Original Article

The Role of anti-HBc IgM in Screening of Blood Donors

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Abstract

Background: Transfusion transmitted hepatitis B has always been a dreaded disease, with incidence of increased transmission through donated blood. The screening test for hepatitis B infection is detection of HBsAg that does not rule out the risk of transmission of hepatitis B as the donor may be in the 'window period'. During this period, detection of the antibody to the hepatitis B core antigen (anti-HBc) IgM type serves as a useful serological marker. The aim of this study was to screen blood donors for anti-HBc type IgM and anti - HBc Ag total for detection and to find their incidence amongst blood donors.

Methods: 2552 voluntary blood donors were screened by the ELISA method for HBsAg and anti – HBc IgM and other mandatory screening markers. 704 of the test blood samples were also screened for anti-HBc total.

Result: Of the 2552 donor, 47 (1.84%) cases were HBsAg positive. A total of 11 (0.43%) blood units were reactive for HBcAg IgM and of these, 10 (0.39%) were HBsAg negative and reactive for anti-HBcAg IgM. Of the 704 samples tested for anti – HBcAg total, 112 (15.9%) samples were reactive.

Conclusion: Screening of blood for anti-HBc total is practical in the western world as the incidence of HBsAg and anti-HBc is low in these countries and these positive blood units for anti – HBcAg total can be discarded. This may not be practical in India as the incidence of anti– HBcAg total is high in our population. It is recommended that all blood units should be tested for anti – HBc IgM for infectivity status of the blood donors in the window period and to discard blood if positive.

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Key Words : Window period; Hepatitis B surface antigen; Anti hepatitis B core antigen

Introduction

Transfusion transmitted hepatitis B has always been a dreaded disease, which has an unholy reputation of being transmitted fairly often through donated blood. The discovery of the hepatitis B surface antigen (HBsAg) was a major breakthrough in decreasing the incidence of post transfusion hepatitis. Following infection by the hepatitis B virus (HBV), the first serological marker to appear in the blood is the HBV DNA, followed by HBsAg, the DNA polymerase and the hepatitis B 'e' antigen (HBeAg). Thereafter, the antibodies to the hepatitis B core antigen (anti-HBc), hepatitis B 'e' antigen and the HBsAg can be detected. Screening of donated blood by enzyme-linked immunosorbent assay (ELISA) for HBsAg is the common method for detecting hepatitis B infection. Screening of blood for the detection of this viral marker, however, does not rule out the risk of transmission of hepatitis B totally, because during the host serological response to infection, there is a phase during which the HBsAg cannot be detected in the blood although hepatitis B infection is present. This phase is called as the 'window period'. It represents a carrier state of the disease. Therefore a definite hazard of transmission of hepatitis B to recipients of such units of donated blood exists. During this 'window period', detection of the antibody to the hepatitis B core antigen (anti-HBc) serves as a useful serological marker for hepatitis B infection. The IgM class of the anti-HBc is the first to appear, and indicates a recent infection. The IgG variety of anti-HBc appears later during the infection and points to a past HBV infection. Individuals with IgG variety of anti-HBc may not be infectious as they may have sufficiently high titres of antibodies to HBsAg (anti-HBs), which are protective in nature and the affected individuals may actually be disease free. With the fairly high incidence of HBsAg in India, there is a definite risk of inadvertently transfusing HBV infected blood. It is therefore strongly felt that a marker must be utilized for screening of blood in the Indian population to detect the presence of hepatitis B during the window period [1,2]. The aim of this study was to screen blood donors for anti-HBcAg antibody of the IgM type and to find the incidence of antibodies to hepatitis B core antigen IgM type (anti-HBcAg IgM) in our subject population of blood donors.

Material and Methods

This study was conducted at the Blood Bank of Armed

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Forces Medical College where 2552 voluntary blood donors were studied. The blood donors were selected after they fulfilled the mandatory criteria for donation eligibility as per the guidelines laid down for blood banks in the gazette notification by the Government of India. At the time of blood donation, 5 ml of venous blood was collected in a clean sterile glass tube for screening for transfusion-transmitted diseases. The screening was done the same day, else, the blood sample was centrifuged and the serum was kept in a refrigerator at 4°C. These samples were tested the next day along with the fresh samples of that day. All the blood samples were subjected to the mandatory screening tests for detection of transfusion transmitted diseases. The blood was tested by the ELISA method for anti-HIV 1 and 2, anti-HCV, HBsAg, VDRL and malaria. The ELISA test used for detection of HBsAg had sensitivity of 0.2 ng/ml. The screening of the donated blood units for anti-HBcAg IgM by the ELISA method was done over and above these screening tests. Testing for anti-HBcAg IgM was performed using the anti-HBc IgM IEMA well kit manufactured by Radim, Italy. In addition, 704 of the test blood samples were also screened for anti-HBcAg total by the ELISA method using kits manufactured by Radim, Italy for evaluating the incidence of anti-HBcAg total amongst our blood donors and comparison with the anti-HBc IgM.

Results

A total of 2552 voluntary blood donors were studied, of which 47 (1.84%) cases were HBsAg positive. A total of 11 blood units tested reactive for anti-HBcAg IgM and of these, one was HBsAg positive and 10 were negative, giving a positivity rate of 0.43% amongst the total of 11 anti HBcAg IgM reactive blood donors, and 0.39% amongst the 10 HBsAg negative anti-HBcAg IgM reactive blood donors.

For determining the incidence of anti-HBcAg total amongst the blood donors, 704 blood donor samples were tested and 112 of these samples were reactive for anti-HBcAg total. The incidence of anti-HBcAg total in our blood donor population was therefore pegged at 15.9%. The blood units negative for HBsAg but positive for both anti-HBcAg total and anti-HBcAg IgM are shown in Table 1.

Discussion

The transmission of hepatitis B following transfusion of blood / blood products containing antibody to the hepatitis B core antigen was first described by Hoofnagle in 1978 [1]. The most widely used marker for diagnosing HBV infection in donated blood is by screening it for HBsAg. However, HBsAg is not detected during the window period of the infection. Therefore, transfusion of blood collected from a donor who is in the window period may lead to post transfusion hepatitis B in the recipient [3,4]. A marker which would be indicative of hepatitis B infection during the window period, is therefore of paramount importance in blood banking. Anti-HBc has been found to be an excellent indicator of occult HBV infection during the window period [1-3]. Other markers for detecting occult HBV infection in an HBsAg negative blood donor such as detection of HBV DNA by polymerase chain rection (PCR) may not be cost effective [5]. Detection of anti-HBc has contributed significantly in reducing the incidence of post transfusion hepatitis B amongst patients [6-8].

Table 1

Results showing reactivity of blood samples for anti-HBc total

Blood samples tested for anti-HBcAg total	Samples positive for anti-HBcAg total	Samples positive for both anti-HBcAg total and anti-HBcAg IgM
704	112 (15.9%)	3 (0.42%)

The prevalence of anti-HBc in the prospective blood donors is proportional to the incidence of HBsAg in the general population. It varies greatly in different ethnic groups and geographical locations. It is higher among groups known to be at increased risk of HBV infection e.g. intravenous drug abuse, sexual promiscuity, low economic status, health care workers etc [2,8]. In India, the incidence of anti-HBc amongst blood donors ranges from 17-29% [9,10].

The sero-prevalence rate of anti-HBc IgM in the general population in our country is not available. Earlier studies done in India for estimation of anti-HBc amongst blood donors have used kits, which estimate anti-HBc total (i.e. both IgG and IgM). Makroo et al [11], pegged the prevalence of anti-HBc total amongst blood donors in New Delhi at 11.6%. Anti-HBc IgM is a marker of recent infection, whereas, anti-HBc IgG positivity indicates a past infection. Anti-HBc IgG may remain positive for life in an affected individual although the individual has protective levels of anti-HBs and therefore, this does not necessarily mean that blood of such a donor is infectious. So, anti-HBc IgM is considered to be a more specific marker for HBV infection during the window period [12,13]. As the western countries have a low incidence of HBsAg, the prevalence of anti-HBc in their blood donors is also low. The blood banks in the western countries therefore prefer to screen blood units using kits estimating anti-HBc total as all blood units would get screened for HBV infection. As the prevalence of anti-HBc in these countries is not high, there would not be any significant wastage of blood units. Studies have shown that all blood units reactive for 'anti-HBc alone' may not be infectious, especially if the donor sera have adequate titres of protective anti-HBs [7,14]. Blood from such donors has been evaluated and found suitable for transfusion. This not only encourages voluntary blood donation, but also helps in increasing the inventory of blood units available for stocking in the blood bank [15]. In India, however, as the prevalence of

anti-HBc is quite high, screening donor blood for anti-HBc total may not be practical.

The incidence of HBsAg amongst our blood donors was 1.84%. We had one case, which was positive for both HBsAg and anti-HBc IgM, which was not included in this study. The balance of 10 HBsAg negative but anti-HBc IgM positive cases, were included in this study. The percentage of potentially infectious blood units identified is lower and realistic. A positivity of 15.9% as seen by anti-HBc total is unacceptably high as compared to 0.43 % as seen by anti-HBc IgM. This blood bank would have been forced to discard an unacceptable number of blood bags screened positive for anti-HBc total, which perhaps would have been non infectious. Screening of blood for anti-HBc total is practical in the western world as the incidence of HBsAg and anti-HBc is low in these countries. They can afford to discard such blood units positive for these screening tests. This may not be practical in India. It is therefore recommended that all blood units should be tested for anti-HBc IgM to see the infectivity status of the blood donors in the window period in this country.

Conflicts of Interest

None identified

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