Original Article

Effectiveness of blood donor questionnaire directed at risk factor for transfusion transmitted infections in Pakistani population

Nuzhat Salamat

Department of Pathology, Combined Military Hospital, Multan Cantt, Pakistan

Abstract:

Background: Deferring blood donors who admit to high-risk behavior on questioning are likely to eliminate those in window period for transfusion transmitted infections (TTI). However, many questions have been implemented in some countries as part of donor history questionnaire, based on precautionary principle and not on evidence, and can result in increased donor losses. This study aims to identify effective risk-directed questions having high predictive value, in local context which can form part of blood donor deferral policies. For this, a case control study in a hospital blood bank having donation services was carried out prospectively over a period of three years. **Materials and Methods:** Two hundred and twenty donors, who were repeatedly reactive for HBsAg, anti-HCV, anti-HIV with EIA, and syphilis with TPHA, were the cases. Eight hundred and eighty four controls were the donors who tested negative for all TTI test. All donors answered seven hepatitis risk directed questions and their responses and reactivity status for TTI were used for statistical analysis with SPSS ver. 15. **Results:** Positive predictive value for history of jaundice at any age for HBsAg was 20%, while PPV for history of surgery in previous six months for both HBsAg and anti-HCVHCV was also around 20%, based on pretest probability of 7%. The post-test probability for these questions was around 30%. Odds ratios with 95% CI did not reveal any significant association of hepatitis with any of seven questions. Donor losses after deferring on basis of two questions were 5.3% per year, while deferral rate after all seven questions was 20%. **Conclusions:** Donors should be permanently deferred if there is history of jaundice at any age, while deferral period after surgery should be one year. Other risk-directed questions should not be used to defer donors. Donor deferral policies should be evidence based and questions with proven efficacy should be made part of donor history questionnaire to minimize donor losses.

Key words:

Blood donor, donor deferral, donor history questionnaire

Access this article online

Website: www.ajts.org

DOI: 10.4103/0973-6247.98929

Quick Response Code:

Correspondence to:
Dr. Nuzhat Salamat,
Department of Pathology, Combined Military Hospital, Kharian Cantt 50070, Pakistan.
E-mail: nuzhatsalamat@yahoo.com

Introduction

Different blood donor screening strategies contribute towards safety of blood transfusion and have been introduced in USA, Europe, and UK over time.[1] One of these is high-risk donor deferral prior to donation, based on risk assessment from donor history questionnaire. Not all questions put up to donors have been rigorously assessed for their sensitivity, specificity, and predictive value before their implementation in developed countries.[2,3] Although different methodological approaches to prove effectiveness of donor history questionnaire can be undertaken but many donor history questions have been implemented as precautionary measures and without evidence of effectiveness.[1] Countries like Pakistan cannot afford to introduce similar precautionary measures of donor deferral, because it may lead to unacceptable donor losses and spending of precious resources on strategies of unproven effectiveness. The guidelines written for Pakistani blood services by National Institute of Health (NIH) mostly reproduce policies of other countries[4] with out taking into consideration local evidence or realities. Their implementation as such will lead to difficulty in compliance and also loss of many safe donors. Since this country has yet to make transition from directed/replacement and professional donors to all volunteer donors, so there is need for carefully selecting only evidence based effective donor deferral strategies. With this background the aim of present study was to assess the effectiveness of different donor history questionnaire developed on the basis of epidemiological data for TTI (transfusion transmitted infections) in Pakistan[5-9] and find questions with significant predictive value so that these can be recommended for inclusion in donor history questionnaire for Pakistani donors. To achieve this objective, a case control study was conducted, over three years, in hospital blood bank that maintains its own donation services.

Material and Methods

Subjects were all male donors who reported to Hospital Blood Bank during 3 years, from July 2006 to July 2009 and were >18 years of age, weighed

more than 50 kg, with hemoglobin >13 g/dl, felt healthy on day of donation, and were seroreactive for any TTI screening test done on their blood samples. These tests include HBsAg, anti-HCV, anti-HIV, and syphilis tests. Subjects not fulfilling above criterion or not consenting to fill questionnaire, or who had unsuccessful donation were excluded. Controls were all donors having same criterion as subjects except that they tested negative in viral screening tests. The purpose of questionnaire and testing and need for consent was explained to donor by reading out standardized information written in Urdu, read to the donors by the blood bank staff. Only consenting eligible subject and control donors were given hard copy of donor questionnaire for self completion.

Sample size

On line calculator[10] was used for computing sample size required to detect a difference between proportions in two groups. The significance level (alpha) of 0.05 and power of 80% was targeted. Assumed proportion of subjects, i.e., donor testing positive for any of the TTI is 0.04. Assumed proportion of group 2, i.e., donor testing negative for any of the TTI is 0.01. The relative ratio of two groups (controls/subjects) was selected to be 4, based on the average prevalence of positive viral screening results each previous year.

Sample size computed with classical calculation was:
Group 1 (subjects): 220
Group 2 (controls): 881

Sampling technique

Non probability purposive sampling

Data-collection procedure

A donor questionnaire was devised in Urdu. The questions pertained to donor risk factors that were formulated on the basis of epidemiological studies from Pakistan. A hard copy of the donor questionnaire in Urdu was the data-collection instrument and was made available to blood bank staff. This included the information on demographics of donor, personal information, and consent and following seven questions:

History of therapeutic injections in previous 6 months;
History of surgery in previous 6 months;
History of dental treatment in previous 6 months;
History of jaundice at any age;
History of family contact of jaundice;
Travel abroad in previous 1 year;
Tattooing of body in previous 6 months;
History of blood transfusion in previous 1 year;

No questions to elicit sexual behavior and preferences were included in this questionnaire because a previous piloting of questions pertaining to sexual behavior and illicit drug usage showed that none of the donors responded to such questions.

The donors were required to fill the questionnaire themselves and were encouraged to seek help in case they had any confusion or were illiterate or did not understand the questions.

All eligible donors whether subject or controls had 3 ml of their blood drawn in plain tube at the time of sampling for hemoglobin estimation by KX 21 Sysmex hematology analyzer. The serum was separated and kept in refrigerator and tested for HBsAg, anti-HCV, and HIV by ELISA (LiNEAR Chemicals, Barcelona Spain), within 12 hours of donation, applying appropriate commercial control (BioRad Virotrol 1).The donor result was reported as reactive if S/Co ratio was >1. Reactive samples were repeated by obtaining sample from the blood bag. Only repeat reactive donors were considered seroreactive and no confirmatory tests were carried out. The syphilis was tested with TPHA (Treponema Pallidum Haemagglutination Test) (IMMUTREP TPHA by Omega Diagnostics UK). The result of same was recorded on the performa.

Ethical approval

The study protocol was approved by the institutional ethics committee of hospital in compliance with Helsinki Declaration of 1975.

Data analysis and statistical procedures

SPSS ver. 15 was used for recording all the data written on the questionnaire. The variables that were included were the basic demographic information, responses to donor questions and viral and syphilis screening test. SPSS ver. 15 and interactive online calculator at www.statpages.org[11] were used for statistical analysis. Descriptive statistics, frequency, and association data to represent these were also obtained with SPSS ver. 15. Comparisons were performed with Chi-square test where values in cells were > 5, while Fishers exact test was used where cell values were less than 5 in 2 × 2 contigency tables. ORs (Odds Ratios), sensitivity, specificity, PPV (positive predictive value), and NPV (negative predictive value) were obtained along with 95% CI (confidence interval), for HBsAg, anti-HCV, HIV, and syphilis separately. A probability smaller than 0.05% was considered significant. A 95% CI of OR that does not overlap with 1 is considered significant association. Calculations of post test probabilities of hepatitis was derived from pretest probabilities of 7% for HBsAg and anti-HCV based on weighted averages of Pakistani blood donors obtained from systematic review[12]

Results

All donors reporting during 3 years period, from July 2006 to July 2009, were directed or replacement male donors only. Average donations at the centre were 4800 per year. Total of 1104 donors were included. Those testing negative were consecutive donors, while all positive cases were pooled from 3 years time, to obtain the desired sample size of 220. These either tested positive for HBsAg, anti-HCV, or syphilis.

Number of anti HCV seroreactive donors were 123, while 78 were HBsAg positive donors. Eight donors were reactive for both types of hepatitis. There was no positive case of HIV among the 1104 subjects included in the study. Three had positive test for syphilis, i.e., TPHA. None of TPHA positive donors indicated any risk factors on preliminary questionnaire as well as on direct questioning when they were interviewed again. The mean age of all donors was 27.5 years (range 16–58 years). No significant difference was found between mean age of HBsAg positive (28.7 years) vs. HBsAg negative (27.46) years by independent sample T-test. The comparison of anti-HCV positive donors age by same test showed significant difference (P 0.004) as anti-HCV positive donors had mean age of 29.2 vs. anti-HCV negative donors mean of 27.3 years. Donors testing positive for syphilis were of ages 22, 23, and 26 years. Odds ratios with 95% CIs and P values for each risk factor are shown in Tables 1 and 2 for HBsAg and anti-HCV,

Table 1: HBsAg and risk factors in donors

Risk factor	ORs*	95% CI†	*P* value	Sensitivity	Specificity	PPV‡	NPV§
injections in previous 6 months	0.73	0.237 - 2.22	0.79	0.119 0.119 - 0.122	0.95 0.93-0.96	0.05 0.005-0.12	0.92 0.91-0.93
Surgery in previous 6 months	2.98	0.44-20.	0.33	0.012	0.996	0.200 0.15-0.55	0.923
Dental treatment in previous 6 months	1.59	0.4-6.3	0.38	0.09 0.083-0.092	0.98 0.97-0.98	0.11 0.03-0.27	0.92 0.90-0.93
History of jaundice	4.05	1.16-14.1	0.06	0.035 0.012 - 0.074	0.991 0.989 - 0.994	0.25 0.05 - 0.49	0.92 0.90 - 0.93
Family contact with jaundice	0.91	0.15-5.5	1	0.012 0.002-0.05	0.98 0.98-0.99	0.071 0.013-0.30	0.92 0.921-0.925
Travel abroad	0.925	0.34-2.52	1	0.047 0.018-0.10	0.95 0.94-0.95	0.073 0.004-0.144	0.92 0.920-0.927
Tattoo on body	0.0	0.00-7.66	1	0.0 0-5.09	0.99	0.00	0.83 0.79-0.083
History of blood transfusion	0.0	0.0-7.66	1	0.0-5.09	0.99	0.00	0.83 0.79-0.083

*Odds ratio, †Confidence intervals, ‡Positive predictive value, §Negative predictive value

Table 2: Anti-HCV and risk factors in donors

Risk factor	OR*	95% CI†	*P* value	Sensitivity	Specificity	PPV‡	NPV§
injections in previous 6 months	0.00	0.00-0.53	0.003	0.00 0.00-.027	0.94 0.94-0.95	0.00 0.00-.00	0.87 0.876-0.879
Surgery in previous 6 months	1.86	0.27 - 12.5	0.06	0.008 0.001-0.24	0.98 0.995-0.998	0.20 0.15 - 0.55	0.882 0.881-0.884
Dental treatment in previous 6 months	0.46	0.077-2.74	0.7	0.008 0.001-0.034	0.98 0.0983-0.987	0.059 0.053-0.17	0.88 0.880-0.884
History of jaundice	0.46	0.077-2.14	0.7	0.008 0.001-0.04	0.94 0.983-0.987	0.08 0.07-0.23	0.88 0.88-0.884
Family contact with jaundice	0.56	0.095-3.4	1	0.008 0.001-0.033	0.98 0.98-0.99	0.07 0.13-0.31	0.88 0.88-0.884
Travel abroad	0.41	0.136-1.27	0.19	0.023 0.008-0.04	0.947 0.945-0.952	0.055 0.019-0.145	0.87 0.87-0.88
Tattoo on body	0.00	0.00-41.7	1	0.00 0.00-0.18	0.994 0.994-0.996	0.00 0.00-0.38	0.881 0.881-0.883
History of blood transfusion	0.00	0.00-41.7	1	0.00 0.00-0.18	0.994 0994-0996	0.00 0.00-0.38	0.881 0.881-0.883

*Odds ratio, †Confidence intervals, ‡Positive predictive value, §Negative predictive value

respectively. It also shows sensitivity, specificity, and positive predictive value, negative predictive value for all the risk factor directed questions. 95% CI of ORs of all questions, except one include 1 so association of questions with HBsAg and anti-HCV is not proved at 5% significance level. 95% CI of ORs for history of jaundice does not include 1 which indicate an association but P value of this risk factor with Fishers exact test is also >0.05% (0.06%) and therefore not significant. The PPV (positive predictive value) of two risk directed questions, i.e., history of surgery in previous 6 months and history of jaundice, is >20% for HBsAg, while for HCV the PPV for history of surgery is 20%. The PPV calculation was based on pretest probability of 7% for both types of hepatitis. A PPV of any risk factor that is >20% would increase the post test probability to 27% or more. All the questions have high specificity; therefore, questions with high PPV [>20%; Tables 1 and 2], if used as donor deferral criterion, would translate into donor loss of 1.5%. When all the seven questions are used as donor deferral criteria, then the total donor loss calculated is 14.49%. These are in addition to 16% lost donors due to seroreactivity in blood serology tests for hepatitis while having no history of any risk factor. This 16% would translate into 5.3% hepatitis seropositive donors per year, as the positive donors were consecutive in 3 years for this study. Total loss would become 14.49% plus 5.3% (19.79%).

Discussion

Donor screening strategies enhance safety[13] of blood but only few have been evaluated for effectiveness before implementation[14,15] Some predonation screening procedures are of questionable significance, especially after introduction of TTI screening tests of high sensitivity and specificity.[16,17] Developing countries like Pakistan are faced with challenge of extending same standard of care as developed countries, but have poor infrastructure, nonsustainable health care funding, illiteracy and uninformed public, and above all absence of evidence for formulation of locally relevant policies. It has been seen that screening policies, predonation, and others that have evolved in developed countries is made part of local regulatory guidelines, which may not be relevant, practical, or affordable in present conditions. Some of these may have adverse impact on the transfusion services and therefore need for local evidence is urgent. This study tries to fill one of the gaps about effectiveness of donor health history questionnaire as a tool to defer unsafe donor, who are more likely be in window period of TTI. Seven questions are initially tested which were framed in simple, easily understandable language that could be answered without assistance, and are based on risk factors[5-9] that have been systematically reviewed by Syed

et al.[12] The cases and controls were a cohort of directed donors/replacement donors.

The introduction of educational material and direct questioning about HIV risk factors has been effective in decreasing risk of its transmission before tests for HIV were available.[18] This study, however, did not include questions directed towards HIV and illicit drug use related high risk behavior because piloting of such risk directed questions in same center showed that no such question were answered by the donors. The reasons could be that directed and replacement donors completed the questionnaire with their relatives and friends around them and they probably did not trust the privacy and confidentiality of information with the blood bank. Social and religious taboos to answer such questions even to health care workers is well known in the society as exemplified by the denial of high risk behavior by the donors who tested positive for syphilis, even on one to one interview. Failure to acknowledge risk behavior is complex in every society, and some degree of nondisclosure is expected in predonation screening.[19] Nonvolunteer donors selected as subjects were the important limitation of the study; therefore, the results may not be completely applicable to all volunteer donors. However since the questions were taken as not crossing the threshold of privacy of donors, and were answered enthusiastically, therefore the author concludes that these will be applicable to all types of donors.

Tables 1 and 2 ORs for any risk factor did not prove significant association of risk factors with seroreactivity for hepatitis in this study. Previous history of jaundice irrespective of age for HBV and history of surgery in previous 6 months for both HBV and HCV had PPV of 20% or more [Tables 1 and 2]. The calculations were based on pretest probabilities of 7% derived from the weighted averages of hepatitis prevalence in Pakistani blood donors.[12] The post-test probability of hepatitis was increased to 30% for these questions, which makes these two questions having highest efficacy and therefore are recommended to be part of Donor History Questionnaire (DHQ) and used for deferring donor. Similar observation has been made by Zou *et al.*, who found that questions regarding risk of viral hepatitis and history of intravenous drug use, correlated better with hepatitis markers positive donors.[20] Permanent deferral is recommended for Pakistani donors having history of jaundice at any age because 40% of HBsAg in Pakistan is acquired in perinatal period,[9] which will be in contrast to USA where history of jaundice after 11 year age is criteria for permanent deferral. Donors with history of surgery should be temporarily deferred for 1 year which is sufficient time for seroconversion after last intervention especially if screening is done with reagents of high sensitivity and is similar to what is being recommended by Federal Drug Agency USA and American Association of Blood Banks.[21]

The 5.3% deferral rate is expected to be lower if DHQ comprising seven questions is implemented because some donors with viral markers will be excluded in predonation screening. However, the ORs in this study have shown that there is no significant association of risk factors with TTI; therefore, this seropositivity rate will persist and will have to be added to other causes of donor deferral and sums up to 20% of all donors at the center. This seems to be excessive when compared with 14% in USA where donors are asked more than 40 questions and takes into consideration the miscollected units as well.[22]

It is important to note that one fourth of donors in this study needed assistance to fill up the questionnaire because of illiteracy or primary education alone. This has implications for introducing "self exclusion" policy in this country in which donor decide to refrain from donation after comprehending the educational material about risks of donations from high risk donors. Therefore, either the volunteers will have to be recruited from educated classes or primarily audiovisual techniques will have to be applied.

This type of study or those employing different strategies need to be duplicated in all volunteer donors who are provided adequate privacy and have assurance about the confidentiality at blood bank. Such studies may be supplemented with anonymous donor surveys to assess the magnitude of high risk donors and truth challenged donors. Sexual behavior/preferences and drug intake directed questions need to be assessed as well to define effective donor health questionnaire that are more likely to defer donors in window periods of TTIs and could not be undertaken in present study. For hepatitis-related questions, this present study is sufficient to extrapolate results to other groups of donors and may form basis of much abbreviated questionnaire until more studies are available.

Since none of donors in study happen to have history of transfusion, therefore its PPV could not be calculated. However, this is important risk factor for hepatitis in our country as shown in many studies[12,23] and although only minority of donors will probably become volunteer donor after having indications to receive blood transfusion, therefore this history should also constitute criteria for temporary deferral as is also approved by FDA and AABB[21] Only limited number of questions should be made as donor deferral criteria at donor interview and should explicitly be stated in the national guidelines, keeping in view the structural, organizational, and financial limitations of country.[24] TTIs for which laboratory test are not yet available, DHQ remains the only way to defer donor with high risk [e.g., Creutzfelt Jacob Disease (VJD), variant CJD], however surveillance of blood transfusion recipients and epidemiological data for such infections, should be available for the country before introducing deferral policies, directed at these even if they are deemed effective for other countries.

In an era of very effective and sensitive laboratory testing for TTI, the developing countries should set their priorities on evidence and not necessarily have to adopt non evidence-based policies based on precautionary principle only. The meager resources should be primarily directed at ensuring universal screening for TTI with high quality reagents, at grass root level.

Acknowledgement

I thank technical staff of blood bank that provided and helped donors to complete the questionnaire and carried out TTI tests.

References

1. Kleinman S. Impact of blood donor screening procedures on transfusion safety. In: Linden JV, Bianco C, editors. Blood safety and surveillance. New York: Mercel Dekker Inc.; 2001. p. 145.
2. Eder A, Goldman M, Rossmann S, Waxman D, Bianco C. Selection Criteria to Protect the Blood Donor in North America and Europe: Past (Dogma), Present (Evidence), and future (Hemovigilance). Transfus Med Rev 2009;23:205-20.

3. Kleinman S. Donor selection and screening procedures. In: Nance SJ, editor. Blood Safety, Current Challenges. Bethesda, MD: American Association of Blood Banks; 1992. p. 169.
4. Ministry of Health Government of Pakistan. Standards and Guidelines for Blood Transfusion Services. Islamabad; 1999. p. 2-10.
5. Jafri W, Jafri N, Yakoob J, Islam M, Tirmizi SF, Jafar T, *et al*. Hepatitis B and C: Prevalence and risk factors associated with seropositivity among children in Karachi, Pakistan. BMC Infect Dis 2006;6:10.
6. Luby SP, Qamruddin K, Shah AA, Omair A, Pahsa O, Khan AJ, *et al*. The relationship between therapeutic injections and high prevalence of hepatitis C infection in Hafizabad, Pakistan. Epidemiol Infect 1997;119:349-56.
7. Akhtar S, Moatter T. Intra-household clustering of hepatitis C virus infection in Karachi, Pakistan. Trans R Soc Trop Med Hyg 2004;98:535-9.
8. Irfan A, Arfeen S. Hepatitis C virus infection in spouses. Pak J Med Res 2004;43:113-6.
9. Sarwar Zuberi J. Seroepidemiology of HBV/HCV in Pakistan. Int Hepatol Comm 1996;5:19-26.
10. Available from: http://www.sampsize.sourceforge.net/iface/index.html/. [Updated 2005 Aug 9; Cited 2011 May 23].
11. Pezzullo JC (Georgetown University). Interactive Statistical Calculations web site [Internet]. Washington (DC): John C. Pezullo; 2000-2011. Available from: http://www.StatPages.org/. [Rev. 2011 Feb 17; Cited 2011 May 23].
12. Ali SA, Donahue RM, Qureshi H, Vermunda SH. Hepatitis B and hepatitis C in Pakistan: Prevalence and risk factors. Int J Infect Dis 2009;13:9-19.
13. Glynn SA, Kleinman SH, Schreiber GB, Busch MP, Wright DJ, Smith JW, *et al*. Trends in incidence and prevalence of major transfusion-transmissible viral infections in US blood Donors, 1991 to 1996. JAMA 2000;284:229-35.
14. Grossman BJ, Kollins P, Lau PM, Perreten JL, Bowman RJ, Malcolm S, *et al*. Screening blood donors for gastrointestinal illness: A strategy to eliminate carriers of Yersinia enterocolitica. Transfusion 1991;31:500.
15. Appleman MP, Shulman IA, Saxena S, Kirchhoff LV. Use of a questionnaire to Identify potential blood donors at risk for infection with *Trypansoma cruzi*. Transfusion 1993;33:61.
16. Lawson-Ayayi S, Salmi LR. [Infection risk and efficacy of Clinical selection techniques for volunteer blood donors]. Transfus Clin Biol 1997;4:513-21.
17. Van den Burg PJ, Vrielink H, Reesink HW. Donor selection: The exclusion of high risk donors? Vox Sang 1998;74 Suppl 2:499-502.
18. Busch MP, Young MJ, Samson SM, Mosley JW, Ward JW, Perkins HA. Risk of human immunodeficiency virus transmission by blood transfusions prior to the implementation of HIV antibody screening in the San Francisco Bay Area. Transfusion 1991;31:4-11.
19. O'Brien SF, Xi G, Yi QL, Goldman M. Understanding non-disclosure of deferrable risk: A study of blood donors with a history of intravenous drug use. Transfus Med 2010;20:15-21.
20. Zou S, Fujii K, Johnson S, Spencer B, Washington N, Iv EN, *et al*. Prevalence of selected viral infections among blood donors deferred for potential risk to blood safety. Transfusion 2006;46:1997-2003.
21. American Association of Blood Banks. Bethesda. [Internet]. The Association; c 2011. Available from: http://www.aabb.org/resources/donation/questionnaires/Pages/dhqaabb.aspx. [Updated 2011; Cited 2011 Mar 23].
22. Custer B, Johnson ES, Sullivan SD, Hazlet TK, Ramsey SD, Hirschler NV, *et al*. Quantifying losses to the donated blood supply due to donor deferral and miscollection. Transfusion 2004;44:1417-26.
23. Jafri W, Jafri N, Yakoob J, Islam M, Tirmizi SF, Jafar T, *et al*. Hepatitis B and C: Prevalence and risk factors associated with seropositivity among children in Karachi, Pakistan. BMC Infect Dis 2006;6:101.
24. Lee HH, Allain JP. Improving blood safety in resource-poor settings. Vox Sang 2004;87:76-179.

Cite this article as: Salamat N. Effectiveness of blood donor questionnaire directed at risk factor for transfusion transmitted infections in Pakistani population. Asian J Transfus Sci 2012;6:169-73.

Source of Support: Nil, **Conflict of Interest:** None declared.