# Clinical relevance of hepatitis B core total antibody in the detection of occult hepatitis B infection in patients with liver disease and blood donors

Sir,

Recently, occult hepatitis B virus infection (OBI) has drawn much attention, because such patients are hepatitis B surface antigen (HBsAg) negative but are potentially infectious because of the presence of hepatitis B virus (HBV) DNA in the blood of infected patients.[1] Furthermore, in many developing countries including India which is moderate endemic for HBV infection, screening of blood donors for HBV is only done by HBsAg alone. The prevalence of OBI in blood donors has been confirmed from different geographic areas and ranges from <1% to 16% depending on the endemicity of HBV infection.[2] Molecular testing is not routinely performed in laboratory and in blood banks because these are not cost-effective testing. Our objective was to find out the prevalence and importance of anti-HBc as a predictive marker of occult hepatitis B (who are usually HBsAg negative) infection in patients with liver disease and in healthy blood donors. This prospective study was done over a period of 5 months (September 2015–January 2016) in a tertiary care liver hospital. All the patients with liver disease who were screened for HBV infection in the outpatient and inpatient department were enrolled. Furthermore, all the age-matched healthy blood donors coming to the department of transfusion medicine and fulfilling the general criteria for blood donation as per the Drugs and Cosmetics Act, 1940, during the study period, were included as the control group. Both the patients with liver disease and blood donors were screened for HBsAg test. HBsAg-positive patients with liver disease and blood donors were excluded and HBsAg-negative individuals were included in the study. HBsAg-negative patients with liver disease and blood donors were further tested for anti-HBc and anti-HBs. All tests were performed by a chemiluminescence microparticle assay (ARCHITECT i2000SR Immunoassay Analyzer, Abbott Diagnostics, Germany). Among anti-HBc-positive individuals, detection of HBV-DNA was also performed. Samples with HBV-DNA load 6 IU/mL or more than 6 IU/mL were considered as HBV-DNA positive. "Probable" OBI was defined as the presence of anti-HBc alone (anti-HBc positive, HBsAg negative, and anti-HBs negative). "Confirmed" OBI was defined as the presence of HBV-DNA ≥6 IU/mL in probable OBI cases. One thousand one hundred and twelve patients with liver disease and 970 healthy blood donors who were HBsAg negative were included in the study. The mean age ± standard deviation of the study population

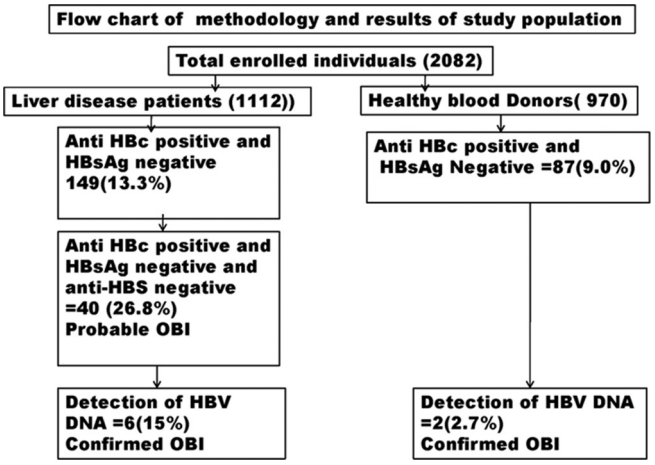


**Figure 1:** Work algorithm. HBV = Hepatitis B virus, Anti-HBc = Hepatitis B core total antibody, OBI = Occult hepatitis B virus infection, Hbs Ag = Hepatitis B surface antigen, anti-HBS = Antibody against hepatitis B surface antigen

**Table 1: Baseline characteristics and underlying etiology of the study population**

| Parameters | *n* (%) |
|---|---|
| Mean age±SD | 76 (50.66) |
| Gender (male:female) | 3:1 |
| Healthy blood donors | 970 |
| Patients with liver disease | 1112 |
| LFT of patients with liver disease | |
| AST (5-35 IU/l) | 70.44 |
| ALT (7-56 IU/l) | 105.11 |
| ALP (38-126 IU/l) | 200.66 |
| Total bilirubin (0.3-1.2 mg/dl) | 1.7 |
| Total albumin (6-8 g %) | 6.7 |
| Underlying etiology of patients with liver disease | |
| CLD | 76 (50.66) |
| ACLF | 16 (10) |
| AVH | 14 (11) |
| Family screening | 18 (12) |
| Health-care checkup | 6 (3) |
| Nonalcoholic steatohepatitis | 8 (5.3) |

SD=Standard deviation, LFT=Liver function test, AST=Aspartate transaminase, ALT=Alanine transaminase, ALP=Alkaline phosphatase, CLD=Chronic liver disease, ACLF=Acute-on-chronic liver failure, AVH=Acute viral hepatitis

was 47.6 ± 8.0 years with male-to-female ratio of 3:1. Baseline characteristics of the study population and underlying etiology of patients with liver disease are detailed in Table 1. Among HBsAg-negative individuals, the prevalence of anti-HBc seropositivity was seen in 149 (13.3%) patients with liver disease and 87 (9%) healthy blood donors ($P$ = 0.36). The prevalence of anti-HBc positive with anti-HBs negative, i.e., only anti-HBc positivity, was seen in 40 (26.84%) patients with liver disease, indicating probable OBI. Of them, confirmed OBI by the detection of HBV-DNA was seen in 6 (15%) patients with liver disease. HBV-DNA ranged from log 2.19 to 4.93 IU/ml with median log value of 3.16 IU/ml. Of relevant note, 2 (2.7%) healthy blood donors with anti-HBc seropositivity also had HBV-DNA positivity with median log value of 2.65 (0.77–3.16) IU/ml. True OBI was seen significantly in more patients with underlying liver disease (15%) than healthy blood donors (2.7%; $P$ = 0.01). Workflow algorithm is shown in Figure 1.

The present study has primarily assessed the clinical significance of anti-HBc alone as a representative marker of OBI in different population groups. In developing countries including India, HBsAg test is the primary way to definitively diagnose chronic HBV infection, but this can miss a large number of occult HBV infections, because the patients having occult HBV infections are HBsAg negative.[3] Anti-HBc is a cost-effective serological marker in comparison with molecular testing like HBV-DNA and important marker to screen for underlying occult HBV infection and must be done along with HBsAg screening. The frequency of posttransfusion HBV infection is apparently due to the fact that HBsAg is in circulation at very low and undetectable level for screening assays. HBsAg screening must be practiced for blood safety as well as robust screening of asymptomatic cases for HBV infection. Prevalence of anti-HBc ranges from 8% to 18% in the blood donor population in different part of India. In a recent study by Panigrahi *et al*., it was found that out of 220 blood donors nonreactive for HBsAg, anti-HBc was positive in 30.1% of population.[4,5] Testing blood donors for anti-HBc will minimize transfusion-associated hepatitis, but will increase the service charges of blood products. In resource-poor setting where the nucleic acid testing (NAT) is not available, inclusion of anti-HBc testing for donor screening is more cost-effective than treating posttransfusion hepatitis. Although a large number of donations will be rejected, rejection of these donations will be valuable in reducing the risk of HBV transmission with its potential consequences, particularly among immunocompromised recipients. In blood banks with NAT testing available, anti-HBc additional testing will help confirm the occult hepatitis in transfusion patients and to counsel them from the complication of liver disease. We recommend universal inclusion of anti-HBc testing along with existing HBsAg testing in the screening of liver disease patients and healthy blood donors.

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## Conflicts of interest

There are no conflicts of interest.

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