Evaluation of Abnormal Liver Tests

Tinsay A. Woreta, MD, Saleh A. Alqahtani, MD*

KEYWORDS

• Aminotransferases • Alkaline phosphatase • Hepatocellular injury • Cholestasis
• Bilirubin metabolism

KEY POINTS

- Serum aminotransferases are sensitive markers of hepatocellular injury.
- Assessing the pattern and degree of elevation in aminotransferases can help suggest the cause of liver injury.
- Elevation in serum alkaline phosphatase occurs as a result of cholestasis, which may result from intrahepatic causes, extrahepatic obstruction, or infiltrative disorders of the liver.
- Hyperbilirubinemia may occur as the result of both hepatocellular and cholestatic injury.
- Albumin and prothrombin time are true markers of liver synthetic function.

INTRODUCTION

The use of serum biochemical tests plays an important role in the diagnosis and management of liver diseases. The routine use of such tests has led to the increased detection of liver diseases in otherwise asymptomatic patients, often providing the first clue of the presence of liver pathology. Such laboratory tests, in addition to a careful history, physical examination, and imaging tests, can help clinicians determine the cause of liver disease in most cases.

The term "liver function tests" is commonly used to refer to a combination of liver biochemical tests, including serum aminotransferases, alkaline phosphatase (AP), and bilirubin. This is a misnomer, because aminotransferases and AP are markers of hepatocyte injury and do not reflect liver synthetic function. Traditionally, liver injury has been characterized as primarily hepatocellular versus cholestatic based on the degree of elevation of aminotransferases compared with AP (**Table 1**). Although such a distinction can help direct initial evaluation, there is often significant overlap in the presentation of various liver diseases, which often have a mixed pattern.[1] It is

Division of Gastroenterology and Hepatology, The Johns Hopkins Hospital, 1830 East Monument Street, Suite 428, Baltimore, MD 21287, USA
* Corresponding author.
E-mail address: salqaht1@jhmi.edu

Med Clin N Am 98 (2014) 1–16
http://dx.doi.org/10.1016/j.mcna.2013.09.005 **medical.theclinics.com**
0025-7125/14/$ – see front matter

Table 1
Categorization of liver diseases by pattern of elevation of liver enzymes

Liver Disease Category	Aminotransferases	Alkaline Phosphatase
Hepatocellular	↑↑	↑
Cholestatic	↑	↑↑

useful to classify liver biochemical tests into the following categories[2]: (1) markers of hepatocellular injury (aminotransferases and AP); (2) tests of liver metabolism (total bilirubin); (3) tests of liver synthetic function (serum albumin and prothrombin time [PT]); and (4) tests for fibrosis in the liver (hyaluronate, type IV collagen, procollagen III, laminin, FibroTest [BioPredictive, Paris, France], and FibroScan [Echosens, Paris, France]).

Furthermore, when evaluating patients with abnormal liver enzyme or function tests, it is helpful to define the liver injury as acute versus chronic. Liver disease is considered chronic if the abnormalities in liver enzyme tests or function persist for more than 6 months.

MARKERS OF HEPATOCELLULAR INJURY

The liver contains a multitude of enzymes in high concentration, some of which are present in the serum in very low concentrations. Injury to the hepatocyte membrane leads to leakage of these enzymes into the serum, which results in increased serum concentrations within a few hours after liver injury. Serum enzymes tests can be categorized into two groups[2]: enzymes whose elevation reflects generalized damage to hepatocytes (aminotransferases); and enzymes whose elevation primarily reflects cholestasis (AP, γ-glutamyltransferase [GGT], 5′ nucleotidase [5′-NT]).

Aminotransferases

The aminotransferases (previously called transaminases) are located in hepatocytes and are sensitive indicators of hepatocyte injury. They are useful in detecting acute hepatocellular diseases, such as hepatitis.[2] They consist of aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Aminotransferases catalyze the transfer of the α-amino groups from aspartate or alanine to the α-keto group of ketoglutaric acid, forming oxaloacetic acid and pyruvic acid, respectively. The enzymatic reduction of oxaloacetic acid and pyruvic acid to malate and lactate, respectively, is coupled to the oxidation of the reduced form of nicotinamide dinucleotide to nicotinamide dinucleotide. Because only nicotinamide dinucleotide absorbs light at 340 nm, this reaction can be followed spectrophotometrically by the loss of absorptivity at 340 nm, and provides an accurate method to assay aminotransferase activity.[3]

AST and ALT are present in the serum at low concentrations, usually less than 30 to 40 IU/L.[4] The normal range varies among clinical laboratories, based on measurements in specific populations. Several factors have been shown to influence ALT activity, such as gender and obesity.[5] Men tend to have a higher serum ALT activity compared with women.

ALT is found in highest concentration in hepatocytes and in very low concentrations in any other tissues. In contrast, AST is found in many other tissues including muscle (cardiac, skeletal, and smooth muscle); kidney; and brain.[2] Thus, ALT is a more specific marker for liver injury. A ratio of AST/ALT greater than five, especially if ALT is normal or slightly elevated, is suggestive of injury to extrahepatic tissues, such as skeletal muscle in the case of rhabdomyolysis or strenuous exercise.