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## Aminotransaminases: Structures, Functions and Clinical Significance

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**ABSTRACT:** The liver exerts critical functions in metabolic reactions, nutrition, detoxifying toxins, and excretion of wastes from the body. Aminotransferase are: There are two enzymes that are involved in the metabolism of amino acids: ALT and AST. The presence of them is indicative of damage to liver cells. High levels of transaminases can aid health care providers to diagnose frequent and risky hepatic disease. Both nonalcoholic and alcoholic hepatic diseases are the most well-known etiologic factors of high transaminase levels. ALT is made up of 496 amino acids. It can be detected at low levels in serum, and in high levels in the liver. Several health problems can result in increased ALT concentrations, including: celiac disease, some muscle disorders, thyroid disorders, hereditary hemochromatosis, heart failure, hepatitis, obesity, alcohol consumption, acetaminophen, nonalcoholic fatty liver disease. AST is made up of two typical dimers. It is a good indicator of human health and are of great clinical importance. High AST concentrations are frequently associated to septic shock, acute myocardial infarction, drug toxicity, cholestatic syndromes, cirrhosis, alcoholic liver disease, inflammatory liver disease (viral hepatitis), exercise, thyroid disease, myopathy, hemolysis and skeletal muscle injury.

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### 1. INTRODUCTION

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are the two types of enzymes that are classified as proteins that transfer amino acids. Damage to the liver can be identified by the presence of these cells. Aspartic acid and alanine are both involved in the process of gluconeogenesis. This is accomplished by the transfer of amino groups from aspartic acid or alanine to ketoglutaric acid, which ultimately leads to the production of oxaloacetic acid and pyruvic acid, respectively. There are a variety of organs that may contain AST in addition to the cytosol and mitochondria. These organs include the liver, cardiac muscle, skeletal muscle, kidneys, brain, pancreas, lungs, white blood cells, and red blood cells. This is in addition to the fact that AST is present in the mitochondria. When compared to ALT, the sensitivity and specificity of the AST test are lower when it comes to identifying liver disorders. Furthermore, higher AST readings can also be caused by the presence of substances that are not connected to the liver. The activity of AST in neonates and babies is roughly twice as high as that of adults, but it becomes comparable to that of adults by the time the child is approximately six months old (Lala et al., 2024).

In the majority of liver illnesses, the levels of ALT are often greater than those of AST, although both enzymes mostly come from the cytosol of hepatocytes. The secretion of these enzymes into the circulation is initiated by liver cell damage, which does not always result in cell death. Typically, guys who are in good health tend to have greater levels of AST and ALT in comparison to females. Moreover, there is a correlation between these enzyme levels and obesity, as persons with a higher body mass index tend to have higher normal reference ranges (Ruhl & Everhart, 2010). High levels of transaminases are often observed in primary care settings, impacting between 10% to 30% of the population in the United States. Nevertheless, less than 5% of people with high transaminases would suffer from severe liver problems (Ioannou et al., 2006b).

Transaminase levels that are increased are mostly caused by liver problems, including those that are nonalcoholic and those that are alcoholic. There are a few instances of etiologies that are less common, such as drug-induced hepatotoxicity, infections with hepatitis B and C, and hereditary hemochromatosis. A deficiency in alpha1-antitrypsin, autoimmune hepatitis, and Wilson disease are some examples of reasons that are significantly less common than others. There is a possibility that patients suffering from non-hepatic conditions, such as thyroid problems, celiac disease, hemolysis, and muscular issues, are linked to transaminase levels that are slightly higher than the normal range. It is recommended that the first examination include a test for metabolic syndrome as well as assessment

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of insulin resistance. The patient's waist circumference, blood pressure, fasting lipid levels, and fasting glucose or A1C readings are some of the factors that might be evaluated during this test. Additionally, a thorough blood test must be carried out without fail. A complete blood count, which should include platelets, as well as measurements of serum albumin, iron, total iron-binding capacity, and ferritin, should be included in this examination. In addition, a test for hepatitis C antibodies and hepatitis B surface antigen is an essential component of the diagnostic procedure (Oh et al., 2017).

Many risk factors believed to be associated to high ALT levels, these include: The variables included in this study are blood total cholesterol concentration, glycemic status, alcohol intake, cigarette smoking, ethnicity (non-Hispanic white, non-Hispanic black, Mexican-American, other), sex, and age (in years). Within a specific subset of patients who underwent a morning test following an overnight period of abstaining from food, researchers observed elevated levels of plasma blood triglycerides, serum C-peptide, and glucose (Ruhl & Everhart, 2010).

### ALANINE AMINOTRANSFERASE

A critical enzyme that is involved in the secondary metabolic processes of glucose and protein is alanine aminotransferase (ALT), also referred to as glutamate pyruvate transaminase (GPT). The reversible transfer of amino groups between alanine and 2-oxoglutarate is facilitated, leading to the production of glutamate and pyruvate. For both patients and clinical researchers, ALT is considered a biomarker for liver injury (Yang et al., 2009).

ALT is a cytosolic enzyme highly concentrated in the liver, with a half-life of approximately  $47 \pm 10$  hours. Elevated ALT levels can be caused by various factors, including celiac disease, certain muscle disorders, thyroid disorders, hereditary hemochromatosis, heart failure, hepatitis A, B, or C, obesity, alcohol consumption, acetaminophen, and nonalcoholic fatty liver disease (Lala et al., 2024). ALT consists of 496 amino acids and is commonly found in blood at low levels (usually below 30 IU/L). Nevertheless, any ailment that undermines the integrity of hepatocyte membranes or leads to cell necrosis leads to the discharge of elevated levels of ALT into the bloodstream (Moriles et al., 2024).

The activity of the enzyme known as alanine aminotransferase (ALT) in the serum is dramatically elevated in a variety of liver illnesses, including viral infections, cirrhosis, non-alcoholic steatohepatitis (NASH), and drug toxicity. On the other hand, increased levels of serum ALT activity can also be found in conditions that are not connected to the liver, such as celiac disease and muscle disease, and even in people who appear to be in excellent health. On the other hand, certain people who have been diagnosed with liver illnesses by histological examination, such as cirrhosis, NASH, and hepatitis C infection, do not have increased levels of ALT in their blood. Similarly, in preclinical evaluations of medication toxicity, rats frequently display increased levels of serum ALT without accompanying histological harm. Hence, the interpretation of serum ALT data might pose difficulties in both clinical diagnosis and preclinical drug toxicity assessment (Ozer et al., 2008).

ALT has traditionally served as a significant indicator of liver damage since it is found in great amounts in the liver and in low amounts in other tissues, both in rats and humans. It is hypothesized that the enzyme is released into the serum as a result of liver injury, causing an increase in ALT levels. Currently, serum ALT levels are assessed based on the enzyme's catalytic activity. However, it has not been definitively proven that liver damage directly increases ALT protein levels in the serum (Moriles et al., 2024).

It has been hypothesized that both ALT isoenzymes are present in the serum and that they make a contribution to the total activity of the ALT. As a consequence of this, the measurement of ALT isoenzymes has the potential to provide information that is both innovative and relevant in the context of preclinical drug safety studies and clinical diagnostic methods (Yang et al., 2009). Several studies have shown that levels of AST can rise by a factor of 10 to 20 times or more over the typical range, while levels of ALT can reach even greater levels (up to 50 times the normal range). On the other hand, the AST to ALT ratio (AST/ALT) can occasionally help in identifying if there is liver injury or damage to a different organ (Huang et al., 2006).

Nonalcoholic fatty liver disease (NAFLD) and alcoholic liver disease are the factors that are most likely to be responsible for high transaminase levels. Ruhl & Everhart (2010) noted that trunk fat plays a critical role in increasing ALT levels, suggesting that metabolically active intra-abdominal fat may contribute to liver injury. Additionally, Qiu et al. (2023) The ratio of ALT to HDL-C was found to have a significant and positive relationship with the prevalence of non-alcoholic fatty liver disease (NAFLD). For every standard deviation increase in the ratio of ALT to HDL-C, the adjusted odds ratio (OR) for non-alcoholic fatty liver disease (NAFLD) among the participants increased by 3.05.

Regarding alcoholic liver diseases, Sinn et al. (2022) observed that even modest alcohol consumption was linked to increased mortality from liver-related and overall causes among individuals with elevated ALT levels. Therefore, those with elevated ALT levels should be advised to completely abstain from alcohol. Similarly, Ioannou et al. (2006a) When there is a rise in serum ALT activity in the blood, and it is not caused by viral hepatitis or excessive alcohol consumption, it is often due to nonalcoholic fatty liver disease (NAFLD). This is something that has been observed from time to time. There are risk factors for nonalcoholic fatty liver disease

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(NAFLD) that are comparable to those for coronary heart disease, such as insulin resistance and central obesity. A recent study by Zheng et al. (2023) An investigation has revealed that there is a direct correlation between the levels of alanine aminotransferase (ALT) and the probability of developing non-alcoholic fatty liver disease (NAFLD). This was found to be the case. If, on the other hand, ALT levels were lower than 0.5 times the upper limit of normal in the study, it was discovered that the greatest mortality rates from cardiovascular diseases and death rates from any cause were recorded. This was the case throughout the whole study. It is interesting to note that having normal or lower levels of ALT was connected with higher death rates in comparison to having increasing ALT levels. This was the case regardless of the severity of non-alcoholic fatty liver disease! As a result, it is essential for medical professionals to recognize that raised levels of ALT serve as a signal of liver damage, whereas lower levels of ALT are associated with an increased risk of mortality.

On the other hands, high liver enzymes are common among patients with inflammatory bowel disease (IBD) and typically resolve on their own. The use of immunomodulators was found to be independently linked to higher ALT levels (Parisi et al., 2016).

### ASPARTATE AMINOTRANSFERASE

Aspartate aminotransferase (AST), formerly referred to as glutamic oxaloacetic transaminase (GOT), is an established enzyme that relies on pyridoxal 5'-phosphate (PLP) for its function. It acts as a catalyst for the reversible transformation of aspartic acid and  $\alpha$ -ketoglutarate into oxaloacetic acid and glutamic acid, enabling the transfer of amino groups between amino acids and  $\alpha$ -keto acids (Toney, 2014). The structure of AST is built in the form of two symmetrical dimers, with each dimer comprising of a large domain and a small domain. There are 413 amino acid residues that make up the cytoplasmic AST monomer, which is formed of a polypeptide chain. The molecular weight of this substance is around 45 kilodaltons, and it is composed of  $\alpha$ -helices and  $\beta$ -strands (Ndrepepa, 2021).

Aspartate aminotransferase exists in human tissues as two separate isoenzymes: one is present in the cytoplasm (c-AST) and the other is found in mitochondria (m-AST). AST, mostly derived from striated muscle, heart, and liver tissues, is becoming more well acknowledged for its diagnostic usefulness in assessing organ injury. AST isoenzyme analysis is useful for evaluating liver necrosis and predicting prognosis in hepatic disorders. Additionally, it can aid in the identification of individuals who have active alcoholic liver disease. evaluating AST isoenzymes in persons with acute myocardial infarction gives unique diagnostic information that is different from what can be gained by evaluating total creatine kinase and lactate dehydrogenase enzyme tests and their related isoenzymes (Panteghini, 1990).

In the liver, 80% of AST actions is located in mitochondria, with the remaining 20% in the cytoplasm. In human cardiac tissue, mitochondrial AST constitutes approximately 65% of total AST activity. The primary mechanism by which AST protein is eliminated from the bloodstream is through liver sinusoidal cells. The mean plasma half-life for total AST is 17 hours, but for mitochondrial AST it is 87 hours. AST activity has been detected in virtually all human tissues. The proportional ratio of AST activity in different human tissues, compared to serum activity, is as follows: The number of red blood cells is 40, in the lung it is 500, in the spleen it is 700, in the pancreas it is 1,400, in the brain it is 2,500, in the kidney it is 4,500, in the skeletal muscle it is 4,800, and in the liver it is 7,000. However, in the heart, it is 7,700 (Ndrepepa, 2021).

Various variables alter the amount of circulating AST. There are four primary processes that have been suggested to account for the increase in AST (and ALT) levels in the circulation. The primary cause is direct tissue injury, which occurs when the plasma membrane is damaged, resulting in the leaking of proteins or cell death caused by hazardous chemicals or stimuli. Alternatively, apoptosis, occurring during normal cellular turnover or under conditions of increased apoptotic stimuli, can also elevate aminotransferase levels, including AST.

Organs that exhibit high AST activity significantly contribute to its increased levels in the bloodstream. Elevated AST levels are frequently linked to conditions including septic shock, acute myocardial infarction, drug toxicity, cholestatic syndromes, cirrhosis, alcoholic liver disease, viral hepatitis, physical exercise, thyroid disorders, muscle disorders (myopathy), hemolysis, and skeletal muscle injury (Ndrepepa, 2021; Murao et al., 2017).

Severe myocardial ischemia or necrosis of myocardial cells during acute myocardial infarction often leads to elevated serum AST levels. However, there is typically a weak correlation between damage to liver cells and the presence of plasma aminotransferases. When there is minor damage to cells, enzymes are mostly released from the soluble cytoplasmic fraction. On the other hand, when there are extensive necrotic lesions, enzymes are released from both the cytoplasm and mitochondria. Another mechanism involves the formation of plasma membrane blebs, which occur when the plasma membrane detaches from the cytoskeleton under conditions of increased cellular stress. These blebs release enclosed cytoplasmic contents, including AST (Ndrepepa, 2021; Josekutty et al., 2013).

Research in adolescents indicates that serum AST levels are impacted by genetic predispositions as well as environmental factors (28, 29). A systematic review conducted by Aloisio et al. (2021) highlighted that aspartate aminotransferase (AST) levels frequently rise in COVID-19, with some studies linking AST abnormalities to increased risk of mortality. Similarly, patients with lower respiratory

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tract infections showed elevated ALT or AST levels, and these markers correlated with an additional day of hospital stay compared to patients with normal enzyme levels (Oh et al., 2016).

### CONCLUSIONS

ALT is made up of 496 amino acids. It can be detected at low levels in serum, and in high levels in the liver. Several health problems can result in increased ALT concentrations, including: celiac disease, some muscle disorders, thyroid disorders, hereditary hemochromatosis, heart failure, hepatitis, obesity, alcohol consumption, acetaminophen, nonalcoholic fatty liver disease. AST is made up of two typical dimers. It is a good indicator of human health and are of great clinical importance. High AST concentrations are frequently associated to septic shock, acute myocardial infarction, drug toxicity, cholestatic syndromes, cirrhosis, alcoholic liver disease, inflammatory liver disease (viral hepatitis), exercise, thyroid disease, myopathy, hemolysis and skeletal muscle injury.

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