Risk factors associated with human immunodeficiency virus infection in blood donors in Iran: A case–control study

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Abstract:

BACKGROUND: Despite setting the stringent criteria for the selection of safe donors, some human immunodeficiency virus (HIV)-positive volunteers manage to give blood. Considering the window period of screening tests, this could endanger the safety of blood supply.

MATERIALS AND METHODS: A frequency match case–control study was conducted on HIV-positive and negative blood donors in Iran from 2007 to 2008. Overall, 61 HIV-positive and 224 HIV-negative blood donors were selected as cases and controls, respectively. Two groups were matched for confounding factors. An identical questionnaire was used to assess risk factors. Univariate regression analysis for calculating crude odds ratio (OR) and 95% confidence interval (CI) was used for detecting eligibility of risk factors to enter the final model. The exposures with \( P < 0.1 \) were entered in the logistic regression model. Adjusted ORs with \( P < 0.05 \) and 95% CIs were reported for statistically significant variables.

RESULTS: Significant effects were detected for the following variables: education, job, tattoo, intravenous (IV) drug abuse, imprisonment, and risky sexual behavior. However, based on multiple analyses, education, IV drug abuse, imprisonment, and risky sexual behavior remain significant.

CONCLUSION: The majority of our findings are in parallel with the other studies performed in other countries. To increase blood safety, special attention should be paid to illiterate, first-time blood donors who are in the 25–40 age range. In addition, having the history of IV drug abuse, imprisonment and risky sexual behaviors put the blood donors more at risk of infecting HIV.

Keywords: Blood donors, human immunodeficiency virus, Iran, risk factor

Introduction

Providing safe and sufficient blood is the most important mission of all blood transfusion services. To this end, Iranian blood transfusion organization (IBTO) developed stringent criteria for selection of safe donors such as encouraging regular blood donation and retaining safe blood donors; providing informative and educational materials about the main risk factors; improving public health programs with a focus on counseling and screening of those engaged in high-risk activities; predonation screening through interviews, filling precise questionnaire, and brief physical examinations; and implementing a uniform self-deferral procedure and confidential unit exclusion.[1] Physicians in donor selection department are trained before starting their work and continuously in related courses.

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IBTO screens 100% of donated blood for transfusion-transmitted infections (TTI). Screening of donated blood for hepatitis B surface antigen (HBsAg) became mandatory since the establishment of IBTO in 1974. However, screening of blood units for human immunodeficiency virus (HIV) and hepatitis C virus (HCV) started from 1989 to 1996, respectively.\cite{2}

In Iran, the overall prevalence rate of HIV infection among blood donors, during the last 5 years, was 0.003%.\cite{3} However, according to the UNAIDS, the number of people living with HIV in Iran is estimated to be 66000 (37,000–120,000) in 2016; in another word, the prevalence of HIV is about 0.1% among Iranian adult population (15–49 years old).\cite{4} As expected, the prevalence of HIV is considerably lower among blood donors comparing to general population. However, despite the policies set to exclude people with high-risk behaviors, some few HIV-infected volunteers manage to donate. Considering the window period of screening tests, this could endanger the safety of blood supply.

Several studies carried out to identify the most important risk factors among HBsAg and HCV-positive blood donors in Iran.\cite{5,6} However, there has not been any comprehensive data about the risk factors of HIV-positive blood donors. This study aims to address this lack of information and evaluates the main risk factors of Iranian HIV seropositive blood donors.

**Materials and Methods**

A frequency match case–control study was conducted on HIV-positive and negative blood donors in Iran from 2007 to 2008. The delay in reporting the data was mainly attributed to the problems that were faced in collecting the data of control group in terms of their consistency and confounding factors. Overall, 61 HIV-positive and 224 HIV-negative blood donors were selected as cases and controls, respectively. To reduce selection bias and confounding, 1:4 cases and control frequency matching by age, gender, and times of donation (first time, regular or repeat donor) was performed. Their ages were matched based on 10-year period categories, and the controls were selected and recalled according to their inclusion in each category. The same method was used for the matching their sex. An identical questionnaire was used for both the cases and controls to assess risk factors for HIV. All participants agreed to complete the questionnaire and signed an informed consent. The questionnaire was developed (to assess HIV risk factors among blood donors) by consulting experts, based on the national standards of procedures in IBTO. To exclude the errors and defects, the questionnaire was firstly filled by 35 HIV-positive blood donors and 100 HIV-negative blood donors in a pilot. The questionnaire contained items on sociodemographic characteristics and risk factors. Sociodemographic characteristics included gender, age, marital status, level of education, and occupation. Risk factors included phlebotomy (Hijamat), tattoo, blood transfusion, intravenous (IV) drug abuse, imprisonment, risky sexual behavior (sex with HIV-positive person, sex with more than one partner, extramarital sex, male–male sex, and history of sexually transmitted disease). The questionnaires were completed by the medical doctors at blood centers in predonation interview at a private room, through a face-to-face process, and were collected in special boxes. To observe confidentiality, the name and donation number was deleted from the questionnaire.

**Case and control definitions**

Based on the policy of IBTO, volunteers who have positive ELISA test are permanently deferred to donate blood. Then, confirmatory test must be done, and the positive cases are recalled and requested to turn back to repeat the confirmatory test with different kits. These donors after positive repeated tests have been requested to fill in the questionnaire as cases. Control group was selected four times more than cases among blood donors who had negative HIV serologic tests from the same database of cases who had accepted our invitation to participate in the study. Control group were frequently matched with cases in terms of age, gender, and times of donation. Phone recalls were made based on the results of HIV + confirmatory tests to the donors. Accordingly for each HIV-positive case, a person from control group was recalled to fill the questionnaire.

**Laboratory methods**

The donations were all screened for HIV antigen/antibody by Vironostika HIV antigen/antibody (Bio Merieux)-Fourth generation or HIV antigen/antibody (Bio Rad)-Fourth generation kits. Every sample that was found to be positive in the screening test was retested; and if it was constantly positive, retesting was performed by HIV BLOT 2.2 (MP Diagnostic) and INNO-LIA, HIV 1/2 score (Innogenetics) as a confirmatory test.

**Statistical analysis**

First, to evaluate univariate analysis between HIV-positive blood donors and the expected exposures, the models were run separately. The models included the risk factors of the questionnaire as independent variables and HIV as the dependent variable. The sociodemographic characteristics of the cases and controls were assessed, and the risk factors were compared with univariate analysis for calculating crude odds ratio (OR) and 95% confidence interval (CI) and eligibility to enter the final model. The exposures with $P < 0.1$ were entered in the multiple logistic regression model.
Consequently, a backward stepwise selection method was used to build multiple models that restricted to all the risk factors that were independently associated with HIV. Adjusted ORs with \( P < 0.05 \) and 95% CIs were reported for significant variables. Confounding bias was identified as a consequence of the change in OR before and after adjustment for the confounding variable. All the analyses were performed with computer software (SPSS 22, SPSS, IBM Inc.).

The study was ethically approved by the Ethics Committee of Iranian High Institute for Research and Education. The confidentiality of data was preserved during the study.

**Results**

Of all 89 confirmative positive HIV blood donors in 2007–2008 who were called, 61 cases filled in the questionnaire. Of 28 excluded cases, 13 were given wrong telephone number and address (47%), 8 did not return despite former willingness during the first recall (29%), and 7 did not have phone number or had remote home address (24%). Compared to 61 cases, 244 controls were selected from blood donors who had negative HIV serologic tests. Of 61 cases, 5 were female (8.2%) and 56 (91.8%) were male. Cases were more likely between 30 and 40 years old (39.3%). Sixty-seven point two percent of cases were first-time blood donors and 32.8% were lapsed donors. Successful frequency matching enrolment approach leads to enhanced age group, sex, and blood donation type distribution in the final sample. The participants’ donation status and sociodemographic and relevant characteristics are presented in Table 1.

Table 2 displays a comparison of potential crude and adjusted OR of significant exposures and 95% CI.

Based on univariate analysis, significant association was detected for the following variables: education, job, tattoo, IV drug abuse, imprisonment, and risky sexual behavior. However, based on multiple analyses, education, IV drug abuse, imprisonment, and risky sexual behavior remain significant. It seems that job and tattoo were confounded by other exposures.

In univariate model HIV positivity in occupied and students were less than jobless patients, tattoo increased the risk of HIV four times compared to control but neither was significant in multiple models. Phlebotomy (Hijamat) (the Hijamat is the name of the traditional Islamic healing technique and the method includes removing blood from the body to attain remedy and consists of cupping and scarification of the specific skin area of the body) and history of blood transfusion based on univariate analysis were not significantly different between two groups.

In terms of educational levels, illiteracy was more frequent among cases (13.1%) comparing to 2.5% among controls. Higher education has a protective role against HIV positivity. The protective roll became robust by increasing the educational level comparing to illiterate participants (academic level OR \(_{adj}\) : 0.04, CI 95%: 0.008–0.2 and high school level OR \(_{adj}\) : 0.11, CI 95%: 0.03–0.42).

In the absence of confounding effect of other exposures, Intravenous Drug Users (IVDUs), prisoners, and persons with high-risk sex behaviors had HIV infection more than controls, about 18, 15, and 3 times, respectively (IVDU OR adj: 18.24, CI 95%: 4.27–77.76; imprison OR adj: 15.63, CI 95%: 1.54–158.12; and unsafe sex OR adj: 3.18, CI 95%: 1.18–8.51).

In HIV-positive cases, having multiple risk factors at the same time were frequent. About 29% (18 blood donors) of HIV-positive cases had all significant risk factors, but in HIV-negative group, there was no participant with multiple risk factors. In 7.3% (17 blood donors) of HIV-positive cases and 96.4% (216 blood donors) of controls, no risk factor was reported.
The study found the main HIV risk factors among Iranian blood donors who donated blood during 2007–2008. Results indicate that, illiteracy, and having the history of IV drug abuse, imprisonment and risky sexual behaviors are associated with the risk of HIV positivity among blood donors. In addition, being in the 30–40 age range and first-time donor were significantly prevalent among cases comparing to general population.

The rate of male/female ratio of HIV seropositive blood donors (91.8/8.2%) did not have any significant difference comparing to general population of blood donors (92/8%) and general population of HIV positives in 2007 in Iran (93/7%).

In our study, we found some demographic characteristics make volunteer to be at more risk. Middle-aged and first-time blood donors are more likely to be at risk of infecting HIV. However, the population of Iranian blood donors was mostly between 20 and 30 years old (36.7%) in 2007. Furthermore, in general population of HIV infected, cases were mostly (46.4%) in the 25–34 age range. In 2012, Mariston et al. found that being at the 29–39 age range is most prevalent among HIV-positive blood donors. In another study carried out in Malawi, there was a highly significant positive association of HIV prevalence with being in the age group of 25–29 years for females and 30–34 years for males. The minor discrepancy that exists in the age group of our study comparing to general population of HIV infected cases may be related to the higher level of knowledge among young blood donors about the negative effects of HIV test-seeking behavior which is the result of growing IBTO awareness-raising campaigns among university students and young people. Furthermore, the majority of our cases were male, and as it was found in the study of Malawi, men tend to be older than women among cases.

Table 2: Comparison of potential crude and adjusted odds ratio of significant exposures and 95% confidence interval

| Exposure          | OR crude (CI 95%) | P   | OR adjusted (CI 95%) | P   |
|-------------------|------------------|-----|----------------------|-----|
| Education         |                  |     |                      |     |
| Illiterate        | Reference        |     |                      |     |
| High school       | 0.23 (0.07-0.7)  | 0.01| 0.11 (0.03-0.42)     | 0.001|
| Academic          | 0.04 (0.01-0.1)  | <0.001| 0.04 (0.008-0.2)     | <0.001|
| IVDU              | 91.42 (26.28-317.99) | <0.001| 18.24 (4.27-77.76) | <0.001|
| History of imprisonment | 159.33 (20.9-1214.19) | <0.001| 15.63 (1.54-158.12)  | 0.02 |
| Unsafe sex        | 10.55 (5.52-20.19) | <0.001| 3.18 (1.18-8.51)     | 0.02 |
| Gender            | 0.38 (0.12-1.25) | 0.14|                      |     |
| Phlebotomy        | 0.85 (0.43-1.67) | 0.63|                      |     |
| Tattoo            | 4.87 (2.17-10.89) | <0.001|                      |     |
| Blood transfusion | 2.65 (0.83-8.44) | 0.14|                      |     |
| Job               |                  |     |                      |     |
| No job            | Reference        |     |                      |     |
| Occupied          | 0.35 (0.15-0.84) | 0.01|                      |     |
| Student           | 0.08 (0.01-0.72) | 0.02|                      |     |
| Age               |                  |     |                      |     |
| <30               | Reference        |     |                      |     |
| 30-40             | 1.42 (0.7-2.88)  | 0.31|                      |     |
| 40-50             | 1.59 (0.74-3.42) | 0.23|                      |     |
| 50<               | 0.88 (0.26-2.89) | 0.83|                      |     |
| Marital status    |                  |     |                      |     |
| Divorce/widow     | Reference        |     |                      |     |
| Married           | 0.36 (0.08-1.59) | 0.2 |                      |     |
| Single            | 0.5 (0.11-2.30)  | 0.37|                      |     |
| Covariate         |                  |     |                      |     |
| Education         |                  |     |                      |     |
| Low               | Reference        |     |                      |     |
| Medium            | 0.23 (0.07-0.7)  | 0.01| 0.11 (0.03-0.42)     | 0.001|
| High              | 0.04 (0.01-0.1)  | <0.001| 0.04 (0.008-0.2)    | <0.001|

IVDUs=Intravenous drug users, OR=Odds ratio, CI=Confidence interval

Discussion

The study found the main HIV risk factors among Iranian blood donors who donated blood during 2007–2008. Results indicate that, illiteracy, and having the history of IV drug abuse, imprisonment and risky sexual behaviors are associated with the risk of HIV positivity among blood donors. In addition, being in the 30–40 age range and first-time donor were significantly prevalent among cases comparing to general population.

However, the population of Iranian blood donors was mostly between 20 and 30 years old (36.7%) in 2007. Furthermore, in general population of HIV infected, cases were mostly (46.4%) in the 25–34 age range. In 2012, Mariston et al. found that being at the 29–39 age range is most prevalent among HIV-positive blood donors. In another study carried out in Malawi, there was a highly significant positive association of HIV prevalence with being in the age group of 25–29 years for females and 30–34 years for males. The minor discrepancy that exists in the age group of our study comparing to general population of HIV infected cases may be related to the higher level of knowledge among young blood donors about the negative effects of HIV test-seeking behavior which is the result of growing IBTO awareness-raising campaigns among university students and young people. Furthermore, the majority of our cases were male, and as it was found in the study of Malawi, men tend to be older than women among cases.

Our results indicate that cases are mostly first-time blood donors (67%). This confirms the findings of another study.
in which Amini et al. found that the frequency of HIV in repeat blood donors is significantly less than first-time blood donors between 2006 and 2007. In another study that analyzed the prevalence of HIV among Brazilian blood donors, it was shown that HIV prevalence was 22% higher among the first-time donors than replacement donors.

Illiteracy was more frequent among cases than controls (13.1% vs. 2.5%). Illiterate individuals were found to present the highest risk of being HIV-positive donor candidates in Brazil. It may be because of lower rate of risky behavior among educated people or higher educated HIV positives may not tend to donate because of their knowledge.

Among known HIV risk factors, we did not recognize any significant association between HIV positivity, doing phlebotomy (Hijamat), and history of blood transfusion. Based on the National Blood Policy in Iran, doing Hijamat defers volunteer from blood donation for 6 months. These results confirm the finding of the report of the Ministry of Health which indicates that since 2007, there has not been any reported case of HIV positive through blood transfusion.

However, being IV drug abuser, having a history of imprisonment and risky sexual behaviors are found to have significant effects on HIV positivity.

Given a large proportion of prisoners is drug addicts, these findings were compatible with other studies conducted in Iran and some countries which suggest that drug injection inside prison carries more risk for HIV infection. The prevalence of HIV is 13.4% among injecting drug users which is dramatically high comparing to general population. In a study among community-based drug users in Tehran, the prevalence of HIV infection was reported 23.2% among male IVDUs. In a multiple analysis, a history of shared drug injection inside prison (OR: 2.5) and multiple incarcerations (OR: 3.13) were associated with a significantly higher prevalence of HIV infection. Other studies conducted among IV drug users in Tehran support our results, in which a history of shared injection inside prison found to be the most important risk factor associated with HIV infection.

After injecting drugs, a significant proportion (17.1%) of registered cases of HIV transmission in Iran is attributed to unsafe sexual contact. Although having male–male sex identified as the most significant risk factor in other countries, (in Brazil and United States) in Iran, having risky sexual behaviors came third of importance. This may due to religious beliefs and criminal laws which bans Iranians from this kind of relation. Nevertheless, in the biobehavioral survey of inmates in 2009, 15.6% of men reported sexual contact with other men. The prevalence of HIV among this subset of MSM was found to be 3.7%. We believe that most of our excluded cases may have some risk factors. These donors gave wrong address or phone number and some did not return despite former willingness during the first recall. They may mostly be test seekers who did not give right personal details to escape from aftermath consequences. In a study conducted in Brazil in 2010, it was reported that test seeker HIV-positive blood donors believe that it is ok not to answer questions truthfully to donate blood and get tested for HIV through donation.

Due to few numbers of cases, we were unable to identify prevalent risk factors in each province. In provinces with more HIV positives such as Kermanshah and Golestan, the rate of deferral from blood donation was lower than average rate of deferral in the whole country which was 25.6% in the same year and in other HIV prevalent provinces such as Tehran, Fars, and Hormozgan, it was equal to that rate. Considering the high prevalence of HIV in those provinces, it is necessary to apply more stringent criteria for the selection of blood donors.

Conclusion

In donor selection step, attention should be paid to the vulnerable population, especially first time who are in the age range of 25–40. The staff of donation department staff should be trained regularly and receive feedback about donors who will be positive for TTI.

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Conflicts of interest

There are no conflicts of interest.

References

1. Pourfathollah AA, Hosseini Divkolaye NS, Seighali F. Four decades of national blood service in Iran: Outreach, prospect and challenges. Transfus Med 2015;25:138-43.
2. Abolghasemi H, Maghsadlu M, Amini Kafi-Abad S, Cheraghali A. Introduction to Iranian blood transfusion organization and blood safety in Iran. Iran J Public Health 2009;38 Suppl 1:82-7.
3. The Statistical Database of Iranian Blood Transfusion Organization;
4. UNAIDS. Islamic Republic of Iran. UNAIDS; 2016. Available from: http://www.unaids.org/en/regionscountries/countries/islamicrepublicofiran. [Last accessed on 2017 Nov 01].

5. Rezaei N, Amini-Kafabad S, Maghsudlu M, Abolghasemi H. Risk factor analysis of hepatitis C virus seropositivity in Iranian blood donors: A case-control study. Transfusion 2016;56:1891-8.

6. Vahid T, Kafaei J, Kabir A, Yektaparast B, Alavian SM. Hepatitis B prevalence and risk factors in blood donors in Ghazvin, Iran. Hakim Health Syst Res 2005;8:8-15.

7. Iran Country Report on Monitoring of the United Nations General Assembly Special Session on HIV and AIDS. National AIDS Committee Secretariat, Ministry of Health and Medical Education; February, 2010.

8. Iran Country Report on Monitoring of the United Nations General Assembly Special Session on HIV and AIDS. National AIDS Committee Secretariat, Ministry of Health and Medical Education; March, 2011.

9. Queiroz NM, Sampaio Dde A, Santos Ede S, Bezerra AC. Logistic model for determining factors associated with HIV infection among blood donor candidates at the Fundação HEMOPE. Rev Bras Hematol Hemoter 2012;34:217-21.

10. Kafi-Abad SA, Rezvan H, Abolghasemi H, Talebian A. Prevalence and trends of human immunodeficiency virus, hepatitis B virus, and hepatitis C virus among blood donors in Iran, 2004 through 2007. Transfusion 2009;49:2214-20.

11. Iran Country Report on Monitoring of the United Nations General Assembly Special Session on HIV and AIDS. National AIDS Committee Secretariat, Ministry of Health and Medical Education; March, 2015.

12. Mir-Nasserri MM, Mohammadhkani A, Tavakkoli H, Ansari E, Poustchi H. Incarceration is a major risk factor for blood-borne infection among intravenous drug users: Incarceration and blood borne infection among intravenous drug users. Hepat Mon 2011;11:19-22.

13. Vanichseni S, Kitayaporn D, Mastro TD, Mock PA, Raktham S, Des Jarlais DC, et al. Continued high HIV-1 incidence in a vaccine trial preparatory cohort of injection drug users in Bangkok, Thailand. AIDS 2001;15:397-405.

14. Rahimi-Movaghar A, Amin-Esmaeili M, Haghdoot AA, Sadeghizadeh B, Mohraz M. HIV prevalence amongst injecting drug users in Iran: A systematic review of studies conducted during the decade 1998-2007. Int J Drug Policy 2012;23:271-8.

15. Zamani S, Kihara M, Gouya MM, Vazirian M, Nassirimanesh B, Ono-kihara M, et al. High prevalence of H incarceration IV infection associated within among community-based injecting drug users in Tehran, Iran. J Acquir Immun Defic Syndr 2006;42:342-6.

16. Kheirandish P, Seyedinagh SA, Hosseini M, Jahani MR, Shizad H, Foroughi M, et al. Prevalence and correlates of HIV infection among male injection drug users in detention in Tehran, Iran. J Acquir Immune Defic Syndr 2010;53:273-5.

17. Zamani S, Kihara M, Gouya MM, Vazirian M, Ono-Kihara M, Razzaghi EM, et al. Prevalence of and factors associated with HIV-1 infection among drug users visiting treatment centers in Tehran, Iran. AIDS 2005;19:709-16.

18. Islamic Republic of Iran AIDS Progress Report. National AIDS Committee Secretariat, Ministry of Health and Medical Education; March, 2014.

19. de Almeida-Neto C, Goncalx TT, Birch RJ, de Carvalho SM, Capuani L, Leão SC, et al. Risk factors for human immunodeficiency virus infection among Brazilian blood donors: A multicentre case-control study using audio computer-assisted structured interviews. Vox Sang 2013;105:91-9.

20. Crowder LA, Steele WR, Notari EP, Hopkins CK, Lima JL, Foster GA, et al. Prevalence, incidence, and risk factors of human immunodeficiency virus infection in blood donors in the Southeastern United States. Transfusion 2017;57:404-11.

21. Gonzalez T, Sabino E, Sales N, Chen YH, Chamone D, Busch M, et al. Human immunodeficiency virus test-seeking blood donors in a large blood bank in São Paulo, Brazil. Transfusion 2010;50:1806-14.

22. Musavi H, Rahimi H, Kooti W, Dorostkar R, Azami M, Sharghi M, et al. Prevalence of Human Immunodeficiency Virus in Iranian Blood Donors: A Systematic Review and Meta-Analysis. Arch Iran Med 2018;21:260-7.

23. Birjandi F, Gharibaghian A, Delavari A, Rezaie N, Maghsudlu M. Blood donor deferral pattern in Iran. Arch Iran Med 2013;16:657-60.

24. Attarchi Z, Ghafori M, Hajibaygi B, Assari S, Alavian SM. Donor deferral and blood-borne infections in blood donors of Tehran. Sci J Blood Transfus Organ 2006;2:353-64.