



Stringent Donor Selection Still Holds the Key in Prevention of Transfusion Transmissible Infection: Results of a Fifteen Year Study

KEYWORDS

Transfusion transmissible infections, Trends, Blood donors, Stringent donor selection

Dr R S Mallhi

Assoc Prof, Dept of Immunohaematology and Blood Transfusion, AFMC

Dr U Dimri

Resident, Dept of Immunohaematology and Blood Transfusion, AFMC

ABSTRACT *Background: Despite the availability of more sensitive testing methodologies for screening of blood components, voluntary donors still hold their forte when it comes to prevention of transfusion transmissible infections (TTIs).*

Aim and Objectives: We studied the effect of shifting our donor base from replacement to voluntary donors on the prevalence of TTIs among blood donors in the past 15 years (2000- 2014).

Study Design and Methods: 1,28,068 allogeneic donations from 2000 to 2014 were screened for hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), malaria and syphilis. The prevalence was calculated per 1000 donations. Results were also analyzed for pre and post 2009 seroprevalence levels.

Results: The seroprevalence per 1000 donations for entire study period was 14.9 for HBV, 5.5 for HIV, 4.5 for HCV and 3.6 for syphilis. A significant reduction in HIV, HBV and Syphilis is seen in total donor population in pre and post 2009 seroprevalence values. Surprisingly a significant increase is observed for HCV in pre and post 2009 seroprevalence values. Seroprevalence values differed significantly between the voluntary and replacement donors, with higher values seen in the latter category.

Conclusion: Our study results show that in a developing country like India, though universal implementation of NAT screening is much desirable, the focus should still be on increasing voluntary non remunerated donors for TTI prevention, coupled with a sensitive ELISA based screening programme.

Introduction:

The medical and surgical practice was revolutionized when James Blundell performed the first human to human blood transfusion in 1818, which eased the path for longer and more complicated procedures that are accompanied with significant blood loss(1). However transfusion of blood and its components in medical and surgical practice has always been associated with the possibility of an undesired complication occurring like transfusion transmissible infections (TTIs).

Every unit of blood being transfused carries with it a 1% chance of transfusion associated problems including TTIs (2). The list of TTIs is long and each country carries out TTI screening of blood donations according to its own national policies. In India, according to the National AIDS Control Organization (NACO) guidelines, all blood donor samples must be tested for human immunodeficiency virus (HIV) 1 and 2, hepatitis B virus(HBV), hepatitis C virus(HCV), syphilis and malaria(3). The importance of testing for these infections can be gauged from the fact that, according to the latest estimates, India harbors 5.7 million cases of HIV, 43 million cases of HBV and 15 million cases of HCV positive individuals (4). Amongst all plausible routes of transmission of these infections, transfusion of blood still constitutes a major and efficient route of transmission.

Transfusion of blood and its components can be made safer by a number of ways that include voluntary blood donation, better donor screening questionnaires, increasing the number of TTIs tested, use of more sensitive testing methodologies like nucleic acid testing (NAT), etc. Use of ID NAT has brought down the window period of HIV, HCV and HBV to 5, 3-5 and 21 days respectively (5). With the advancements in TTI screening, blood transfusion

practice has become increasingly safe but transmission of TTIs still occurs. It happens primarily because of window or pre-seroconversion phase transmission of TTI. NAT for TTI screening is also hampered by lack of well-trained technical manpower and ever emerging newer viral variants. Also NAT is beyond the economical scope of a vast majority of Indian blood banks even today and they still have to rely on ELISA/ Rapid tests for TTI screening. Thus it may be seen that still the best way forward in a developing nation like us is self-exclusion by voluntary non remunerated blood donors that is coupled with sensitive ELISA screening tests.

In our Centre, we have made great efforts to shift our donor base from replacement to voluntary donors, along with up gradation of existing TTI testing kits. We have also tried to study the effect of these measures on the prevalence of TTIs among blood donors in the past 15 years (2000-2014).

Material and Methods:

Ours was a retrospective cross-sectional plus record based study conducted at a hospital based blood bank of a tertiary care teaching hospital situated in Western India. Donor data for blood donations for 2000-2009 time period was retrieved from our donor archives. Like most of the hospital based blood banks, we also used to be heavily dependent on replacement donors as our source of blood supply. However in 2009, a ten year road map was formulated in order to achieve a complete voluntary non remunerated blood donors based blood supply. Essentially it consisted of tapping into local committees of colleges and various non-government organizations of the region. A revised donor questionnaire form based on NACO and WHO guideline was also brought out. Implementation of

donor screening was rigorous and continued up gradation and maintenance of technical and interviewing skill levels of blood bank officers and technicians was ensured. Yearly reviews of the trend of preceding year were performed and appropriate measures for identifiable lacking areas were undertaken.

All eligible blood donors were screened for HBsAg, HIV antigen/antibody, anti-HCV, malaria antigen and treponemal antibodies for syphilis by NACO approved commercial kits (Enzyme Linked Immunosorbent Assay (ELISA), Immuno-chromatographic assay and Rapid Plasma Reagin (RPR) tests respectively). Tests were performed according to the manufacturer's instructions. For HIV till 2011, 3rd generation HIV ELISA kits (targeting IgG and IgM type of anti HIV 1 & 2) were used following which 4th generation HIV ELISA kits (same targets as 3rd generation plus p24 antigen of HIV-1) were used in our blood bank. For HCV and HBV, 3rd generation ELISA kits have been in use since 2002. Necessary ethical clearance was taken from institutional ethical committee. The seroprevalence of TTI was calculated per 1000 donations. To analyze any significant changes observed in pre and post 2009 levels of seroprevalence, Chi square test was used to calculate the p values using SPSS ver 21. p-value of ≤ 0.05 was considered significant.

Results:

A total of 1,28,068 allogeneic donations took place during the study period and consisted mainly of male donors (96%) (Table 1). Majority (77%) of donors were from 20-39 years age group (Fig 1). Blood donations per year have shown an increasing trend since 2002, with a preponderance of voluntary donations since 2009 (Fig 2). A general trend of decrease in overall seroprevalence of HBV, Syphilis and HIV was observed during the 15-year study period from 2000 through 2014 (Fig 3). The seroprevalence of HCV showed a stable trend till 2010 after which it has shown an increase. The seroprevalence per 1000 donations for entire study period was 14.9 for HBV, 5.5 for HIV, 4.5 for HCV and 3.6 for syphilis (Table 2). Only two cases of Malaria positive donations came during the entire study period. When we compare the pre and post 2009 seroprevalence values, a significant reduction in HIV, HBV and Syphilis is seen in total donor population (Table 2). Surprisingly a significant increase is observed for HCV when we compare pre and post 2009 seroprevalence values. On further splitting the TTI seroprevalence values into voluntary and replacement donors, some interesting patterns emerged (Fig 4a & 4b). Seroprevalence values differed significantly between the voluntary and replacement donors, with higher values seen in the latter category. Voluntary donors showed a declining trend in both HBV and syphilis seroprevalence, which was more marked since 2009. HIV also showed a declining trend in both voluntary and replacement donors except a spike in 2012 (the following year when HIV 4th generation ELISA was introduced in our blood bank). HCV had also shown a declining trend in voluntary donors till 2008, after which it has shown mainly an increasing trend till 2014, with a minor dip in 2013. When we analyze seroprevalence trend in the replacement donors, both HBV and HCV had shown a declining trend till 2008 after which both of them have shown an increasing trend. Syphilis seroprevalence had shown an overall declining trend in replacement donors. On account of being positive for TTIs markers, a total of 3623 units of seropositive blood were discarded as per biomedical waste disposal policy in place.

Discussion

Transmission of residual TTIs is still an issue that crosses every physician and blood bank administrators mind whenever a blood unit is transfused. Western developed countries have brought down this residual risk of transmission of TTIs by blood transfusion to quite negligible figures (6). Developing nations like us are still grappling with these issues due to reasons enumerated before. However, there are some positive trends in form of increasing voluntary donations due to concerted effects of the various agencies. As per 2012-13 data of computerized management Information System of NACO quoted by Mammen and Nair (2015), the percentage of voluntary donors has been upto 73% (7). In our study also voluntary non remunerated donors formed the majority of our donor population i.e. 67% as compared to replacement donors (33%) (Table 1). A most heartening trend of significant increase in proportion of voluntary donations was observed (from 37% (pre 2009) to 69% (post 2009)) in our study. A large number of Indian as well as international studies have shown that voluntary donors are indeed safer as compared to replacement donors (8-13). However it may be noted that barring few (11,13-15), most of the hospital based blood banks in India even today have a replacement donor based blood supply with proportion of replacement donors ranging from 68.6% to 99.48% (2,9,10,16-18). This observation only highlights the fact that conversion of blood supply to total voluntary donation is not an easy task. These data also reflect that a large section of our general population still lack awareness about the need of voluntary blood donation.

Major chunk of our donor population was derived from age group of 20-39 years (77%). It could be due to the fact that we had specifically targeted college going students as our donor population. These are the well-educated and motivated youth which are most amenable to become repeat voluntary blood donors and also encourage others to donate blood voluntarily.

It has been seen that even though females form about half of Indian population, still they constitute quite low percentage of blood donors. This may be because of the high incidence of anaemia in Indian women especially in the age of child bearing, which incidentally also overlaps with the eligibility age range of blood donation in India (11). In our study also female donors formed a minor component of our donor study pool because a majority of female donors that turned up, had to be deferred because of low hemoglobin counts (less than 12.5 gm/dL), a finding supported by many other Indian studies (2,10,11,13). Still an impressive increased participation from female donors is seen when we compare pre and post 2009 values (02% v/s 09%, respectively) (Table 1).

In our donor population Hepatitis B was the most common TTI with seroprevalence of 1.45% (14.5/1000 donations). The seroprevalence of HBsAg among blood donors from other parts of India has been reported to range from 0.66% to 2.23% (2,10,11,13,19,20). In our study even though HBV seroprevalence has shown a declining trend in both overall and voluntary donors, it showed an increase in replacement donors post 2008 (Fig 3 & 4). This observation could be due to an ineffective penetrance of HBV immunization in general population of Western Maharashtra. In a study conducted among the locals of a part of Western Maharashtra the prevalence of HBsAg was found to be 1.82% (21). But the lesser seroprevalence in voluntary donors can be attributed to an increased awareness of HBV due to better education levels leading to better com-

pliance to HBV immunization.

In India blood donation is the third most common cause of HIV transmission (22). Also amongst all the modalities of transmission of HIV, transfusion of infected blood is the most dangerous as it has been estimated that HIV infected blood is more than 90% efficient in transmission of HIV (23). The prevalence of HIV among blood donors from other parts of India has been reported to range from 0.084% to 0.56% (2,10,11,13,19,20). The prevalence rate of HIV in Maharashtra as published in HIV Sentinel Surveillance 2010-11 was found to be 0.42% (24). In our study the seroprevalence of HIV has also shown a significant declining trend from 2000 till 2011 with a sudden increase in 2012 followed by decline in 2013-14 albeit still at higher levels than 2011 (Fig 3). It could be due to the fact that we had introduced HIV 4th generation ELISA kits in year 2012, which are known to reduce window period. Introduction of these kits could have resulted in the increased detection rates, leading to a safer blood supply.

The prevalence of syphilis among blood donors from other parts of India has been reported to range from 0.01% to 1.6 % (2,10,11,13,19,20). In our study the seroprevalence of syphilis has shown a declining trend overall as well, in voluntary and replacement donors, with zero detection in voluntary donors in 2014 (Fig 3 & 4). Syphilis spirochetes lose their viability rapidly in refrigerated blood and possibly also in the high oxygen content of platelet (PLT) concentrates on making chances of transfusion transmitted syphilis quite slim(25). If we compare the western data, only 01 case of transfusion transmitted syphilis has been reported in United States in last 50 years and there is a big debate there that whether testing for syphilis serves useful purpose anymore(25). Coming to Western India population, despite extensive research, there was no study that gave seroprevalence of syphilis in general population. However in high risk group population (female sex workers, men having sex with men) of Maharashtra, syphilis prevalence was 7.4%-13.4%(26) which is quite worrying. Thus it may still be prudent to keep continuing the syphilis screening in our donor population.

One surprising trend seen in our study is that of HCV prevalence which had shown a decrease till 2008 after which it has shown significant increase in both voluntary and replacement donors (Fig 3 & Table 2). Similar increasing trend in HCV seroprevalence has also been shown in the donor population of Northern India in a recently done study(6). Increased seroprevalence of HCV among the donors also brings to fore the apprehension about increasing subclinical infection of HCV in the general population, as significant increase is seen in supposedly healthy voluntary donors. The prevalence of HCV among blood donors from other parts of India has been reported to range from 0.11% to 1.09% (2,10,11,19,20). There is lack of large population based studies for prevalence of HCV in general population of Western India. Only one study that was undertaken also showed an insignificant (0.09%) prevalence among 1000 villages of Maharashtra (27). The rise in HCV prevalence can also be attributed to lack of an effective vaccination programme and to the better modalities of screening diagnostics available. Further research in pertinent areas is required to find out the exact scenario.

Only two blood units were found positive for malarial antigen. This may be due to the fact that western Maharashtra is not an endemic area for malaria with annual parasite index of less than two(28).

It may be seen that we were able to reduce the overall seroprevalence and wastage of precious blood units by increasing the voluntary donor population base. It is by no means an easy task especially for hospital based blood bank. But its necessity cannot be overlooked as the seroprevalence rates in replacement donors have been unacceptably high and are even showing rising trends.

TTIs screening of blood and blood components has come a long way since screening for blood donations for syphilis was first instituted in United States in 1940s(29). Enforcement of stringent guidelines for blood transfusion and testing the donor serum for various antibodies have been efficacious in successfully bringing down the seroprevalence rates of TTIs. Still these preventive approaches are beleaguered by innumerable virus immunological variants and the inherent drawback of the serological tests that they may miss diseases detection during their window period. This problem is further compounded by new emerging pathogens and difficulty in adopting the highly sensitive test like DNA hybridization and Polymerase Chain Reaction for generalized utilization due to cost factor, and due to the non-availability of trained manpower.

As a result TTIs still remains a major hazard of blood and its components transfusion. Further increase in the number of voluntary donations and self-exclusion by donors will go a long way in substantially reducing TTIs.

One important finding that came out of our study while going through contemporary medical literature was that the seroprevalence of HIV and HBV in blood donors in our study and the general population of Western Maharashtra were comparable (Table 3). Similar studies for comparing seroprevalence of HCV and syphilis in donors vis a vis general population are lacking. Our observations further affirm that the evaluation and monitoring of the prevalence of TTIs among blood donors is not just a valuable index of blood safety but it is also an indicator of the prevalence of these infections in the general population(30). Thus the results about TTIs prevalence donors in our study can also be carefully extrapolated to provide estimate about the burden of these infections in the general population of Western India.

Conclusion:

In our study apart from HCV, the declining trend in prevalence rate obtained for other TTIs was found to be in consensus with various previous reports. These declining trends of prevalence of TTIs in blood donors and therefore by proxy, the general population of western Maharashtra can be ascribed to better education in general population, better screening procedures and informational campaigns driven by many health related agencies and NGOs leading to heightened awareness about TTIs among the donor populations. However still more attention needs to be given towards prevention of HCV in general population, in the form of effective vaccine development and targeted educational measures. Also our study results show that in a developing country like India, though universal implementation of NAT screening is much desirable, the focus should still be on increasing voluntary non remunerated donors for TTI prevention, coupled with a sensitive ELISA based screening programme.

Table 1
Total blood collection and sex distribution of donors

Duration	Total collection	Male donors	Female donors	Voluntary donors	Replacement donors
2000-2014	1,28,068	1,22,945(96%)	5,123(4%)	78,044(67%)	38,439(33%)
Pre 2009 (2000-08)	71633	70200(98%)	1433(2%)	26738(37%)	44895(63%)
Post 2009 (2009-14)	56435	51355(91%)	5080(9%)	39179(69%)	17256(31%)

Table 2 : Prevalence of TTIs per 1000 donations (O –overall, V – voluntary, R – replacement, p value between V and R)

Serial no	Time period	HIV				HBV				HCV				SYPHILIS			
		O	V	R	p	O	V	R	p	O	V	R	p	O	V	R	p
1	Overall	5.5	2.8	8.4	0.00000	14.9	7.5	22.5	0.00000	4.5	3.7	5.2	0.00008	3.6	2.0	5.3	0.00000
2	Pre 2009 (2000-08)	7.3	4.1	9.2	0.00000	17.2	9.7	24.7	0.00000	3.5	2.6	4.1	0.001	5.0	3.6	5.9	0.00002
3	Post 2009 (2009-14)	3.4	2.0	6.6	0.00000	11.9	6.3	21.6	0.00000	5.7	4.3	8.9	0.00000	1.8	0.9	3.8	0.00000
4	p value (between 2 & 3)	0.000	0.000	0.000	----	0.000	0.000	0.000	----	0.000	0.000	0.000	----	0.000	0.000	0.000	----

Table 3 : Comparison of seroprevalence rates of TTIs in donor population and general population of Western Maharashtra

TTI	Seroprevalence		
	Present study (as in 2014)	Other studies in donor populations	General (G)/High risk(H) Maharashtra population
HIV	0.56%	0.08-0.56%	0.42% (G) ¹
HBV	1.49%	0.66-2.53%	1.82% (G) ²
Syphilis	0.37%	0.01-1.6%	7.4%-13.4% (H) ³
HCV	0.45%	0.11% to 1.09%	0.09% (G) ⁴

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Fig 1 : Age Composition of donor population

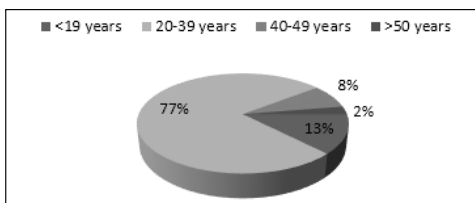


Fig 2 : Trend in pattern of blood donations

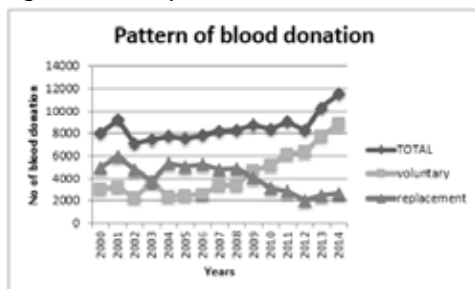


Fig 3 : Trend regarding prevalence of TTIs per 1000 donations during study period (2000-2014)

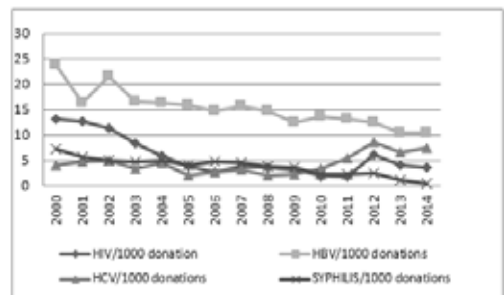
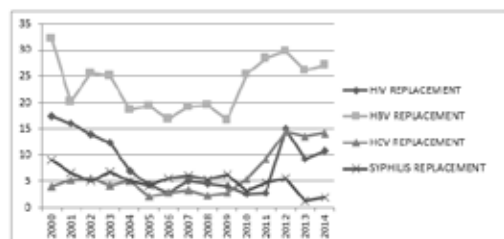


Fig 4 a and b – Trends in prevalence of TTI per 1000 donations seen in voluntary and replacement donors



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