

## Systematic Review

# Prevalence of Human Immunodeficiency Virus in Iranian Blood Donors: A Systematic Review and Meta-Analysis

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## Abstract

**Background:** The probability of HIV transmission through contaminated blood and blood products is eye catching. 5%-10% of blood products are contaminated with HIV. Therefore, it is essential to provide safe blood supply to prevent transmission of infectious diseases. Current systematic review and meta-analysis was conducted to evaluate the weighted prevalence of HIV in Iranian blood donors.

**Methods:** This study was reported according to PRISMA checklist for systematic reviews and meta-analysis. Required data were collected by using key words such as "HIV", "blood donation" OR "blood donors", "epidemiology" OR "prevalence", "blood transfusion" and "Iran", in international databases including PubMed, Scopus, Web of Science, Cochrane, Embase and national databases including Magiran, IranMedex and Scientific Information Databank. Papers were searched until December 2017. Cochran's Q test and I<sup>2</sup> index were used to assess the heterogeneity among studies.

**Results:** A total of 49 studies including 5 403 170 donors entered this meta-analysis. According to analysis, the prevalence of HIV-positive patients among Iran blood donors was estimated 7.9/100 000 (95% CI: 0.000052-0.000121%). The highest prevalence was related to the central region of Iran (11.3/100,000 [95% CI:0.000063-0.0002%]) and Kermanshah province (49.2/100 000 [95% CI:0.000273-0.000888%]) and the lowest prevalence was related to the eastern region (1/100 000 [95% CI:0.000001-0.000072%]) and Khorasan Razavi province (0.9/100 000 [95% CI:0.000001-0.000139%]).

**Conclusion:** The overall HIV prevalence in Iranian blood donors is low and satisfying. However, the high prevalence in some regions and provinces should be reviewed more meticulously.

**Keywords:** Blood donors, Human immunodeficiency, Meta-analysis, Prevalence, Virus

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## Introduction

Transfusion of blood and blood products is the only way to save patients in many cases, but it sometimes transmits some pathogenic factors (transfusion transmitted infection: TTI). Blood safety is a concern in the world. Supplying safe blood and preventing the transmission of infectious diseases are among the most important goals in any blood transfusion organization.<sup>1</sup> The health of stored blood in every country depends on the quality of screening measures. The risk of TTI can be reduced by using screening measures as well as performing serological tests. For this reason, blood transfusion organizations have prepared educational programs and screening methods to reduce risk of TTI.<sup>2</sup>

The World Health Organization (WHO) recommends that all donated blood samples should be screened for TTI before being used. Therefore, it is obligatory to screen all donated blood samples for viral diseases such as HIV, all around the world.<sup>1,3</sup> Acquired immunodeficiency syndrome (AIDS) is one of the blood-borne diseases. HIV was discovered in 1981, and the first case was reported after a blood transfusion in 1982. The probability of HIV transmission through contaminated blood and blood products is 90%–100%. And 5%–10% of those affected by HIV have been infected through transfusion of blood and blood products.<sup>4</sup> AIDS has been named as the sixth fatal disease by WHO. Currently, about 36.7 million people around the world are living with HIV, and

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5000 people are being affected by HIV every day, most of whom at young ages. Ninety percent of these cases occur in developing countries. The largest number of cases infected with HIV in Asia, belongs to India and Thailand. Its prevalence has been reported to be less than 0.01% in Iran.<sup>5</sup> In various studies in Iran, the prevalence of HIV is ranging from 0.003% to zero.<sup>6,7</sup> According to the Joint United Nations Program on HIV/AIDS (UNAIDS) statistics until 2016 in Iran, about 5000 new HIV infections and 4000 AIDS-related deaths had been identified.<sup>8</sup> Due to the importance of this issue, certain strategies have been presented by WHO to reduce the risk of TTI, especially HIV/AIDS.<sup>9</sup>

According to WHO, the HIV growth rate in Iran is alarmingly on the rise.<sup>10</sup> While the statistics of being affected by HIV/AIDS and the mortality due to this disease are decreasing in the world, in the region where Iran is located (EMRO), the situation is quite opposite, and the statistics are increasing.<sup>8</sup> Seroepidemiological studies on TTI have been conducted all around the world. The information obtained from these studies not only can help estimate the magnitude of the transmission of these diseases, but also to some extent give information about the status of these infections in the society.<sup>11</sup> Determining the prevalence of these infections can also help blood transfusion organizations attract certain subgroups of volunteers for safer blood supply and even increase the per-capita production of blood products.

A meta-analysis is a method which collects and analyzes the data of multiple research studies with a common goal, to provide a reliable estimate of the effect size of some interventions and/or observations.<sup>12,13</sup> Therefore, by investigating all related documents and providing a general estimate in systematic reviews and meta-analysis, a more complete image of the problem can be provided.<sup>13,14</sup> During recent years, numerous articles have been published about the prevalence of HIV in Iranian blood donors. However, there is no comprehensive study about HIV status in Iranian blood donors. So, current systematic review and meta-analysis was conducted to evaluate the weighted prevalence of HIV in Iranian blood donors.

## Methods

### Study Protocol

This study was reported according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) checklist.<sup>15</sup>

### Characteristics of the Study

This is a meta-analysis review of all research (English and Persian) conducted on the prevalence of HIV among Iranian blood donors regardless of place and time.

### Search Strategy

Required data about the prevalence of HIV among blood donors in Iran were collected by searching keywords such as “HIV” [MeSH Terms], “human immunodeficiency virus” [Text Word], “blood donation”, “blood donors” [MeSH Terms], “epidemiology” [MeSH Terms], “prevalence” [MeSH Terms], “blood” [MeSH Terms], “blood transfusion” [MeSH Terms], “Iran” [MeSH Terms], in five international databases including PubMed, Scopus, Web of Science, Cochrane, Embase, and three national databases including Magiran, IranMedex and Scientific Information Databank (SID) until December 2017. A manual search was performed by checking the list of all references. The combine search is shown in Figure 1.

### Inclusion and Exclusion Criteria

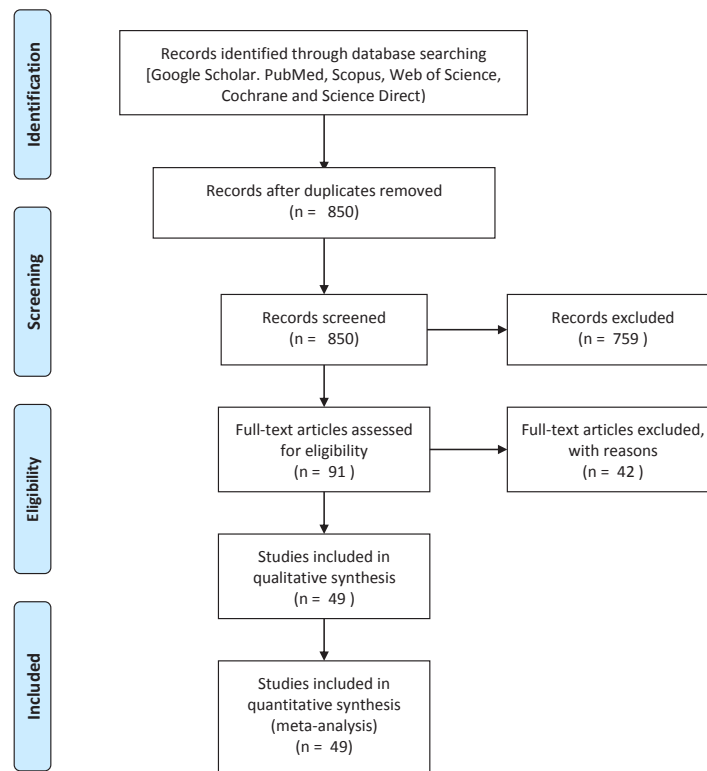
In current systematic review, studies were accepted based on the inclusion and exclusion criteria. The inclusion criterion was accepting the studies which included the total number of blood donors and the number of HIV-positive donors (subjects infected with the human immunodeficiency virus with confirmed laboratory tests), as well as studies that included standard laboratory tests. The included papers were cross-sectional, and published as original articles or short communication. The exclusion criteria included irrelevancy of the studies to the subject matter, non-Iranian samples, non-standard laboratory tests, inadequate data in the study, and lack of access to the articles full texts. Reviews, case reports/case series and letters to editor were excluded.

### Data Extraction

The abstracts of the studies were reviewed by two reviewers based on inclusion and exclusion criteria. In case of any inconsistency, both reviewers matched the results together and solved the discrepancy. The data extracted from all studies were included in the study and checklist was completed after the quality of data was confirmed. The information checklist for the study included the author's name, year of publication, place of study, sample size, prevalence of HIV and risk factors of HIV infection in blood donors.

### Statistical Analysis

The variance of prevalence in each study was calculated with respect to binomial distribution formula. For evaluation of heterogeneity and inconsistency among studies, we used Cochran's Q test and I<sup>2</sup> index. A value of 0% indicates no heterogeneity, while 100% indicates significant heterogeneity for I<sup>2</sup> index. Values of 0%–25%, 25%–50% and 50%–75% represent low, medium and high heterogeneity, respectively. In this review, point



**Figure 1.** Flowchart Describing the Study Design Process.

estimates and their 95% confidence intervals (CI) of HIV prevalence were calculated using random effects model and presented in a forest plot to visualize the heterogeneity among studies. To discover the cause of heterogeneity among studies, subgroup analyzes was done based on region, province.

Egger's and Begg's tests was used for checking publication bias. Furthermore, the meta-regression model was done based on the year of study. In order to evaluate risk factors of HIV, odds ratio (OR) was used. Moreover, sensitivity analysis was performed to verify the data stability in this study.

The meta-analysis was performed with Comprehensive Meta-Analysis software version 2 and  $P < 0.05$  considered as significant.

## Results

### Search Results

During the first stage of search process, 1130 articles were identified. After reviewing the articles and abstracts, a total of 850 irrelevant or repetitive articles were excluded. Finally, after examining the information and quality of the articles, 49 records from 20 provinces had the eligibility to be included in the current systematic review (Figure 1).

### Total HIV Prevalence of Blood Donors

The heterogeneity among studies was high for prevalence

of HIV (Q test  $< 0.001$  and  $I^2 = 98.56\%$ ). In 49 studies with a total sample of 5403170 Iranian blood donors, the prevalence of HIV was estimated to be 79/100000 (95% CI: 0.000052-0.000121%). The highest and lowest prevalence were reported in studies of Kazeminezhad (398.3/100000 [95% CI: 0.003403-0.00466%]) and Yazhan (0.9/100000 [95% CI: 0.000001-0.000139]) (Figure 2).

### Sensitivity Analysis

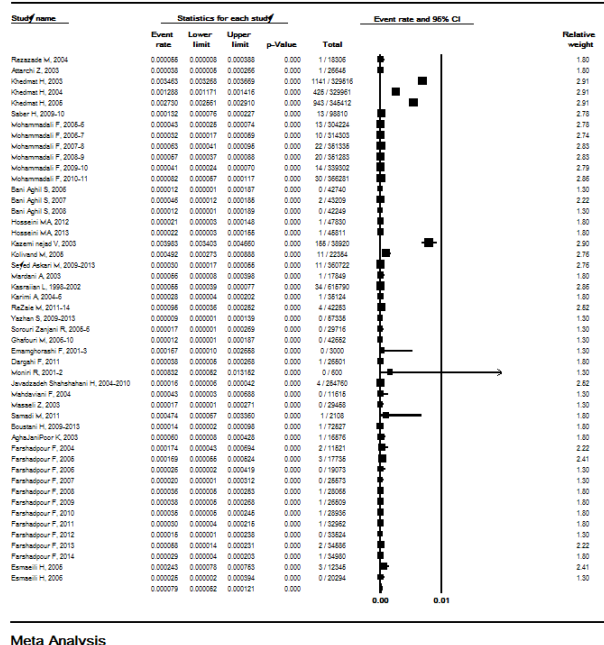
Figure 3 shows the sensitivity analysis. Deletion of a study at the same time showed that the results are reliable.

### Sub-group analysis based on geographical areas

Among region subgroups, the lowest and highest prevalence of HIV were seen in East 1.0/100000 (95% CI=0.000001-0.000072%) and Center 11.3/100,000 (95% CI: 0.000063-0.000200), respectively. The difference between subgroups was not significant ( $P = 0.158$ ) (Table 1).

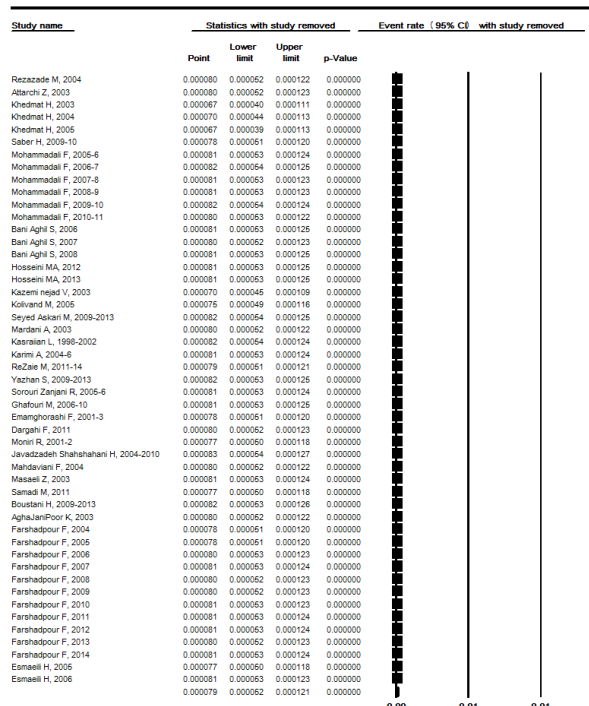
### Sub-group Analysis Based on Provinces

Sorted by province, the lowest prevalence of HIV was seen in South Khorasan province (1.2/100000 [95% CI: 0.000001-0.000187%]) and Khorasan Razavi province (0.9/100000 [95% CI: 0.000001-0.000139]), and the highest prevalence of HIV was seen in Kermanshah province (49.2/100000 [95% CI:0.000273-0.000888%])



Meta Analysis

Figure 2. The Forest Plot of the Systematic Review and Meta-Analysis Based on Overall Prevalence.



Meta Analysis

Figure 3. Sensitivity Analysis of Overall Prevalence.

and Khuzestan province (47.4/100000 [95% CI: 0.000067-0.003360]). The difference between subgroups was significant ( $P < 0.001$ ) (Table 1).

### Meta-Regression Model

According to year of studies, meta-regression model for HIV prevalence revealed that the prevalence of HIV in Iranian blood donors has decreased over the time ( $P < 0.001$ ) (Figure 4).

### Publication Bias

Publication bias for HIV prevalence studies has been illustrated in Figure 5, and  $P$  values of Egger's and Begg's tests were  $P < 0.001$  and  $P < 0.001$ .

### Risk Factors

Complying with the included related risk factors such as gender, education level and marital status, it was revealed that prevalence among males was 2.34 times higher than females (95% CI: 1.16–4.72,  $P = 0.017$ ), and among educated people 9.1 times higher than uneducated (95% CI: 3.2–25.84,  $P < 0.001$ ). Finally no significant difference was observed between single or married people (OR: 1.39; 95% CI: 0.776–2.51,  $P = 0.26$ ) (Table 2).

### Discussion

The importance of blood transfusion and blood products are undeniable. HIV is a life threatening virus that jeopardizes human safety through transfusion of blood products. Therefore, blood donation safety is a priority for Iranian blood transfusion organization. They

try to provide safe blood products with the best quality for patients according to the national standards.

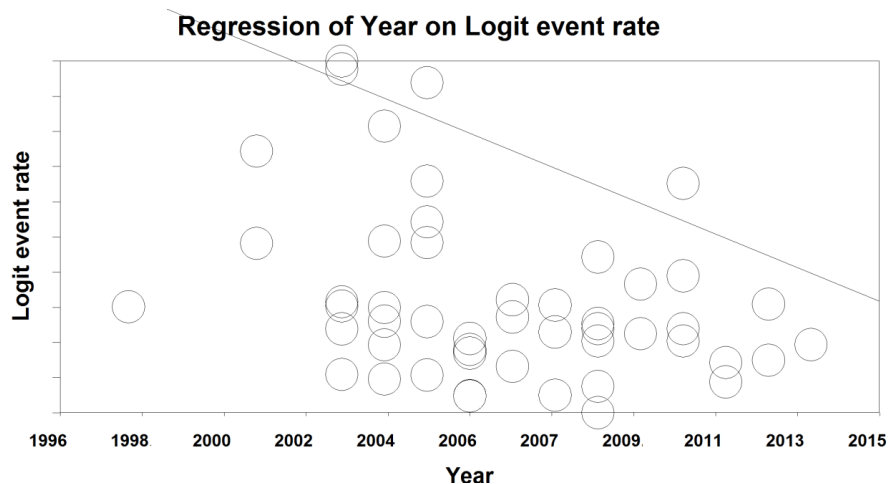
The current systematic review is the first to describe the prevalence of HIV infection in Iranian blood donors, by using data documented from the studies in various provinces. Moreover, various risk factors that have significant association with blood transfusion have been studied. We searched national and international databases among which 49 records were obtained overall. According to this meta-analysis, it has been revealed that the prevalence of HIV among 5403170 samples of blood donors with 2877 positive samples among Iranian people is 7.9/100000 which is low compared to other parts of the world such as Ethiopia with 11.7%,<sup>44</sup> Nigeria with 0.96%,<sup>45</sup> India with 0.39%,<sup>46</sup> and China 13.22/100000 with a range of 0.74–125.97 per 100000.<sup>47</sup> According to studies conducted in 1991–1996, one in 677000 US blood donors, are infected with HIV.<sup>48</sup> Amini et al conducted an investigation in which the prevalence of HIV virus among Iranian blood donors from 2004–2007 was 4 per 100000 respectively.<sup>49</sup> Our data are relatively low, in comparison to European countries' surveys conducted in 1990–2004.<sup>50</sup> This diversity in prevalence is due to differences in the general population. Additionally, types of participations, screening methods and laboratory tests have great impacts on diversity of HIV distribution.<sup>51</sup> The results of this study showed that the prevalence of HIV in most cities of Iran is less than

**Table 1.** Characteristics of All Eligible Studies

Variable	Studies (N)	Sample (N)		Heterogeneity		95% CI	Overall (Per 100000)	References
		All	Positive	I <sup>2</sup>	P Value			
<b>Region<sup>a</sup></b>								
Center	19	3 578 447	2642	99.181	0.000	0.000063–0.000200	11.3	
East	2	99987	0	0.000	0.002	0.000001–0.000072	1.0	
North	8	376 363	162	95.642	0.000	0.000005–0.000583	5.1	
South	17	1 307 713	61	36.964	0.063	0.000041–0.000097	6.3	
West	3	40 660	12	86.712	0.001	0.000008–0.000875	8.3	
<b>Provinces<sup>b</sup></b>								
Arak	1	11 615	0	0.00	1.0	0.000003–0.000688	4.3	(16)
Ardabil	1	26 501	1	0.00	1.0	0.000005–0.000268	3.8	(17)
Bushehr	13	326 093	15	16.768	0.275	0.000041–0.000119	7.0	(18-20)
Fars	1	615 790	34	0.00	1.0	0.000039–0.000077	5.5	(21,22)
Golestan	6	260 759	159	95.98	0.00	0.000003–0.000960	5.2	(23-25)
Hamadan	1	18 306	1	0.00	1.0	0.000008–0.000388	5.5	(26)
Ilam	1	72 527	1	0.00	1.0	0.000002–0.000098	1.4	(27)
Isfahan	2	30 058	0	73.595	0.052	0.000003–0.005365	11.9	(28,29)
Fars(Jahrom)	1	3 000	0	0.00	1.0	0.000010–0.002658	16.7	16.7
Kerman	1	360 722	11	0.00	1.0	0.000017–0.000055	3.0	(30)
Kermanshah	1	22 354	11	0.00	1.0	0.000273–0.000888	49.2	(31)
South Khorasan	1	42 652	0	0.00	1.0	0.000001–0.000187	1.2	(32)
Khorasan Razavi	1	57 335	0	0.00	1.0	0.000001–0.000139	0.9	(33)
Khuzestan	1	2 108	1	0.00	1.0	0.000067–0.003360	47.4	(34)
Mazandaran	1	16 576	1	0.00	1.0	0.000008–0.000428	6.0	(35)
Qom	1	17 849	1	0.00	1.0	0.000008–0.000398	5.6	(36)
Semnan	1	42 253	4	0.00	1.0	0.000036–0.000252	9.5	(37)
Charmahalobakhtiari	1	35 124	1	0.00	1.0	0.000004–0.000202	2.8	(38)
Tehran	11	3 157 072	2632	99.499	0.00	0.000087–0.000325	16.8	(11,39–41)
Yazd	1	254 760	4	0.00	1.0	0.000006–0.000042	1.6	(42)
Zanjan	1	29 716	0	0.00	1.0	0.000001–0.000269	1.7	(43)

Test for subgroup differences:  $Q = 6.611$ ,  $df(Q) = 4$ ,  $P = 0.158$ .

Test for subgroup differences:  $Q = 3337.145$ ,  $df(Q) = 48$ ,  $P = 0.00$ .

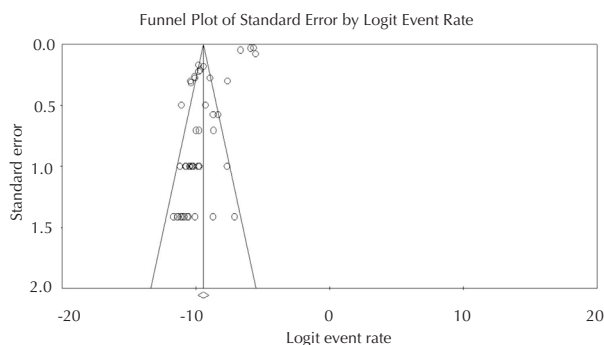


**Figure 4.** Meta-regression Model for Association of HIV Prevalence and Years of Studies.

that of neighboring countries and therefore shows a better health status. Mismatches can be attributed to the implementation of national vaccination programs, the differences in individual characteristics of the donors, the prevalence of high-risk behaviors and socioeconomic factors. In our study, heterogeneity was calculated using

$Q$ -test and  $I^2$ , and its level was reported to be high. One of the reasons for the increased level of heterogeneity can be the small sample size in different studies.

The climate of different regions of Iran is a vital parameter. Therefore, HIV prevalence in five geographical areas of Iran was studied. There was a



**Figure 5.** Publication Bias for Current Studies

significant relationship between geographical regions/provinces and HIV prevalence. It has been revealed that the prevalence of HIV was 8.3/100000 in West, 5.1/100000 in North and 5.1/100000 in Center of Iran. Furthermore, this percentage was 1.0/100000 in East and 6.3/100000 in South of Iran (Table 1).

In this study, the prevalence of HIV among blood donors varies in different provinces, so that in the central regions of the country, the prevalence of HIV is higher than other parts, which due to differences in the number of studies and the size of the samples, cannot be reasoned. It seems that there are other causes for this difference in various provinces: differences in education levels and ethnicities. The highest prevalence of HIV was in provinces of Kermanshah, Khuzestan, Tehran, Fars and Isfahan, respectively. The lowest prevalence was in Khorasan, Ilam, Yazd and Zanjan, respectively. Some Socio-economic factors such as income, sanitary status, culture and religious beliefs cause diversity in the percentage of infected people.

According to Figure 4, the prevalence of HIV donors has decreased significantly in recent years and over time. Relative reduction in the incidence of infected people has been noticed, which might be the result of enhanced hygiene such as utilizing personal drug needles. Furthermore, it has been suggested that social support and mental health counseling interventions can reduce sexual transmission risk behaviors.

Association between HIV infection and gender is meaningful based on our analysis. According to statistics, men are more vulnerable than women (OR: male to female: 2.18 [1.12–4.24,  $P = 0.021$ ]) (Table 1). Since most females are anemic and do not fulfill the required criteria for blood donation, infection is low among them. However, men are more capable to donate blood. Moreover, women have less inclination to have hazardous sexual behaviors in comparison to men. Therefore, women are introduced as a healthier source of blood in the community. Test-seeking behavior is also a very important issue. If a person donates blood when the virus is at its Window’s Period, it would be impossible to detect the virus by screening methods. So being aware about test-seeking behaviors may impress the final result in men and women.<sup>52</sup> These data are inconsistent with Kulmirzayeva and Igissinov survey, in which there was not any statistically significant difference between sex and HIV infection ( $P > 0.05$ ).<sup>53</sup> However, gender is considered significant for HIV cases in Federal Republic of Germany.<sup>54</sup>

Marital status and level of education are other important factors that may impress HIV infection outbreaks.<sup>55,56</sup> In the present study, the frequency of the virus infection between married and single individuals did not show a significant difference. In a study conducted in Brazil between 1992 and 1995, the prevalence of HIV in single people was higher than that of married ones.<sup>57</sup> A

**Table 2.** Risk Factors Associated to Seroprevalence of HIV in Blood Donors

Demographic Factors	No. of Studies	Sample		Heterogeneity		OR (95% CI, P Value)
		Total	HIV	I <sup>2</sup>	P Value	
<b>Gender</b>						
Male	16	1 115 458	58	0	0.99	Male to female: 2.34 (1.16–4.72, $P = 0.017$ )
Female		69839	2			
<b>Education level</b>						
Educated	9	224 412	13	0	0.99	Educated to uneducated: 9.1 (3.2–25.84, $P < 0.001$ )
Uneducated		6405	0			
<b>Marital status</b>						
Single	13	226 557	13	0	0.99	Married to single: 1.39 (0.776–2.51, $P = 0.26$ )
Married		723 744	41			

Abbreviations: OR, Odds ratio.

similar result was obtained in Zimbabwe in 1966.<sup>58</sup> Also, in a study on blood donors in China during 1994–1995, the number of HIV cases in married individuals was higher than singles.<sup>59</sup> This is probably due to the higher average age of married people and, as a result, the longer exposure time to the virus.

The findings of this study showed that the prevalence of HIV in educated people was significantly (9.1%) higher than non-educated people. It may be due to lack of accurate demographic information such as education level and also low number of participants.

There are many risk factors on which the outbreaks of HIV infection depend. A single risk factor could change the statistics significantly, since it could have a great impact on epidemiological scheme of disease. Some of the risk factors were not included in this study as they were not mentioned in surveys. It could be considered as a limitation for this study. Also lack of information from all cities of Iran and small sample size in some studies are considered as other limitations in this study.

In conclusion, the overall HIV prevalence in blood donors in Iran is low and satisfying. However, the high prevalence in some regions and provinces should be reviewed more meticulously. Furthermore, more educational programs are required to encourage women to donate blood. Therefore, in order to overcome some limitations and increase the safety of blood supply, public health efforts must be passed to provide adequate population-based programs to ensure safety of blood products.

#### Authors' Contribution

All authors contributed equally to this study.

#### Conflict of Interest Disclosures

The authors declare that they have no conflicts of interest.

#### Ethical Statement

Not applicable.

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