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Testing Donor For Anti HbcIgM to Enhance Blood Safety

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Blood transfusion is a life-saving intervention and millions of lives are saved each year globally through this procedure. However, blood transfusions are associated with certain risks which can lead to adverse consequences. It may cause acute or delayed complications and carries the risk of the transmission of infections (1).

Unsafe blood remains a major threat for the global spread of transfusion transmissible infections (TTIs). There is a long list of viruses, parasites and bacteria, which can be transmitted through blood transfusions. Amongst them, important ones are human immunodeficiency virus (HIV-I/II), hepatitis B virus (HBV), hepatitis C virus (HCV), syphilis and transfusion associated malaria infection. The magnitude of TTI varies from country to country depending on the prevalence of these infections in the population from where the blood units are sourced. There is a risk of 1–2 per 1000 recipients receiving contaminated blood with viral, bacterial or parasitic agents (2).

Amongst the viruses HBV presents a higher residual risk of transmission by transfusion than HCV or HIV (3). The current residual risk of HBV has been reported to be more than 20 fold higher than that for HIV and HCV. Also this risk is 5 times higher for countries with moderate to high prevalence of HBV as compared to countries with low prevalence (4). The high residual risk of HBV transfusion is mainly related to blood donations that have been carried out either during the pre-seroconversion window period or during stages of occult HBV infection (5,6). Concealing of medical history by paid or professional blood donors, who widely exist in developing countries, also pose a great threat to safe blood supply.

If we look at the Indian scenario, despite mandatory screening for HBsAg for more than 20 yrs, transfusion transmitted HBV continues to be a major problem, more so in patients receiving multiple transfusions, like thalassemics, hemophiliacs, those suffering from hematological malignancies, undergoing cardiac surgery or dialysis. Transfusion associated-HBV (TAHBV) is estimated at approximately 1.5 percent in postsurgical recipients and 50 percent or more in multiple-transfusion recipients in India. (7).

It has been demonstrated that some HBsAg negative individuals and those reactive for Anti-Hbc continue to replicate HBV (8). Thus the absence of HbsAg in the blood of apparently healthy individuals may not be sufficient to ensure lack of circulating HBV. Blood containing Anti-Hbc with or without detectable presence of HBsAg might be infectious; therefore routine blood donor screening for Anti-HBc was introduced in some countries resulting in a decrease in the risk of post transfusion HBV infection (9).

Anti-Hbc testing is still not mandatory in blood banks in India and only HbsAg testing is used as screening test for HBV.

I. Aims And Objectives

The present study was undertaken by the department of Microbiology of SGGRIM&HS along with Blood Bank of the Institute, with the aim of evaluating the use of Anti-HBc IgM as a routine donor screening tool for enhancing blood safety and preventing post transfusion hepatitis B.

The objectives of the study were

To estimate the prevalence of hepatitis B surface antigen in blood donors. To estimate the prevalence of hepatitis B core antibody (Anti-HbcIgM) in blood donors and evaluate its effectiveness as a donor screening tool.

II. Material Methods

The present study was carried out over a period of 12 months from September 2013 to August 2014. The donors were either voluntary or replacement. Voluntary donations were taken in the blood banks or at voluntary blood donation camps. Replacement donors were either relatives or friends of patients. All prospective donors were asked to fill the donor questionnaire form. Consent for blood donation and infectious marker testing was obtained at the time of donor selection. A detailed history and clinical examination was carried out for all the donors by qualified staff trained to screen donors for blood donation. This is a descriptive

cross-sectional study. The blood donors were selected after they fulfilled the mandatory criteria for donation, as per the Drugs and Cosmetics Act, 1940 and the amendments there of (10).

Sample Collection and processing

As part of standard protocol, two samples were collected from all blood donors in vacutainers, after 350 ml of whole blood donation. One clotted sample for infectious diseases screening and another sample in an EDTA tube for blood grouping. The screening was done either on the same day or else, the blood samples were centrifuged at 3000 rpm for 10 min, serum separated and kept in the refrigerator at -18◦ C or lower.

All the blood samples were subjected to the mandatory screening tests for detection of transfusion transmissible diseases. The blood samples were tested by the ELISA method for anti-HIV 1 and 2, anti-HCV, HBsAg. RPR method was used for syphilis and rapid card test for malaria. Test for Anti-HBcIgM was done by Chemiluminescence method for all blood donors who were HbsAg negative (Fig 1)

Test for HBsAg was done by ELISA method using Monolisa™ HBsAg ULTRA manufactured by BIO-RAD, France and test for anti-HBcIgM was done using VITROS Anti-HBc IgM assay, Orthoclinical Diagnostics, Rochester, New York, performed on the VITROS ECi Immunodiagnostic System as per manufacturer's instructions.

III. Results

A total of 2,488 healthy blood donors were recruited for this study.

Average age of donors was 27.4yrs. Majority of donors were between 18-30 years of age(52.57%). A decreasing trend of donation was seen with increasing age.

Amongst the donors 2,275 (91.44%) were males and 213 (8.56%) were females(Fig 2). Majority were voluntary donors (68.01%) while the rest were replacement donors (31.99%). Repeat donors comprised just 13.2% of the total. Thirty two (1.29%) donors were found positive for HBsAg and 15 (0.6%) donors were found positive for Anti-HBcIgM alone. No donor was found positive for both markers. Therefore a total of 47(1.89%) donors showed serological evidence of Hepatitis B virus infection in the form of either HbsAg reactivity or reactivity for Anti-HbcIgM (Fig 3). Higher percentage of male donors showed seroreactivity for HBV markers as compared to female donors (1.98% vs. 0.94% respectively). This difference however was not found to be statistically significant ($p > 0.05$).

The highest percentage of HBsAg seroreactive donors were found in 41-50 years age group and this difference was found to be statistically significant (3.17%; $p=0.01$). The least number of HbsAg seroreactives were found in the 18-30 years age group and this difference was also found to be statistically significant (0.69%; $p=0.01$). Therefore an increasing trend of HBsAg seroreactivity was seen with increasing age of donors. The highest percentage of Anti-HBcIgM donors was seen in 31-40 years age group. This difference was however not found to be statistically significant ($p>0.05$) (Fig 4).

Overall a significantly higher number of seroreactives were seen amongst replacement donors as compared to voluntary donors (3.14% vs 1.30%; $p<0.05$) (Fig 5).

The seroprevalence in first time donors for HBsAg was 1.3% and for anti-HBcIgM was 0.56%.This was not very different from that of repeat donors (1.21% for HbsAg and 0.91% for anti-HbcIgM ; $p>0.05$).

IV. Discussion

Despite mandatory screening of donor blood for HbsAg, transfusion associated HBV (TAHBV) infection continues to be a major problem in India, more so in patients receiving repeated transfusions (11). This is largely explained by the undetectable levels of HBsAg in following conditions.

- Donor is in the window period of infection.
- Donor is a typical Occult Hepatitis B Infection carrier with suppressed viral replication and gene expression.
- Donor is affected with variant HBV strains(S escape mutants) that are replication-competent but produce abnormal surface proteins that are not recognized by the commercially available HBsAg detection kits (12).

HBV DNA has been detected in 1.6 to 38% of HBsAg negative donors (13,14,15). Therefore screening of donors for HBsAg alone does not totally eliminate the risk of HBV infection and a marker which would be indicative of hepatitis B infection in the absence of HbsAg, is of paramount importance.

HBV DNA testing is the ideal test for diagnosing Occult Hepatitis B infection (12). However studies indicate that the added benefit of pooled-sample NAT is relatively small in areas of low endemicity, with greater yields in areas highly endemic for HBV. Single-sample NAT would offer more significant early window period closure and could prevent a moderate number of residual HBV transmissions not detected by HBsAg assays;

however in a resource crunched country like ours it may not be cost effective. Also even single-sample HBV NAT may not substitute for anti-HBc screening, as indicated by studies of donors with isolated anti-HBc who have extremely low DNA levels undetectable by standard single-sample NAT and who have been associated with transfusion-transmitted HBV(9).

Detection of Anti-HBc has been found to be an excellent indicator of occult HBV infection especially during the window period (11) and can be used as a surrogate marker for diagnosing seropositive OBI (12). In fact, detection of anti-HBc has contributed significantly in reducing the incidence of post transfusion hepatitis B amongst patients (16, 17). Therefore blood banks of many developed countries like USA, France and Japan have adopted for Anti-Hbc screening of their donors (17). However, in India it is still not a mandatory donor screening test.

Most of the studies done for estimation of anti-HBc among blood donors have used kits for total anti-HBc (both IgG and IgM). Anti-HBcIgG may be found positive in an affected individual who has had past infection of HBV, even in presence of protective levels of anti-HBs antibodies, and therefore may not be infective. But Anti-HBc IgM is a marker of recent infection (18). Seroprevalence of total Anti-HBc being quite high, screening of donor blood for total anti-HBc cannot be the criterion to discard blood units in India, whereas the Anti-HBc IgM-reactive samples with negative HBsAg test may identify the potentially infectious blood units without substantially increasing the cost of screening or the unnecessary wastage of blood units.

The result of this study emphasizes upon the need to include anti-HBcIgM in routine screening of blood donors in endemic nations like India. It also confirms the fact that testing blood donors for HBsAg alone is not sufficient to eliminate HBV from blood supply. Although, the possibility of achieving zero risk of transfusion associated HBV infection depend largely on DNA testing of all the collected units of blood before transfusion; however, since this is not done in many developing countries including India due to cost factors, this study recommends the inclusion of anti-HBcIgM in routine screening of blood donors in countries where DNA testing is not being done. This will go a long way in reducing transfusion associated Hepatitis B Virus (TAHBV) infection.

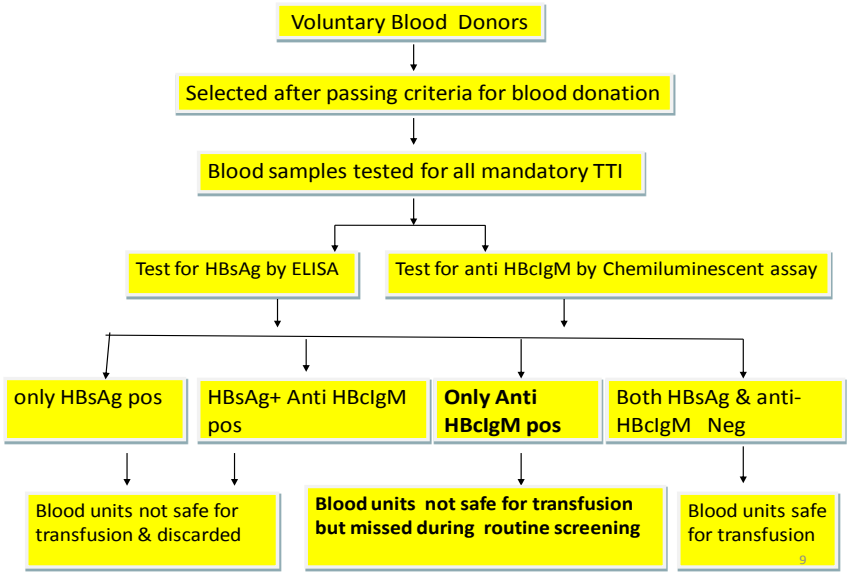

Fig 1: Flow Chart Depicting Study Protocol

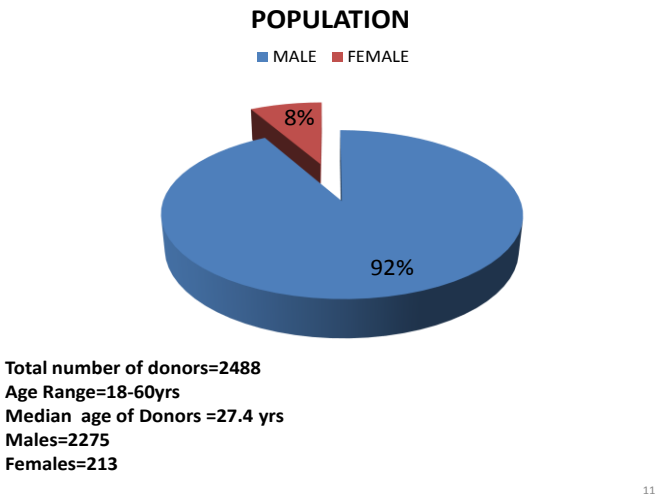

Fig 2: Demographic profile of donors

Fig 3:Donors Showing Serological Evidence of HBV Infection

Seroreactive	Number	Percentage
Hbs Ag reactive	32	1.29%
Anti-Hbc IgM reactive	15	0.60%
Total seroreactive	47	1.89%

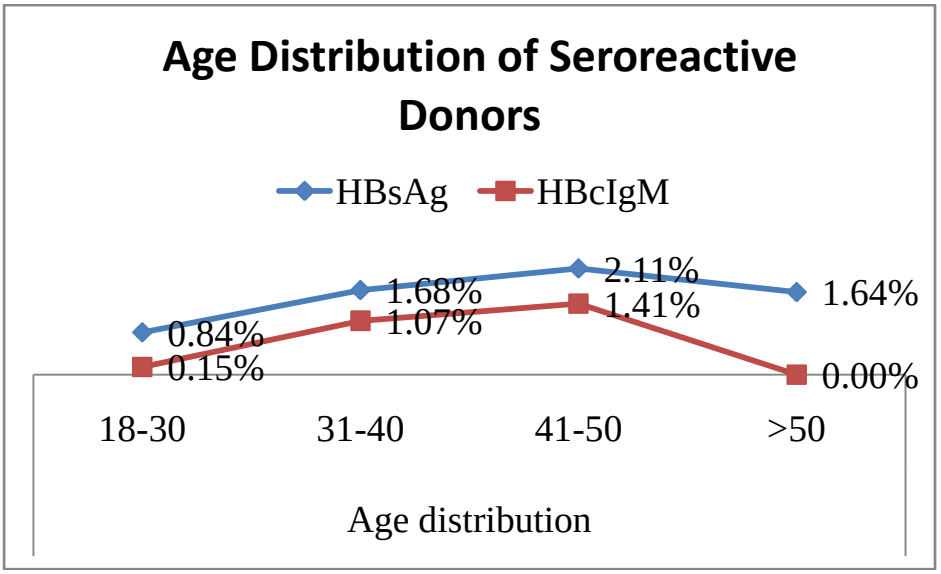

Fig 4:Age Distribution of Seroreactive Donors

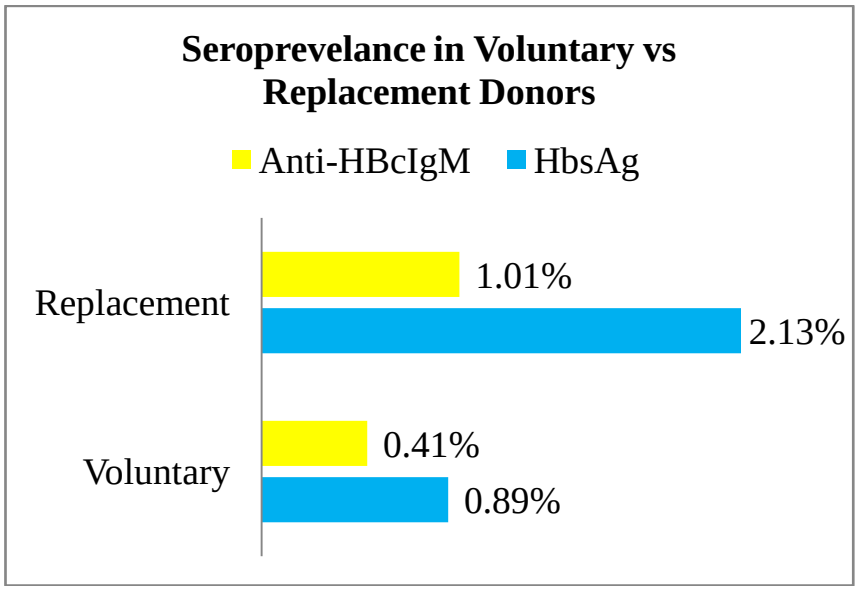

Fig 5:Seroprevelance in Voluntary vs Replacement donors

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