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Short Communication

Markers for Transfusion-Associated Hepatitis in North Indian Blood Donors: Prevalence and Trends

Bharat Singh*, Monika Verma[1] and Karttikaye Verma[2]**

Department of Regional Blood Transfusion Centre (East) and Pathology and
[2]Department of Orthopaedics, University College of Medical Sciences and Guru Teg Bahadur Hospital and
[1]Pathology Department, University College of Medical Science, Delhi 110095, India

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SUMMARY: Transfusion-associated hepatitis is a great problem in developing countries including India due to endemic hepatitis infections and a lack of voluntary donors, trained personnel, and funds. The prevalence of post-transfusion hepatitis B and C in India is about 1 - 5% and 1%, respectively. A total of 128,589 blood donors were screened for hepatitis B surface antigen (HBsAg) and 76,089 donors were screened for anti-hepatitis C virus (HCV) from 1997 - 2002. Data were tabulated annually. Out of the total, 83.6% were replacement donors. Our study concluded that the prevalence of HBsAg and antibodies for HCV ranged between 1.7 - 2.2% and 0.25 - 0.9%, respectively among all of the donors. Seropositivity was definitely higher in replacement donors than in voluntary donors. Based on these results, we recognize an urgent need to establish a non-remunerated voluntary donor base in India. A stringent deferral system should be developed. The use of sensitive laboratory tests and the addition of antibody to core antigen (anti-HBc) to the mandatory screening test list would further reduce the incidence of post-transfusion hepatitis.

Transfusion-transmitted infections continue to be a threat to the safety of the blood supply. In developing countries, the prevalence of transfusion-transmitted disease is much higher and far from attaining a "zero risk" level at the present moment. Viral infections cause the major part of mortality and morbidity in blood recipients. The majority of known cases of post-transfusion hepatitis has been caused by hepatitis B (HBV) or hepatitis C virus (HCV). A few studies have indicated that hepatitis G virus and hepatitis A virus can also be transmitted by blood transfusion (1,2). The safety of blood transfusion is compromised in India due to its dependence on replacement donors, endemic hepatitis infections in this region, the high cost of screening, and a lack of funds and trained personnel. The use of low-sensitivity tests such as reverse passive hemagglutination (RPHA) are also allowed by the existing law (3).

A total of 128,589 blood units were collected from blood donors (replacement and voluntary) at a Regional Blood Transfusion Center, Guru Teg Bahadur Hospital, Shahdara, Delhi, India from January 1997 to December 2002. The replacement donors were family members, friends, or close relatives who donated blood for their respective patients. Donors were selected based on questionnaire. Professional blood donors or those with a history of jaundice were discouraged and excluded from the study.

All 128,589 serum samples were screened for hepatitis B surface antigen (HBsAg) using ELISA kits from omega glaxo III. Among them, 76,089 serum samples were screened for HCV antibodies from 2000 to 2002. ELISA 3rd generation kits from the J. Mitra & Co., New Delhi, India, were used for anti- HCV. Tests were performed according to manufacturer's instructions. All reactive samples were repeated in duplicate. Repeat reactives were labelled as ELISA-positive and were discarded.

The data were tabulated annually. Out of the total, 107,538 (83.6%) were replacement donors and 21,051 (16.4%) were voluntary donors (Table 1). The number of blood donors progressively increased from 12,126 in 1997 to 27,428 in 2001 with a small decrease in 2002. The number of voluntary donations steadily increased over the 6 years period. Donors' seropositivity for HBsAg and HCV antibodies and comparative studies of seropositivity among replacements and voluntary donors are shown in Table 2. The prevalence of HBsAg has remained steady and ranged from 1.7 to 2.2%. Without exception, seropositivity was lower in voluntary (1.2%) than in replacement donors (1.9%). A total of 76,089 donors were screened for anti-HCV; only 408 (0.5%) were found positive. Similarly, the prevalence of anti-HCV was lower in voluntary (0.2%) than in replacement (0.6%) donors.

Replacement donors constitute the largest group of blood donors in India (4). In our study, 83.6% of the total donors were replacement donors, supporting the previous data. This may be due to a lack of awareness in the public and an indifferent attitude of government bodies. However, a change to

Table 1. Total blood collection and distribution in different categories

Year	Total donors	Replacement donors (%)	Voluntary donors (%)
1997	12,126	10,715 (88.4)	1,411 (11.6)
1998	19,165	16,001 (83.5)	3,164 (16.5)
1999	21,209	18,090 (85.3)	3,119 (14.7)
2000	23,238	19,549 (84.1)	3,689 (15.9)
2001	27,428	22,320 (81.4)	5,108 (18.6)
2002	25,423	20,863 (82.1)	4,560 (17.9)
Total	128,589	107,538 (83.6)	21,051 (16.4)

*Corresponding author: Mailing address: Department of Regional Blood Transfusion Centre (East) and Pathology, University College of Medical Sciences and Guru Teg Bahadur Hospital, Shahdara, Delhi 110095, India. Tel & Fax: +91-11-22130973, E-mail: monika4k@hotmail.com, drbharat@bloodbanksdelhi.com

**Present address: Old Church Hospital, Romford, United Kingdom.

Table 2. Number and percent seropositives for HBsAg and anti-HCV in different blood donor groups

Year	HBsAg			Anti-HCV		
	R (%)	V (%)	T (%)	R (%)	V (%)	T (%)
1997	236 (2.2)	17 (1.2)	253 (2.2)	–	–	–
1998	288 (1.8)	35 (1.1)	323 (1.7)	–	–	–
1999	326 (1.8)	41 (1.3)	367 (1.7)	–	–	–
2000	370 (1.9)	43 (1.2)	413 (1.8)	51 (0.3)	7 (0.2)	58 (0.25)
2001	409 (1.8)	50 (1.0)	459 (1.7)	237 (1.1)	14 (0.3)	251 (0.9)
2002	397 (1.9)	63 (1.4)	460 (1.8)	95 (0.5)	4 (0.1)	99 (0.4)
Total (%)	2,026 (1.9)	249 (1.2)	2,275 (1.8)	383 (0.6)	25 (0.2)	408 (0.5)

R, Replacement donors; V, voluntary donors; T, total donors.

100% voluntary donors may require many more inputs. These issues should be urgently addressed by health care authorities. Indeed, in Japan a mere change in practice from paid donors (1963 - 1964) to voluntary donations (1968 - 1972) decreased the incidence of transfusion-associated hepatitis from 51 to 16% (5). In this study, the prevalence of markers for transfusion-transmitted hepatitis is definitely higher in replacement donors (Table 2). So, it is important that voluntary donations be encouraged and replacement donations be discouraged.

The prevalence of HBV infection is low in the United States (U.S.) and in Western Europe (0.1 - 0.5%), while in Southeast Asia and China it ranges from 5 - 15% (6). The prevalence of HBV infection in India is 1 - 5% in the general population (7) with 1 - 3% in voluntary and 10 - 12% in commercial donors. The prevalence of anti-HCV in blood donors in various countries is given in Table 3. Our study showed prevalences of HBsAg and anti-HCV of 1.8 and 0.5%, respectively, in blood donors, supporting the findings of the previous studies.

According to the Drugs and Cosmetics (1st amendment) Rules, 1992 (3) act, each blood unit has to be tested for HBV, human immunodeficiency virus (HIV), syphilis, and malaria prior to transfusion. HCV testing has been mandatory since June 2001. Information on HCV infection is still sketchy and only few studies are available. In India, approximately 87% of blood banks test for hepatitis B and only 6% for hepatitis C (16). The Drugs and Cosmetics Rules, 1992 allow testing for HBsAg to be carried out by either ELISA or RPHA. Only 17% of blood banks currently use ELISA methods (16). This is probably because of limitation of resources and lack of funds. Another reason for high prevalence of hepatitis B is that HBsAg may be undetectable in the window period, in the convalescent phase, in asymptomatic carriers, and due to laboratory errors. Prevalence rates and infectivity risks also could have been underestimated for HBV, assuming that the test for antibody to the hepatitis B core antigen (anti-HBc) was not done uniformly. In the U.S., anti-HBc was made mandatory in 1986 - 1987. In view of the high (5 - 15%) seropositivity in India, it is worthwhile to evaluate the use of anti-HBc screening. If this test is also implemented in addition to HBsAg, it may help to prevent post-transfusion hepatitis to certain extent. In many western countries, nucleic acid amplification testing (NAT) has been made mandatory in blood donors from 2000. A small study done in India showed that 5% of HbsAg-negative donors turned out to be HBV DNA-positive by DNA hybridization assay (17).

Table 3. Prevalence of antibodies to HCV in blood donors around the world

Country	Prevalence (%)	Reference
India	0.12 - 4	8, 9
Japan	1.2	10
Germany	0.42	11
France	0.68	12
Italy	0.87	13
UK and US	0.01-0.55	14,15

Around the world, more than 75% of transfusion-associated hepatitis is caused by HCV. The incidence of HCV-related transfusion-associated hepatitis in the U.S. and Japan in 1970 was 7.12 and 45%, respectively. With the use of specific assays for HCV in 1994 - 1995, the incidence in the U.S. was reduced to less than 1% and in Japan to nearly zero (5). The Japanese Red Cross uses a unique gelatine particle agglutination test, with a nearly 100% sensitivity for the detection of HCV (5). Due to the delay in the implementation of HCV tests, India may have grossly underreported post-transfusion hepatitis per year. The majority of HCV transmissions could have been prevented if anti-HCV tests had been carried out in India in the early 1990's.

In conclusion, this study has determined prevalences of HBsAg positivity of 1.8% and HCV of 0.5% in Indian donors. Seropositivity is definitely higher in replacement donors. Based on these results, we suggest that in order to further reduce the prevalence of post- transfusion hepatitis, a stringent donor deferral system should be created. Shortcomings of the current approaches both in regard to policy design and program implemented should be removed. There is urgent need to establish a concrete non-remunerated repeat voluntary donor base in India. Feedback to the blood banks regarding the occurrence of transfusion-transmitted hepatitis should be given. Routine screening for HBV and HCV in each blood unit should be performed using a properly evaluated, sensitive ELISA method. There is also a need to include anti-HBc to the list of mandatory screening tests. NAT, a very sensitive test, may be implemented in a cost-effective manner in the near future.

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