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ORIGINAL ARTICLE

Incidence and Residual Risk of HIV, HBV and HCV Infections Among Blood Donors in Tehran

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Abstract Estimation of residual risk is essential to monitor and improve blood safety. Our epidemiologic knowledge in the Iranian donor population regarding transfusion transmitted viral infections (TTIs), is confined to a few studies based on prevalence rate. There are no reports on residual risk of TTIs in Iran. In present survey, a software database of donor records of Tehran Blood Transfusion Center (TBTC) was used to estimate the incidence and residual risk of hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infections, by applying the incidence rate/window period (IR-WP) model. A total of 1,207,155 repeat donations was included in the analysis and represented a mean of 8.4 donations per donor over 6 years. The incidence amongst repeat donors was estimated by dividing the number of confirmed seroconverting donors by the total number of person-years at risk. The residual risk was calculated using the incidence/window period model. Incidence rate and residual risk for HBV, HCV and HIV infections were calculated for total (2005–2010) and two consecutive periods (2005–2007 and 2008–2010) of the study. According to the IR-WP model, overall residual risk for HIV and HCV in the total study period was 0.4 and 12.5 per million units, respectively and for HBV 4.57/100,000 donations. The incidence and residual risk of TTIs, calculated on TBTC's blood supply was low and comparable with developed countries for HIV infection but high for HCV and HBV infections. Blood safety may therefore be better managed by applying other techniques like nucleic acid amplification tests.

Keywords Incidence estimation · Residual risk · Blood donors · Iran

Introduction

Appropriate donor selection and highly sensitive laboratory blood screening procedures for major transfusion transmitted viral infections (hepatitis B, hepatitis C and human immunodeficiency virus) are two main measures to prevent transfusion of infected bloods [1]. Despite these measures, there is still a residual risk of entering infected donations to the blood supply. The greatest portions of this residual risk were due to donation of blood in the infectious window period, the time between infections and detect ability by screening tests. Estimation of these risks is essential to monitor and improve blood safety [2]. In past two decades, various mathematical models have been developed to calculate the residual risk. One of the most accepted models is that of retrovirus donor study of United States (incidence/window period model) that has been used to estimate window period donation risk (residual risk) since early 1990 in U.S, and now been applied successfully worldwide [3, 4].

In Iran, screening of blood donations for hepatitis B virus (HBV) became obligatory since 1974. However, screening of blood donations for human immunodeficiency virus (HIV) and hepatitis C virus (HCV) became

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mandatory since 1989 and 1996 respectively. Our epidemiologic knowledge, in the Iranian donor population, regarding transfusion transmitted viral infections (TTIs), is confined to a few studies based on prevalence rate [5].There are no reports on residual risk of TTIs in Iran.

Tehran Blood Transfusion Center (TBTC) is the largest center of Iranian blood transfusion organization (IBTO), which accounts for more than 30 % IBTO activities. [6] In this survey, a software database of donor records of TBTC was used for the first time in Iran, and followed the incidence rate/window period (IR-WP) model to estimate the incidence and residual risk of HBV, HCV and HIV.

Materials and Methods

Study Population

Data about all repeated donations tested during 2005–2010 were obtained from MAK data base system at all blood collection centers in Tehran. This study has been approved by the Research Committee of TBTC for ethical issues.

Definitions

A new donor is a donor who had not attended previously, according to Tehran blood centers records. A repeat donor is a donor who had a previous recorded attendance as a donor. A seroconverter was defined as a repeat donor who had made a seropositive donation during the study period (2005–2010) and had previously made a seronegative donation. Anti HCV, anti HIV and HBs Ag were screened by commercial third-generation assays. Only donations confirmed positive by western blot for HIV, by immunoblot for HCV and by a neutralization test for HBs Ag were included in the study. In addition, all donations were simultaneously tested for syphilis.

Estimation of Incidence Amongst Repeat Donors

A total of 1,207,155 repeat donations were included in the analysis. The annual donation per donor rate was 1.4 (8.4 $\div$ 6 = 1.4 donations in year). The incidence in repeat donors was estimated by dividing the number of seroconverting donors by the total number of person-years at risk. The number of person-years at risk was calculated as the number of donations made by repeat donors multiplied by an estimate of the average interval (in years) between donations from repeat donors [4, 7]. An inter donation interval (IDI) estimate was derived from data provided from blood centers in Tehran over the 6-year period 2005–2010. Inter donation interval was calculated via dividing the mean IDI for all donors by median IDI for seroconverting donors. The average IDI for all donors was therefore estimated as 365 $\div$ 1·4 $\sim$260 days, that is about 37 weeks (0·72 years). The IDI for the seroconverters was calculated directly from the dates of the last negative and first positive donation. Crud incidence rate and residual risk for HBV, HCV and HIV infections were calculated for total (2005–2010) and two consecutive periods (2005–2007 and 2008–2010) of the study.

HBsAg Adjustment

As HBsAg is generally transient in adults, the incidence of HBsAg seroconversion was adjusted for the probability of detection of an incident infection by subsequent HBsAg testing. In order to adjust for this, we calculated the weighted probability that donation testing would detect seroconversion. We assumed that 5 % of donors would have persistent antigenaemia, 85 % would have typical transient antigenaemia lasting an average of 63 days [7, 8], and 10 % would have a heightened and more rapid clearance of antigen, lasting just 30 days [9]. The chance that an incident HBV-infected donor would be detected by HBsAg testing was calculated as follows: $(0{\cdot}05 \times 1) + (0{\cdot}85 \times T1) + (0{\cdot}1 \times T2)$, where T1 is the probability that a donor with typical transient antigenaemia was HBsAg positive at the time of donation, and T2 is the probability that a donor with rapid transient antigenaemia was HBsAg positive at the time of donation. Assuming that the timing of donations was independent of the timing of infection, the probability of HBsAg positivity at the time of donation was taken as the duration of antigenaemia divided by the IDI. The average IDI for the all 173 HBsAg seroconverting donors, detected during the total study period, was 177.5 days. Therefore, T1 was 63 $\div$ 177.5 = 0·354, and T2 was 30 $\div$177.5 = 0·169. The overall probability of detecting an HBV incident infection by HBsAg testing was therefore 0·368, and the observed HBsAg incidence was multiplied by 1 $\div$0·368 = 2·7 to give an estimate of the total HBV incidence rate [7].

Adjustment for Longer IDIs Preseroconversion

Donors with new infections may have shorter or longer IDIs before their post-seroconversion donation; in this situation, probability of an infectious window-period donation may actually be greater or less than the 'average' probability, as calculated by the basic formula of the incidence estimation. Therefore, we adapted the basic incidence method, according to Soldan et al. [7], by adding an adjustment(S) that represented the mean IDI for all donors divided by the median IDI for seroconverting donors: seroconverting HIV donors (S_{HIV}) = 260 $\div$ 474 $\sim$ 0·54; and seroconverting HCV donors

(S_{HCV}) = 260 ÷ 519 ~ 0·5. Because the IDIs of detected HBsAg seroconverters were biased towards shorter intervals owing to the transient nature of HBsAg, this adjustment was not applied to the calculations for HBV risk. For HBV, it was assumed that the detected HBsAg seroconverters had the lower rank of all the (inferred) HBV incident donors with respect to IDIs. This made them the lowest 35 % of IDIs. The distribution of IDIs for the lowest 35 % ranking HIV and HCV seroconverters was similar to that for the observed HBsAg seroconversions. It was assumed that this held true for the total (65 % Unobserved) group of HBV-infected repeat donors, and the most appropriate value of seroconverting HBV donors (S_{HBV}) was calculated using the IDI for all anti-HIV and anti-HCV seroconverters. SHBV = 260 ÷ 496 ~ 0·52. Considering the small number of seroconverting donors, we used non-parametric test including Mac Nemar test.

Results

From 2,026,603 donations 1,207,155 repeat donations were recorded from 2005 to 2010. A total of 283 new viral infections were detected in repeat donations. 173, 99 and 11 donors seroconverted for HBV, HCV and HIV infection, respectively. During the study period, 2005 through 2010, 2,026,628 donations in Tehran blood transfusion center were collected. The estimates of residual risk only took account of donations from repeated donors. The total number of incident cases increased over time for each marker (Table 1).

The incidence rate of positivity for HBs Ag decreased significantly over time ($P = 0.01$). For HCV, the incidence rates during the study period increased significantly ($P = 0.001$), but an increase in observed incidence rate for HIV was not significant ($P = 0.09$).

We estimated the residual risks of transmitting a viral infection by transfusion of blood components for each period (Table 1).

Residual risk for HBV showed a significant decrease ($P = 0.01$) in second period of study compared with first period, but residual risks for HIV and HCV showed a non significant increase at that time period.

Discussion

Overall, the incidence and residual risk of TTI calculated on TBTC's blood supply was low and comparable with developed countries for HIV infection, but high for HCV and HBV infections. According to the IR-WP model, the risk was 0.3 and 0.5 per 1 million units in two consecutive study periods for HIV infection, with incidence of 0.44 and 0.86 per 100,000 person-years in these two periods respectively. Overall residual risk for HIV in total study period was 0.4 per 1 million units with the incidence of 0.7 per 100,000 person -year. The risk of acquiring a transfusion-transmitted HIV infection in Iran falls below the range of risks reported in other industrialized countries in pre nucleic acid amplification tests (NAT) era. Before implementation of NAT screening, the residual risk of 1.95 per 1 million and 0.7 per 1 million donations reported for Spain [10] and France [11] respectively. The HIV residual risk of U.S. was reported from 2.0 to 0.7 per 1 million donations in different studies on repeat donors before implementation of NAT screening, [3, 12] this may resulted from low

Table 1 Incidence and residual risk of HIV, HBV and HCV infections among blood donors in Tehran

Time-period (years): Repeat donor person-years	2005–2007 347282	2008–2010 511946	2005–2010 859228	Length of window period (days) Estimate (range)
HBs Ag				59 (37–87)
Seroconversions in RDs	83	90	173	
Incidence in RDs per 10^5 person-years	23.90	17.58	20.18	
HBV				
Adjusted Incidence in RDs per 10^5 person-years	31.22	25	28.3	
Residual risk per 10^5	5.05	4.04	4.57	
Anti-HCV				66 (38–94)
Seroconversions in RDs	26	73	99	
Incidence in RDs per 10^5 person-years	4.17	8.65	6.91	
Residual risk per 10^5	0.75	1.56	1.25	
Anti-HIV				22 (6–38)
Seroconversions in RDs	3	8	11	
Incidence in RDs per 10^5 person-years	0.44	0.86	0.7	
Residual risk per 10^5	0.03	0.05	0.04	

prevalence of HIV infection in Iranian general population (<0.01)15 and effective predonation screening procedures [13]. The difference of prevalence of HIV in Iranian general population and blood donor population (0.004 from 2004 to 2007) [5] supports this statement.

The residual risk of HCV was estimated to be 7.5 and 15.6 per 1 million donations with incidence of 4.17 and 8.65 per 100000 person-years in 2 consecutive study periods respectively. Overall residual risk for HCV in total study period was 12.5 per 1,000,000 units with the incidence of 6.9 per 100,000 person –year. The risk estimated in our study for HCV infection is somewhat higher than the risks reported for Spain (6.7 per 1 million donations) [10] and Italy (7.9 per 1 million donation), [14] but much higher than the risk of France (1.2 per 1 million donations) [11] and U.K. (1 per 0.5 million donation) [7] in pre NAT era. The reported residual risk for HCV infection in U.S. was 9.7 to 3.6 per 1,000,000 donations in different studies before implementation of NAT screening [3, 12].

In recent years, the highest estimation of HCV prevalence in Iranian general population was slightly less than 1 % [15]. The overall HCV frequency in Iranian donor population from 2004 through 2007 was estimated to be about 0.13 % [5]. Interestingly, the HCV rate among US population and American Red Cross (ARC) donors was reported to be 1.8 and 0.38 % respectively [1]. Despite this information, the higher level of residual risk for HCV in Iran versus United States and other countries [7, 10, 11, 12] and [14] may indicate a growing trend of HCV spread in the community and therefore a higher incidence in blood donors.

The prevalence trend of HCV infection among our donor population has a steady state or mildly decreasing pattern in recent years, [5] but in this study, we showed that HCV incidence increased in two consecutive study period, and these may indicate the HCV infection which recently spread through the population.

Our overall estimated incidence of HBV (28.29 per 100, 000 person-years) and residual risk (4.57 per 100,000 donations) reflects the endemic nature of HBV in Iran. Our estimation is considerably higher than the risks reported in industrialized European countries (2.1, 3.7 and 13.5 per 1 million donations, for France, [11] UK, [7] and Spain [10] respectively) and other developed countries (1.9 and 9.7 per 1 million donations, for Australia [16] and the United States [3, 12] respectively). Our HBV risk is somewhat better than the risk reported in Italy (6.9 per 100,000 donations) [17].To evaluate the current residual risk of HBV infection, it must also be considered that Iran's national HBV vaccination campaign, which began in 1993, is beginning to show its effects in corresponding donor's age groups, and we expect to observe its prominent effect in the near future [18]. Also, the incidence of HBV in two consecutive courses of the present study showed a decrescendo pattern. WP risk is probably accounting for 90 % of total risk and 10 % or less of other source of risk (viral variant, chronic seronegative carrier, and testing error) [19]. For infections with a very low prevalence already achieved in the donor population (HIV), WP donation appeared to be the main source of risk, but When the prevalence of infection is relatively high, factors that affect the risk of false-negative test results (rather than of truly negative window-period infections) gain more importance, and this may be of concerns for HBV and HCV in our donor population.

We observed that the incident cases had much longer IDIs before their post serocoversion donation than the average IDIs of all repeated tested donors. The similar finding was reported in some other studies, [8, 20] this indicates that the return of some donors around the time of infection has been delayed. To prevent overestimation of incidence calculation, we had to made an adjustment based on this difference as mentioned earlier (crud incidence multiplied to mean IDI for all repeated donors divided by the median IDI for seroconverting donors).

Although we have acceptable condition for HIV risk, according to the result of this study, we need to improve our blood safety, especially for HCV and HBV infection. Blood safety may therefore be better managed by applying other techniques like NAT. TBTC has implemented mini-pool based NAT screening system in 2011 as a one year pilot study. NAT screenings had much shorter infectious window period and higher sensitivity than 3rd generation EIA-based screening tests, especially in the cases of HCV and HIV; thus, it would lead to a significant improvement in transfusion safety in Tehran.

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Compliance with Ethical Standards

Conflict of interest The authors have declared no conflicts of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study has been approved by the Research Committee of TBTC for ethical issues. For this type of study formal consent is not required, because volunteers, at the time of blood donation have transferred of their agreements to conduct humanitarian research to TBTC.

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