Incidence of anti-HBc antibody (IgG and IgM) among HBsAg negative apparently healthy blood donors

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Abstract

In person who is unable to produce HBsAg, anti-HBc antibody is a helpful marker of hepatitis B virus (HBV) infection. In the present study, we have tried to find out the incidence of anti-HBc (IgG and IgM) among blood donors HBsAg negative. People came for donating blood voluntarily or for their relatives (n = 1000) was selected on inclusion and exclusion criteria. Purposefully selected and collated samples were first tested by HBsAg ELISA of third generation reagent. HBsAg negative sample was tested with anti-HBc ELISA. Positive found in the first test was retested. Out of 1,000 samples on duplicate test, 117 positives were detected. The incidence of anti-HBc antibody among apparently healthy blood donors was found 11.7%.

Introduction

HBsAg is the first marker to appear in the blood, which persists, throughout the period of infectivity and eventually marks for chronic infection.[1,2] In chronic carrier, HBsAg is eventually lost and replaced by anti-HBS. But within this, there is a period (diagnostic not detected by HBsAg window).[3] But anti-HBc antibody is detected in all persons who are infected with Hepatitis B virus (HBV).[4] In acute infection, high levels of IgM anti-HBc appear which persist for 3-4 months and are then replaced by IgG anti-HBc. High titer of IgG anti -HBc can be found in carriers. During the recovery phase of acute hepatitis B, anti-HBc may be present in the absence of HbsAg and anti-HBS.[5] Donations during this time (window period) can transmit HBV (tail end carriers).[6,7] Anti-HBc may be the only circulating marker in such individual and they may only be identifiable by anti-HBc screening or by anti-HBc and HBsAg screening. In addition, anti-HBc screening having value in the detection of HBV infected donor who have mutant HbsAg not detectable by some HbsAg assay. In a small proportion of carriers, only anti-HBc can be detected in the plasma. Such subjects may transmit HBV by transfusion.[8]

In acute infection, high level of IgM anti-HBc have been found which persists for 3-4 months and then replaced by IgG anti-HBc. High titer of IgG anti-HBc can be found in carriers who may have low levels of IgM anti-HBc. So, mixed IgG and IgM assay is beneficial. It will detect both acute and chronic infection.

If anti-HBc can be detected in the plasma, such subjects may transmit HBV by transfusion. Subjects infected with HBV may be HBsAg negative due to point mutation in the precore region which may result in inability to synthesize HBsAg. Fulminant HBV infection developed in recipient of HBsAg negative blood from donors infected with this mutated virus. In all these donors, high levels of anti-HBc are present.[9]

About 50% of cases of HBV that could be transmitted by blood from HBsAg negative donors can be prevented by screening for anti-HBc.[4]

So, anti-HBc screening, in addition to HBsAg, may help in reducing HBV transmission by transfusion.

Materials and Methods

This cross-sectional study was conducted from July 2015 to June 2016. One thousand cases of HBsAg ELISA negative samples of blood donors (properly selected on inclusion and exclusion criteria and properly screened for human immunodeficiency virus (HIV), hepatitis C virus (HCV), HBsAg, syphilis and malaria by rapid immunochromatographic tests) were included.

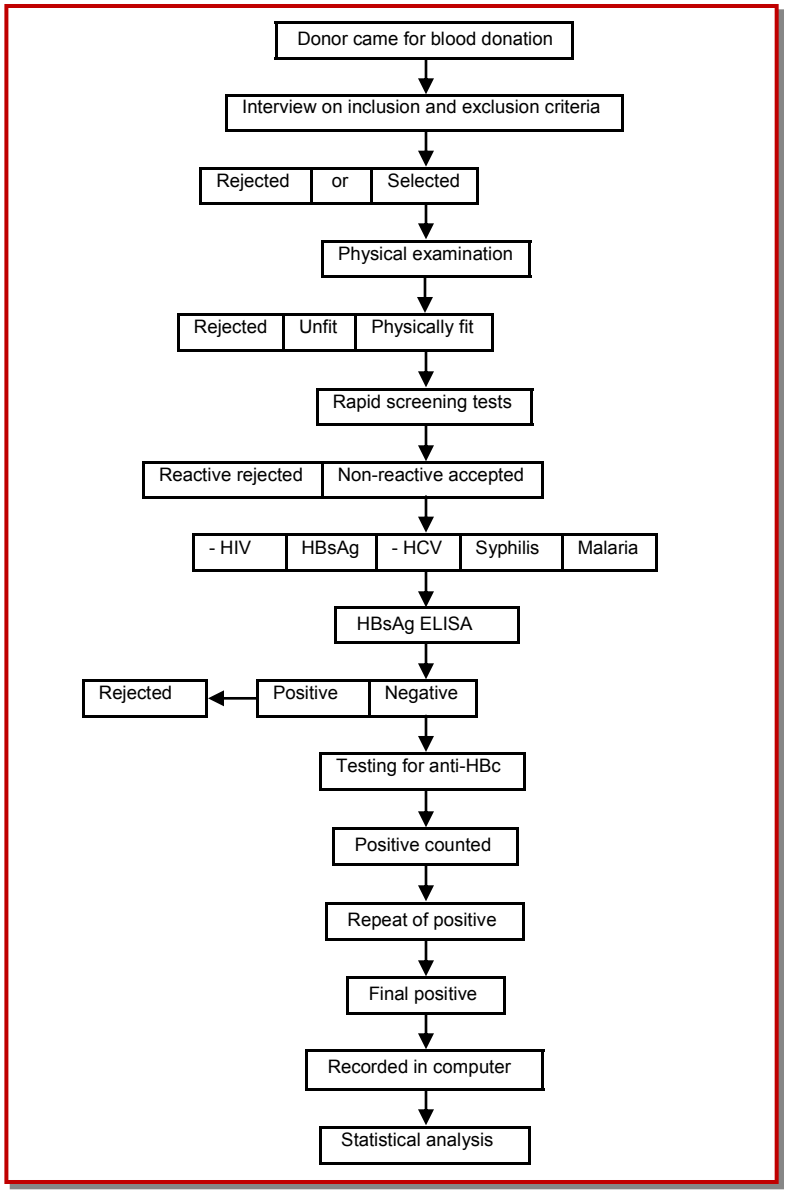

Figure 1: Study design

Inclusion criteria were a) Adult blood donor within the age limit of 18-60 years, b) Donors may have previous history of jaundice, but now physically fit for donation, c) Weight above 45 kg, d) Hemoglobin value >12 g/dL, e) Oral temperature of 97-99°F, f) Blood pressure systolic 100-200 mm Hg and diastolic 60-100 mmHg without drug, g) Pulse 60-100/ min, and h) HBsAg negative by ELISA.

Exclusion criteria were a) Under age 18 years and over 60 years, b) Weight less than 45 kg, c) cardio-vascular diseases, d) History of surgery within one year with blood transfusion, e) History of blood transfusion for one year, f) Acupuncture, tattoo, ear or body piercing within 6 month and g) History of any known exposure to HBV and risk factor.

The selected donors by interview with the help of a written questioner was then examined for physical fitness for donation was determined (Figure 1). These selected donor samples were collected in a 4" test tube with a identification serial number 5 mL of whole blood collected and left for 24 hours at 4°C. Thereafter, the serum samples were separated and kept in Eppendrof tube and stored at below -20°C. When more than 90 samples were collected, they were tested for HBsAG-ELISA. For HBV, HIV, HCV, malaria and syphilis, departmental usual rapid screening process was followed.

ELISA testing for HBsAg

HBsAg was tested by ELISA method using commercial ELISA reagents of One step ELISA-HBsAg of Delta Biologicals, Italy of 3rd generation (sensitivity 100% and specifity 99.5%) Company's instruction was fully followed. HBsAg positive samples were disposed and new samples were included in the study with the same serial identification number. This is the final sample. Information about samples was noted in computer especially HBsAg and H/o jaundice.

ELISA testing for anti-HBc antibody

It was done with ELISA reagents of JAJ, USA. Samples positive were repeated. Repeated positives were taken as positive. Sensitivity of the reagent was not clearly cited in literature. Company's instructions were followed.

Results

Most of the donors (n = 963) belonged to age group of 18-30 years (Table I). Similarly, 91.5% were males. About 50% were students.

Out of 1000 samples on duplicate test 117 samples were found positive for anti-HBc (IgG and IgM). The incidence was 11.7 percent. History of jaundice was found more among males (3.6%) than females (1.2%).

Anti-HBc antibody was found more among donors with the history of jaundice (3.3%) than that of females (0.3%). Donors having anti-HBc positive but no history of jaundice was among males 7.2% and among females 0.90 percent.

Discussion

Anti-HBc is found in all persons infected with HBV. Anti-HBc detects mainly HBV infection at diagnostic window period. It is only the HBV marker at the recovery phase of acute HBV infection. Anti-HBc is produced in the plasma shortly after HBsAg and remain in the circulation for 3-4 months. It may be

Table I

Parameters of patients

Parameters	n
Age (years)	
18-30	963
31-60	37
Sex	
Male	915
Female	85
Occupation	
Student	515
Business	198
Private job	133
Government job	87
Physical labor	54
House wife	13

the only marker present in window period. It may be the only marker present in mutant HBV infection. HBsAg negative person but-HBc positive does not require vaccination. Highly sensitive HBsAg ELISA cannot detect mutant HBsAg, Here- HBc is the only marker except DNA. HBV can be transmitted by many other ways like blood transfusion, surgery, dental procedure, long contact with a HBV infected person, etc. Family history is an important risk factor. These risk factors were excluded in this study by donor selection process. In acute infection, high level of IgM anti-HBc is present which is replaced by IgG anti-HBc. High titer of IgG anti-HBc can be found in carriers in the absence of HBsAg and anti-HBS. Donations taken at this period may cause PTH. In a small proportion of carriers only anti-HBc can be detected in plasma. Such subjects can transmit HBV by transfusion. So, in addition to HBsAg, anti-HBc can detect HBV infection in blood transfusion donor. In present study, highly sensitive HBsAg ELISA reagent (sensitivity 100%) was used. All noticeable risk factors were excluded from donors except history of jaundice, then anti-HBc was tested incidence found was 11.7%. Incidence was higher among aged donors than the young donors and the male than female. High incidence was among the illiterate person. World wide prevalence/incidence having different figure. In Pakistan it is 17.3%.[10] In Spain, it is 4.8% among >65 years of donors. In literature, it is found that the isolated prevalence of anti-HBc is supposed to be 4-50% depending on sensitivity of reagent, age of donor. But the incidence of false positive is 11-3% found in 20 years prospective study. In North-West Greece, the incidence is 15.8%.[11] In Italy identified mutant HB anti-HBc prevalence is 4.8.[11] They proposed not to use mutant HB donor blood for transfusion.

Now the question is whether can we propose to include anti-HBc as screening test in addition to HBsAg As, the reagent require repeated test, single test will loss huge number of valuable donors. There is no more record in our country about actual incidence/prevalence of anti-HBc. So, we cannot propose to include anti-HBc as screening of blood donor in addition to HBsAg. Now HB NAT is a alternative. But it require research about the new screening method. The cost of anti-HBc per test is not very high. But HBNAT is costly. But only HBsAg is not sufficient.

We will have to decide which will be included or added in addition to HBsAg, HBsAg may be added to NAT or anti-HBc. In India, They are trying to include NAT with HBsAg. But NAT plus anti-HBc greatly raise blood safety[12] but of high cost. There is another benefit, about 50% of cases of HBV transmitted from HBsAg negative donors can be prevented by using anti-HBc testing. It is usually due to mutant HBV transfusion from HBsAg negative donor.[12] A study about mutant HBV patient is essential.

Conclusion

The prevalence of anti-HBc Ab was high (11.7%) in Bangladeshi blood donors.

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