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MODERN METHODS OF DIAGNOSING HEPATITIS A

PhD, Assistant **Munavvar Faxriddin qizi Kuchkorova**
Andijan State Medical Institute, Faculty of Postgraduate Medical Education and Retraining;
Department of Pediatric Endocrinology, Phthisiology, Infectious Diseases, and Epidemiology
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Abstract: Hepatitis A is an acute viral infection caused by the hepatitis A virus (HAV), primarily transmitted via the fecal-oral route, and characterized by liver damage. Since the clinical symptoms of the disease resemble those of other acute viral hepatitises, an etiological diagnosis based solely on medical history and clinical examination is insufficient. This article analyzes modern principles for diagnosing hepatitis A, the diagnostic significance of clinical-biochemical markers, the detection of anti-HAV IgM and IgG antibodies, and the capabilities of detecting HAV-RNA using the polymerase chain reaction (PCR) method. Particular emphasis is placed on the role of anti-HAV IgM in confirming acute infection, the indication of immunity from past infection or vaccination by anti-HAV IgG, and the diagnostic value of PCR during the early stages of infection. In modern practice, the comprehensive evaluation of laboratory tests alongside clinical and epidemiological data is considered essential for enhancing diagnostic accuracy.

Keywords: hepatitis A, HAV, viral hepatitis, anti-HAV IgM, anti-HAV IgG, HAV-RNA, PCR, ELISA, ALT, bilirubin, serological diagnosis, differential diagnosis, laboratory diagnostics.

Introduction

Hepatitis A is one of the most widespread forms of acute viral hepatitis globally. Infection is most commonly transmitted through contaminated water and food, as well as through close household or other epidemiological contact with an infected individual. The clinical presentation of the disease can vary depending on the patient's age and immune status. In young children, the infection is often asymptomatic or mild, whereas older patients more frequently exhibit jaundice and signs of general intoxication. A key characteristic of Hepatitis A—unlike other forms of viral hepatitis—is that it does not progress to a chronic infection. Nevertheless, some patients may experience prolonged or relapsing symptoms, and in rare cases, severe liver failure may develop. Diagnosing Hepatitis A based solely on clinical signs is difficult; symptoms such as fever, malaise, loss of appetite, nausea, vomiting, abdominal discomfort, dark urine, and jaundice are also observed in other forms of acute viral hepatitis. Therefore, the etiological diagnosis must be confirmed through laboratory testing.

1. Clinical diagnosis of Hepatitis A

The incubation period of the disease typically lasts several weeks. Initially, during the prodromal phase, nonspecific symptoms such as general malaise, fever, headache, loss of appetite, nausea, and vomiting may appear. Subsequently, darkening of the urine, lightening of the stool, and jaundice (yellowing of the skin and sclera) may be observed. Some patients exhibit liver enlargement and a sensation of pain or heaviness in the right upper quadrant. While the presence of clinical symptoms provides grounds for suspecting Hepatitis A, these symptoms alone are insufficient for a definitive diagnosis. According to the CDC, Hepatitis A cannot be reliably

distinguished from other forms of viral hepatitis based solely on clinical or epidemiological features.

2. Diagnostic significance of biochemical tests

Biochemical blood tests are crucial for assessing liver function in patients suspected of having Hepatitis A.

Key indicators include:

- alanine aminotransferase (ALT);
- aspartate aminotransferase (AST);
- total and direct bilirubin;
- alkaline phosphatase;
- gamma-glutamyl transferase;
- albumin and total protein;
- prothrombin time or INR.

In acute Hepatitis A, a significant rise in ALT and AST levels—particularly high ALT activity—indicates liver cell damage. Elevated bilirubin levels constitute the biochemical basis for jaundice. At the same time, elevated ALT or bilirubin levels are not specific markers for hepatitis A. They indicate the presence of liver damage but do not independently determine the etiology of the disease. Therefore, biochemical markers should be evaluated in conjunction with serological or molecular tests.

3. Anti-HAV IgM — the primary serological marker

One of the most important tests in the modern laboratory diagnosis of hepatitis A is the detection of anti-HAV IgM antibodies (immunoglobulin M against the hepatitis A virus) in the blood. Anti-HAV IgM typically becomes detectable approximately 5–10 days before the onset of clinical symptoms and holds high diagnostic value during the early stages of the disease. In most patients, it persists for several months after the onset of symptoms.

A positive anti-HAV IgM result generally indicates an active or recent HAV infection.

However, evaluating diagnostic results in isolation from the clinical picture can be misleading. In some cases, anti-HAV IgM may persist for an extended period or, rarely, yield a false-positive result. For instance, immunological cross-reactions associated with certain other viral infections may occur. Therefore, positive results that are inconsistent with clinical signs and epidemiological data require cautious interpretation.

4. Diagnostic significance of anti-HAV IgG

Anti-HAV IgG antibodies develop after infection, persist for a long time—effectively for a lifetime—and indicate the presence of immunity.

Therefore:

anti-HAV IgG (+), anti-HAV IgM (-) — may indicate immunity resulting from a past infection or vaccination.

anti-HAV IgM (+) — indicates an acute or recent infection.

anti-HAV IgM (-), anti-HAV IgG (-) — indicates an absence of immunity against HAV.

The total anti-HAV test detects both IgM and IgG antibodies. Consequently, a positive total anti-HAV result alone cannot distinguish between an active acute infection and a past infection or vaccination.

5. PCR and HAV-RNA detection

Molecular diagnostics is a modern approach in laboratory testing for Hepatitis A. HAV-RNA can be detected in biological samples using reverse transcription polymerase chain reaction (RT-PCR). A significant advantage of this method is that viral RNA can be detected even before an immune response has developed. Therefore, PCR offers an additional diagnostic capability during the very early stages of infection. Detecting HAV-RNA is also crucial for epidemiological investigations. By genotyping and sequencing the viral genome, it is possible to determine the relatedness of viral isolates from different patients and to study the source of infection and transmission chains. It should be noted that PCR is not the primary test replacing anti-HAV IgM in all clinical situations. In routine diagnostics, anti-HAV IgM remains the key confirmatory marker, while PCR is employed as a supplementary method depending on available laboratory capabilities and the clinical context.

6. Differential diagnosis

When diagnosing Hepatitis A, it is important to rule out other viral and non-viral liver diseases.

Differential diagnosis is conducted against the following conditions:

1. acute hepatitis B;
2. acute hepatitis C;
3. hepatitis E;
4. drug-induced toxic hepatitis;

5. alcoholic liver injury;

6. autoimmune hepatitis;

7. biliary tract obstruction;

8. certain metabolic and hereditary liver diseases.

Therefore, in a patient presenting with jaundice, it is advisable not to limit testing to anti-HAV IgM alone but also to assess markers for other viral hepatitides and liver function parameters, depending on the clinical situation.

7. Comprehensive assessment of laboratory results

The most effective approach to diagnosing Hepatitis A involves the integrated assessment of clinical, epidemiological, biochemical, serological, and—where necessary—molecular data.

Test	Primary diagnostic significance
ALT/AST	Indicates liver cell damage
Bilirubin	Assessment of jaundice and cholestatic changes
Anti-HAV IgM	Primary marker for confirming acute/recent HAV infection
Anti-HAV IgG	Indicates past infection or immunity
Total anti-HAV	Indicates the presence of immunity but does not distinguish active infection on its own
HAV-RNA PCR	Direct detection of viral genetic material; useful for early diagnosis and epidemiological investigations
HAV genotyping/sequencing	Aids in the epidemiological study of infection sources and transmission chains

8. Modern diagnostic approaches and scientific advances

In recent years, diagnostic approaches for Hepatitis A have been shifting from reliance on a single laboratory marker toward an integrated diagnostic model.

The first key aspect is the interpretation of anti-HAV IgM results in conjunction with clinical and epidemiological data. Although IgM holds high diagnostic value, the possibility of false-positive results must be considered when findings do not align with clinical evidence. The CDC recommends the targeted use of anti-HAV IgM for patients exhibiting symptoms or clinical indications of HAV infection; routine use as part of general liver enzyme screening is not advised.

The second key aspect is the development of molecular diagnostics based on HAV-RNA detection. RT-PCR enables the detection of the virus prior to the development of an antibody

response. This is particularly important in cases of early-stage infection, epidemiological outbreaks, and complex diagnostic scenarios.

A third promising area is molecular epidemiology. Genotyping and sequencing of the HAV genome expand the capacity to identify sources of infection, confirm epidemiological links, and uncover hidden transmission chains.

Thus, the primary scientific and practical trend in modern diagnostics involves complementing serological testing with molecular methods and integrating laboratory results with clinical and epidemiological data.

Conclusion

Timely and accurate diagnosis of Hepatitis A is crucial for limiting the spread of the disease, properly managing the patient, and identifying sources of infection. While clinical symptoms may raise suspicion of Hepatitis A, laboratory testing is required to confirm the etiological diagnosis. Anti-HAV IgM remains the primary serological marker for confirming acute Hepatitis A, whereas anti-HAV IgG is important for assessing immunity resulting from prior infection or vaccination. Detection of HAV-RNA via RT-PCR offers significant added value during the early stages of infection, as well as in epidemiological investigations and genetic analyses. The optimal diagnostic algorithm incorporates clinical examination, epidemiological history, biochemical markers (such as ALT/AST and bilirubin), and anti-HAV IgM testing. The use of HAV-RNA PCR and genotyping, when necessary, expands diagnostic and epidemiological capabilities. Therefore, it is appropriate to base the modern model for Hepatitis A diagnosis on the following sequence: clinical suspicion → biochemical assessment → serological confirmation via anti-HAV IgM → HAV-RNA/PCR (if necessary) → differential and epidemiological analysis.

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