

Aspartate aminotransferase (serum, plasma)

1 Name and description of analyte

1.1 Name of analyte

Aspartate aminotransferase (AST)

1.2 Alternative names

Systematic name L-aspartate:2-oxoglutarate aminotransferase (EC 2.6.1.1); also oxaloacetate aminotransferase, glutamate oxaloacetate aminotransferase; formerly known as aspartate transaminase.

1.3 LMC code

To follow

1.4 Description of analyte

AST is an intracellular enzyme present in both cytoplasm and mitochondria. It is widely distributed throughout the body's tissues, with the greatest amounts in cardiac muscle, liver, skeletal muscle and the kidneys.

1.5 Function of analyte

AST catalyses the transfer of amino groups from aspartate (forming oxaloacetate) to 2-oxoglutarate (forming glutamate). It is a key enzyme in gluconeogenesis.

AST present in the plasma is presumed to be derived from the normal turnover of tissue cells; increased quantities (the enzyme is usually assayed by measuring its activity, see 4.1) are found in tissue damage (particularly hepatic and cardiac and skeletal muscle damage). It is not known to have any function in plasma.

2 Sample requirements and precautions

2.1 AST can be measured in heparin plasma or serum.

2.2 General precautions only.

3 Summary of clinical applications and limitations of measurements

3.1 AST is used to identify tissue damage e.g. arising from damage to cardiac muscle (typically ischaemic in origin), damage to skeletal muscle (e.g. rhabdomyolysis) and liver cell inflammation or necrosis. Its classification as a liver *function* test is erroneous but has become accepted usage and seems likely to continue.

3.2 Limitations

The major disadvantage of AST as an indicator of tissue damage is its lack of specificity to any one tissue. [Alanine aminotransferase \(ALT\)](#) is to be preferred as an indicator of liver cell damage. Furthermore, an increase in serum AST activity does not on its own provide any information about the *cause* of that damage.

4 Analytical considerations

4.1 Analytical methods

In common with the methods used for measuring most enzymes for clinical purposes, AST is assayed by measuring its catalytic activity, not its mass.

The AST reaction involves an amino acid and an oxoacid both as substrates and products. Quantitation makes use of the formation of the oxoacid (oxaloacetate) in a coupled reaction using malate dehydrogenase (malate:NAD⁺ oxidoreductase, EC 1.1.1.38) to reduce it with NADH to form malate. The reaction is followed by measuring the fall in absorbance at 340 nm.

Aspartate + 2-oxoglutarate → (AST) → oxaloacetate + glutamate

Oxaloacetate + NADH + H⁺ → (MD) → malate + NAD⁺

Pyridoxine 5'-phosphate is a coenzyme for the AST reaction; its addition to the reaction mixture ensures that all the apoenzyme is catalytically active and measured. Preincubation is required to remove any endogenous oxoacids from the reaction mixture, the reaction then being started by the addition of 2-oxoglutarate.

4.2 Reference method

This is based on the method described in 4.1.

4.3 Reference materials

IRMM (Institute for Reference Methods and Materials)/IFCC (International Federation of Clinical Chemistry 454).

4.4 Interfering substances

Interference by endogenous oxo acids is eliminated as described in 4.1.

4.5 Sources of error

As with all assays involving measurement of enzyme activity, strict control of reaction conditions, especially temperature, is essential.

5 Reference intervals and variance

5.1.1 Reference interval: (adults and children) ≤34 U/L (women), ≤45 U/L (men)

5.1.2 Reference intervals (others): values above applicable to all ages

5.1.3 Extent of variation

5.1.3.1 Interindividual CV: 24%

5.1.3.2 Intraindividual CV: 16%

5.1.3.3 Index of individuality: 0.66

5.1.3.4 CV of method: 12.5%

5.1.3.5 Critical difference: 65%

5.1.4 Sources of variation: the high degree of intra- and interindividual variation reflect the fact that normal plasma levels of activity are determined by cell turnover and not subject to any form of feedback control.

6 Clinical uses of measurement and interpretation of results

6.1 Indications for measurement

1. See 3.1. AST is measured as an index of liver damage but it is less specific for this purpose than alanine aminotransferase (ALT). Values >20x the upper limit of normal may occur with severe liver damage. Smaller increments (usually <5x ULN) may occur in cholestasis, due to secondary damage to hepatocytes.
2. In established liver disease, a falling AST value usually reflects decreasing cell damage, but in acute liver failure, particularly that caused by paracetamol overdose, there are so few hepatocytes remaining that AST activity falls in parallel with a rising bilirubin concentration.
3. In the context of liver disease, measuring both AST and ALT provides little additional information over that provided by measuring either one. There are two exceptions: in fatty liver disease, an activity ratio AST/ALT of >2 suggests alcohol as a cause; an ratio of ≤ 1 is suggestive of a non-alcoholic cause.
4. Measurement of the ratio of AST activity to platelet count is one of many investigations that may be of value in assessing the presence of liver fibrosis in patients with chronic liver disease.

6.2. Confounding factors: none

7 Causes of abnormal results

7.1 High values

7.1.1 Causes

1. Hepatobiliary disease

- Liver cell necrosis (e.g. in viral hepatitis, toxic liver damage); values may be >20x upper limit of normal (ULN).
- Cholestatic and other forms of hepatobiliary disease; values rarely exceed 5x ULN unless there is accompanying liver cell necrosis.

2. Extrahepatic disease

Relative to plasma, the activity of AST in various tissues is: liver, 2850x, kidneys, 1200x, heart 450x, skeletal muscle 300x. Small increases in plasma AST activity may therefore occur in acute kidney injury, myocardial infarction or skeletal muscle damage typically to a greater extent than any increase in alanine aminotransferase (ALT).

7.1.2 Investigation

Although AST should only be measured when tissue damage is suspected on clinical grounds, in practice it is frequently measured as part of a panel of tests in a 'biochemical profile'. However, chronic liver disease can present non-specifically so that AST measurement is frequently requested in the absence of classic features of liver disease (e.g. jaundice). The important practical question may then arise as to the action to be taken if an unexpected high AST value is found.

In practice, the most common cause of an isolated increase in AST activity is alcohol-related or non-alcoholic fatty liver disease. For any value, a high alcohol intake, diabetes and hypertriglyceridaemia (all of which can cause fatty liver) should be excluded; if present, these should be managed appropriately before repeating the test.

- For increases $\leq 2x$ ULN, and other LFTs normal, repeat in 1–2 months
- If repeat value $\leq 3x$ ULN, further investigation is required
- Values >3x ULN further investigation is appropriate without repeat testing irrespective of results of other LFTs.

First line further liver investigations may comprise:

- hepatitis virus serology,
- full blood count (for alcohol-related macrocytosis or thrombocytopaenia secondary to hypersplenism caused by portal hypertension)
- autoimmune serology (antimitochondrial and antismooth muscle antibodies)
- ferritin (for haemochromatosis) and hepatic ultrasound.

If these do not provide a diagnosis, tests for Wilson's disease, α_1 -antitrypsin deficiency and celiac disease should be considered.

The possibility of skeletal or cardiac muscle damage can be investigated by measuring creatine kinase (CK) activity and a cardiac troponin, respectively. If CK is elevated with no obvious cause, TSH should be measured to exclude occult hypothyroidism.

7.2 Low values

7.2.1 Causes

The lower reference limit is zero: 'low-normal' values are of no significance.

7.2.1 Investigation of low values

Not required.

7.3 Notes

None

8 Performance

8.1 Sensitivity, specificity etc. for individual conditions

Garcia-Monzon C, Martin-Perez E, Iacono OL *et al.* Characterization of pathogenic and prognostic factors of nonalcoholic steatohepatitis associated with obesity. *J Hepatol* 2000;33:716-724. *Data suggest that a cut-off of 40 U/L identifies asymptomatic patients with hepatic steatosis with a sensitivity of 45% and specificity of 100%; for steatohepatitis, the respective values are 45% and 64%.*

Sorbi D, Boynton J, Lindon KD. The ratio of aspartate aminotransferase to alanine aminotransferase: potential value in differentiating nonalcoholic steatohepatitis from alcoholic liver disease. *Am J Gastroenterol* 1999;94:1018-1022. *An ALT/AST ratio ≤ 1.3 provided sensitivity and specificity of 75% for the diagnosis of non-alcoholic steatohepatitis (NASH) in patients with either NASH or alcoholic liver disease; the corresponding figures for a ratio of ≤ 2.0 were approximately 100% and 50%.*

Giannini E, Rizzo D, Botta F *et al.* Validity and clinical utility of the aspartate aminotransferase-alanine aminotransferase ratio in assessing disease severity and prognosis in patients with hepatitis C virus-related chronic liver disease. *Arch Intern Med.* 2003;163:218-224. *One of numerous studies suggesting that a change in the value of the ALT/AST ratio from >1 (normal) to <1 has high sensitivity for diagnosing cirrhosis in patients with chronic hepatitis B or C infection.*

9 Systematic reviews and guidelines

9.1 Systematic reviews

None identified

9.2 Guidelines

1. Goessling W, Friedman LS. Increased Liver Chemistry in an Asymptomatic Patient. *Clin Gastroent Hepatol* 2005;3:852-858. *A succinct review citing classic references.*
2. American Gastroenterological Association. Medical Position Statement: evaluation of liver chemistry tests. *Gastroenterology* 2002;23:1364-1366. *This review is accompanied by a detailed technical review of liver function tests.*

9.3 Recommendations

1. Smellie S, McNulty C, Galloway M. Liver function tests, In: Primary Care and Laboratory Medicine: frequently asked questions. London, ACB Venture Publications 2010, pp. 211-222.
2. There are recommendations for measuring AST in patients on various drugs (e.g. statins, glitazones): the manufacturers' literature should be consulted for further information.

10. Links

10.1 Related analytes

[Alanine aminotransferase](#) (ALT) is also used as an indicator of tissue damage; it is more widely distributed than AST and thus less specific for the liver.

10.2 Related tests

AST is usually measured as part of a panel of 'liver function' tests (or 'liver profile') (but see 3.1,) typically including serum [bilirubin](#) and [albumin](#) concentrations and [alkaline phosphatase](#) activity. [Alanine aminotransferase](#) (ALT) may also be included, but although comparison of ALT and AST activity in a ratio (see 8.1) may provide helpful information, the inclusion of both enzymes in a 'liver profile' cannot be justified. Neither can the routine inclusion of [gamma-glutamyltransferase](#) (GGT) in a liver profile be justified.

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