillins |
| Chronic hepatitis B and C | Ciprofloxacin |
| Steatosis and nonalcoholic steatohepatitis | Nitrofurantoin |
| Autoimmune hepatitis | Ketoconazole and fluconazole |
| Acute hepatitis A or E | Isoniazid |
| Hemochromatosis | **Antiepileptic drugs** |
| Wilson's disease (in patients <40 years old) | Phenytoin |
| Alpha 1-antitrypsin deficiency | Carbamazepine |
| Primary biliary cirrhosis | **Inhibitors of HMG CoA reductase** |
| | Simvastatin |
| **Non-hepatic causes** | Pravastatin |
| Celiac sprue | Lovastatin |
| Inherited disorders of muscle metabolism | Atorvastatin |
| Non-insulin dependent diabetes mellitus | Nonsteroidal anti-inflammatory drugs |
| Hyper- or hypothyroidism | **Hyperglycemic drugs** |
| Active rheumatoid | Sulfonylureas ,Glipizide |
| Acquired muscle diseases | **Herbs and homeopathic treatments** |
| Strenuous exercise | Chaparral |
| **Drugs and substances of abuse** | Chinese herbs |
| Anabolic steroids | Jibuhuan |
| Cocaine | Ephedra (mahuang) |
| 5-Methoxy3,4-methylenedioxymethamphetamine | Gentian |
| | Germander |
| Phencyclidine | Alchemilla (lady's mantle) |
| Glues and solvents | Senna |
| Glues containing toluene | Shark cartilage |
| Trichloroethylene, chloroform | Scutellaria (skullcap) |

it may be surmised that parenchymal function is good and that hypovitaminosis K was responsible for the original prolongation of PT [1].

**8. α-Antitrypsin:** α- antitrypsin is a glycoprotein synthesized by the liver and is an inhibitor of serine proteinases, especially elastase. Its normal concentration is 1- 1.6 g/L. It is an acute phase protein, serum levels increase with inflammatory disorders, pregnancy and after oral contraceptive pills. Deficiency of α-antitrypsin is an uncommon cause of chronic liver disease in adults. Decreased levels of α-antitrypsin can be detected either by direct measurement of serum levels or by the lack of a peak in *α*-globulin bands on serum protein electrophoresis. The diagnosis is best established by phenotype (ZZ) determination.

## CONCLUSIONS

Liver is a versatile organ of the body and it performs metabolic, synthetic and excretory functions. It also helps to maintain homeostasis of systemic blood. Liver plays a central role in

metabolism by providing adequate quantities of metabolic fuel. Besides metabolic function, liver also performs a vital role in host defence. Therefore, it is very much essential to assess the function of liver in healthy individuals.

**Table-2: The common causes of elevated serum transaminases**

| Elevation | Causes |
|---|---|
| **Severe ( > 20 times, 1000I U/L)** | Drug toxicity, particularly paracetamol<br>Acute viral hepatitis<br>Autoimmune hepatitis<br>Ischaemic liver |
| **Moderate (3-20 times, 100–300 IU/L)** | Alcoholic hepatitis<br>Acute hepatitis, neonatal hepatitis, chronic hepatitis,<br>Autoimmune hepatitis, drug induced hepatitis<br>Acute biliary tract obstructions<br>Non-alcoholic steatohepatitis<br>Wilson's disease |
| **Mild (1-3 times,< 100 IU/L)** | Chronic hepatitis C<br>Chronic hepatitis B<br>Haemochromatosis<br>Fatty liver<br>Extrahepatic biliary atresia (EHBA)<br>Non alcoholic steato hepatitis(NASH)<br>Drug toxicity<br>Myositis<br>Duchenne muscular dystrophy<br>Vigorous exercise |

Laboratory liver tests help to make clear the alteration of markers that reflect the liver disease. A single liver function 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 assessment of enzyme abnormalities like, the predominant pattern of enzyme alteration, the magnitude of enzyme alteration in the case of aminotransferases, isolated elevation or in conjugation with some other parameter, the rate of change and the nature of the course of alteration or follow up of 6 months to 1-2 years provide a clear picture and helps to proper diagnosis of the liver disease. The pattern of enzyme abnormality, interpreted in the context of the patient's symptoms can aid in directing the subsequent diagnosis. The pattern of enzyme abnormality, interpreted in the context of the patient's characteristics, can aid in directing the subsequent diagnostic work-up. Awareness of the prevalence of determined liver disease in specific populations and of possible hepatic involvement during systemic illnesses or drug therapies may help the clinician identify the cause of alterations efficiently.

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**Table-3: Biochemical changes for the differential diagnosis of hyperbilirubinemia**

| Disease | Serum Bilirubin | | | Serum Enzyme | | | Urine | | Feces Colour |
|---|---|---|---|---|---|---|---|---|---|
| | Total | Conjugated | Unconjugated | ALT | AST | ALP | Bilirubin | Urobilinogen | |
| Hemolytic Jaundice | ↑ | N | ↑ | N | N | N | (-) | ↑ | Brown |
| Obstructive Jaundice | ↑ | ↑ | N | ↑ | ↑ | ↑↑ | (+) | ↓or (-) | Clay |
| Hepatic Jaundice | ↑ | ↑ | ↑ | ↑↑ | ↑↑ | ↑ | (+) | ↓or (N) | Pale Brown |
| Gilbert's Syndrome | ↑ | N | ↑ | N | N | N | (-) | ↓or (N) | Yellow |
| Crigler-Najjar Syndrome | ↑ | ↓ | ↑↑ | N | N | N | (-) | ↓ | Pale Brown |

↑ = increased , ↑↑ = marked increased , N = normal , (-) = absent , (+) = present

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