

## Diagnosis of Hepatitis

Is only HBsAg testing sufficient?



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### Background

Diagnosis is a vital decision point at which adequate evidence has to be accumulated to get a clear clinical picture about the patient before initiation of the treatment. Laboratory tests for hepatitis are very critical for the physician to confirm his findings about the clinical condition of the patient because of several causative agents of the disease.

Earlier, Hepatitis A virus was considered to be the sole causative pathogen for hepatitis. Infection with Hepatitis A being self limiting was never a fatal disease. Later discovery of Hepatitis B and because of its parenteral route of infection assumed importance, more so from a Blood Bankers point of view as this virus was infectious and could be transmitted through blood transfusion. Clinically also Hepatitis B needs to be treated with caution as it could lead to other complications of the liver. Subsequently Hepatitis C virus also assumed importance as its route of infection is also parenteral and equally harmful. Lately Hepatitis E has joined the list of viruses that cause hepatitis, though not so harmful as the disease progression is similar to that of A. , studies have exposed the high occurrence of HAV and HEV co-infection cases in India which has been implicated as one of the major causes of acute hepatic failure especially in pediatric patients.

With hepatitis being caused by the virus A, B, C, and E diagnosis is even more complicated as all of them present similar symptoms. Therefore laboratory testing is important to identify the exact causative virus so that the appropriate treatment can be initiated accordingly.

### Common trend of Diagnosis

#### Biochemical test Profile

Parameter	Normal Values*	Elevated values*	Remarks
Bilirubin	Direct : >0.2mg/dl	>0.25mg/dl	Elevated results suggest inflammation of liver or 'Hepatitis' only but do not indicate about the causative agent for the inflammation.
	Total : > 1.0mg/dl	>1.8mg/dl	
ALT	5-35U/ml	>45U/ml	
AST	8-40U/ml	>50U/ml	
ALP	Adult : 8-290U/L	>348U/L	
	Children: 245-770U/L	>924U/L	
If above biochemical markers are high then patient is tested for HBsAg, to rule out the Hepatitis B infection.			

\* Ref. No. 3

### Why differential diagnosis is important?

Hepatitis is caused by A, B, C or E virus and relying only on the above method of diagnosis is insufficient to pin point the exact causative pathogen. Since the clinical symptoms and biochemical markers result are alike in all acute viral hepatitis; a quick and accurate therapeutic decision can not be made. Even more HBsAg test is not sufficient because this marker itself has limitation as a HBV detection marker in acute stage of disease. At this point a definitive diagnosis of viral hepatitis by immunological markers has gained importance.

### Importance of HEV detection

Both HAV and HEV have similar pathogenesis and hepatitis by these both viruses almost invariably resolves after acute infection. So diagnosis by clinical symptoms and biochemical markers is difficult. But HEV may be severe in certain cases, especially in pregnant women. The reason behind this occurrence is still unknown.

Further more Hepatitis A and E viruses were found to be associated with 60% of the cases of acute liver failure in a recent study involving a group of pediatric cases admitted to the All India Institute of Medical Sciences in New Delhi, India. In that study, possible co-infections with hepatitis A virus (HAV) and HEV have been implicated as the single largest viral infection causing acute hepatic failure and sporadic fulminant hepatitis in India.

National Institute of Virology, Pune has investigated 100 outbreaks of HEV in India and has reported 1-5% Voluntary donors in Pune positive for HEV. That's indicates transfusion associated Hepatitis E may occur in endemic countries.

In fact HEV may also become a probable threat to blood recipients as reported by NIV Pune and need to be tested as a part of blood donor screening in the near future. Therefore HEV as a test is for acute viral hepatitis is becoming very crucial.

### Complications in HBV and HCV diagnosis

The situation is more complicated in HBV and HCV because of its fatality. Both HBV and HCV can produce a wide spectrum of liver diseases, from a subclinical carrier state to severe or fulminant acute hepatitis. 5 to 10% of all patients with HBV develop chronic hepatitis or become inactive carriers, where as HCV has the highest rate of chronicity (about 75%). Cirrhosis can develop in both cases. Hepatocellular carcinoma can ultimately develop in chronic infection, even without being preceded by cirrhosis.

Even testing for HBsAg is not enough to rule out HBV infection, since in 10-15% of infected patients report HBsAg negative in the acute phase of infection.

In addition, up to 20% of patients with alcoholic liver disease harbor HCV. The reasons for this high association are unclear, because concomitant alcohol and drug use accounts for only a portion of cases. In these patients, HCV and alcohol act synergistically to worsen liver damage.

It is now well established that all four virus viz A, B, C and E can cause Hepatitis but the etiologies of respective viruses are diversified so diagnosis by bio chemical markers and HBsAg is nothing but practicing a game of chance today. It is essential to isolate the exact causative pathogen and differential diagnosis is the only practical way for the same. Some immunological tests are significant to detect relevant serological markers of respective viruses.

### Approach for Differential diagnosis of Hepatitis

Early detection of the specific virus is only possible by detection of serological markers of respective viruses through immunological tests. These diagnostic tests can help in detecting the specific causative virus and can aid in initiating the right treatment.

An ideal approach for detection of specific virus has been discussed below.

#### Immunological Tests Panel:

- Anti HAV - IgM
- Anti HEV - IgM
- HBsAg
- Anti HBc
- Anti HCV

Test Markers	Hepatitis A	Hepatitis E	Hepatitis B	Hepatitis C	Remarks
Anti HAV IgM	+				HAV infection
Anti HEV IgM		+			HEV infection
HBsAg Anti HBc			+ -		Suspected HBV infection, repeat after one month
HBsAg Anti HBc			+ +		Confirmed HBV infection
HBsAg Anti HBc			- +		Confirmed HBV exposure or HBV infection with remission of HBsAg
Anti HCV				+ / -*	HCV exposure or infection

In the initial phase of acute hepatitis C, antibodies to HCV detection may be negative due its prolonged serological window period. Repeat the test after 90 days if suspected. \*

Positivity of the specific marker indicates the infection of specific virus. Multiple markers may be present in case of co-infection. All negative tests indicate the non viral causes of the hepatitis disease. Positivity of Anti HCV confirms the exposure only and does not distinguish between an acute, chronic and resolve infection.

For confirmation of the current HCV infection and monitoring of HCV disease prognosis or effectiveness of the antiviral therapy, measuring viral load by HCV RNA -assay or PCR is the only way.

### Why Anti HBc test is also important along with HBsAg for detection of Hepatitis B infection?

Positivity of Anti HBc confirms exposure to HBV. At the onset of illness, HBsAg will have reached its peak concentration and it is eliminated with a half life of approximately 9 days. Due to this in 5 % cases HBsAg may be negative at the onset of clinical symptoms. In such situation the acute disease can only be diagnosed by the detection of antibodies to Hepatitis B core antigen (Anti HBc).

### Conclusion

Diagnosis of acute viral hepatitis can no longer be restricted to detection of only HBV by HBsAg test as is the practice. HCV is also a growing hazard which can be damaging or fatal in chronic cases. With HEV joining the list of causative pathogens the medical fraternity has to deal with a more complex disease than it is assumed to be.

It is therefore necessary to screen a patient for HAV, HBV, HCV and HEV as a first line approach in diagnosing acute viral hepatitis and putting him/her on to a correct course of treatment. For Hepatitis B positive patient HBV markers like HBeAg, HBeAb, HBAb tests are essential for monitoring the disease prognosis.

Today all the above tests are available in a rapid format with good sensitivity, specificity and are simple to perform. With the availability of these tests medical practitioners can easily pin point the exact causative pathogen without having to wait to decide the correct line of treatment.

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