Am J Blood Res 2020;10(5):145-150
www.AJBlood.us /ISSN:2160-1992/AJBR0115694

Review Article

Incidence of adverse reaction in blood donation: a systematic review

Moslem Taheri Soodejani[1], Ali Akbar Haghdoost[2], Maryam Okhovati[3], Farzaneh Zolala[2], Mohammad Reza Baneshi[4], Abbas Sedaghat[5], Seyyed Mohammad Tabatabaei[6,7]

[1]Research Center of Prevention and Epidemiology of Non-Communicable Disease, Department of Biostatistics and Epidemiology, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran; [2]HIV/STI Surveillance Research Center, WHO Collaborating Center for HIV Surveillance, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran; [3]Medical Library and Information Sciences Department, Faculty of Management and Information Science, Kerman University of Medical Sciences, Kerman, Iran; [4]Modeling in Health Research Center, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran; [5]Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran; [6]Department of Medical Informatics, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran; [7]Clinical Research Development Unit, Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran

Received June 5, 2020; Accepted August 17, 2020; Epub October 15, 2020; Published October 30, 2020

Abstract: There are a lot of reports related to adverse reactions post blood donation. The present study is designed to investigate the incidence of adverse reactions in blood donation around the world. This research was conducted through searching databases such as PubMed, Web of Science, Scopus, EmBase, Ovid, as well as the specialized journal of TRANSFUSION without any time limit by using the keywords including "Adverse Event", "Adverse Effect", "Adverse Reaction", "Complication", "Side Effect", "Vasovagal Reaction", "Local Reaction", "General Reaction", "Allergic Reaction", "Blood Donor", and "Blood Donation". In the initial search, 7054 documents were found, of which 2517 duplicates were excluded. After screening the remaining 4,537 documents, 97 one were reviewed for quality assessment, of which 30 with the appropriate quality were selected for the review process. The results of the study showed that the reactions caused by blood donation are very different. Most reactions were systemic, and ranged from 0.08 to 13 percent in different countries. The incidence of adverse reactions in blood donation differ across the countries which might be related to the donors' characteristics. The difference did even existed in studies conducted in the same country and the same year. This suggests that many factors can cause adverse reactions in blood donation, and that a wide range of them investigated in one study, most of which were systemic.

Keywords: Adverse event, adverse effect, adverse reaction, complication, side effect, vasovagal reaction, local reaction, general reaction, allergic reaction, blood donor, blood donation

Introduction

Blood transfusion is known as a key component in every healthcare system which saves millions lives around the world each year [1]. About 30% of all people have had a need to receive blood or its products during their life [2].

Although blood donation is a very low risk procedure, the incidence of some adverse reactions is inevitable which is the most important factor in reducing the donor's desire to donate again. This would be an obstacle against providing healthy and sufficient blood. Therefore, eliminating or reducing these factors by means of prevention, can help to achieve this goal [3].

Various adverse reactions may occur post blood donation, all of which are divided into two categories of local and systemic reactions [4]. Local reactions include hematoma, hemorrhage, bruising, and associated inflammation, while systemic reactions associated with dizziness, hyperventilation, pallor, bruising, and similar sings [5].

Although the incidence of adverse reactions in blood donation is related to many factors, the sexual distribution of donors, as well as dona-

tion type (First, Regular) and race are the most affecting factors [6-9]. In this study, a systematic review has been done on the incidence of adverse reactions in blood donation in different countries around the world and the incidence, as well as participation rate of women and first donors have been extracted.

Materials and methods

Search strategy

To investigate adverse reactions in blood donation occurred all over the world, electronic databases, reports and documents published by various organizations was searched using keywords including "Adverse Event", "Adverse Effect", "Adverse Reaction", "Complication", "Side Effect", "Vasovagal Reaction", "Local Reaction", "General Reaction", "Allergic Reaction", "Blood Donor" and "Blood Donation". Different Databases such as PubMed, Web of Science, Scopus, EmBase, Ovid, as well as the specialized journal of TRANSFUSION were searched without any time limits.

Inclusion and exclusion criteria

All documents published in Persian and English that possibly contained the estimation of the incidence of adverse reactions in blood donation, such as cohort and cross-sectional studies without any time limits, were considered as inclusion criteria in this step.

Reviews, case-reports and the studies with poor quality which was not possible to extract their data used for estimation of the incidence of adverse reactions in blood donation were excluded.

Quality assessment

The quality of the articles was assessed using the Joanna Brigges Institute checklists for cross-sectional and cohort studies [10]. According to the Quality Assessment Checklist, studies with a score of less than 5 were excluded. In some studies, more than one article was published at a same year and in a same country using data collected from the same sources, but different results were reported. In such studies, if there were annual reports from the ministry or any other international organization, it was considered as the main one and others were excluded as duplicates.

Data extraction

Various data such as the place of the study and the publication year as well as more specialized one such as the study type, the number of blood donations, the number of adverse reactions by type, the number of donations by sex and the number of donations by type were extracted from studies.

Statistical analysis

Cohen's kappa was used to calculate the agreement between two researchers which is a statistical coefficient that represents the degree of accuracy and reliability in a statistical classification. This statistic was introduced by Jacob Cohen in the journal of Educational and Psychological Measurement in 1960 (Formula 1).

Formula 1: $k = \frac{p_o - p_e}{1 - p_e}$

In this formula, p_0 is the relative observed agreement among raters, and p_e is the hypothetical probability of chance agreement.

Results

In the initial search, 7054 documents were found, of which 2517 were excluded as duplicates. After screening the remaining 4537 documents, 97 ones were reviewed for quality assessment, out of which, 30 documents with appropriate quality were finally selected for systematic review (**Figure 1**). Document extraction and quality assessment were performed by two researchers (MTS & MO) independently. The average agreement between the two researchers in document selection, quality assessment and data extraction was good (Cohen's unweighted k = 0.85).

Adverse reactions in blood donation

The incidence of adverse reactions in blood donation were explored continent by continent. In the latest study in the United States of America, which was published in 2016, 30,868 blood donations were investigated, of which 0.34% had caused systemic reactions in blood donors. In this study, the proportion of women among donors was 46% [9].

In Europe, one of the most recent studies on the incidence of adverse reactions in blood

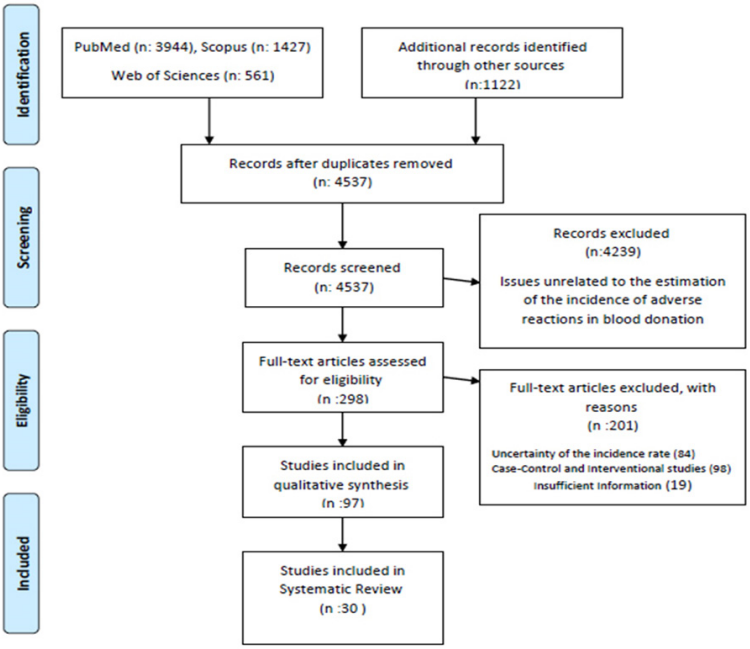

Figure 1. Selection process of documents relevant to the systematic review.

donation was conducted in Germany. The study, which was done in 2012 on 928,411 donations, revealed that adverse reactions had occurred in 0.7% of all blood donations. In this study, women and first donors made up 47.8% and 82% of all donors, respectively [11].

In Asia, India was the country with the most researches done related to adverse reactions in blood donation. Their latest study was conducted in 2017 on 1095 blood donations, the results of which showed that 10.2% of the total blood donations caused adverse reactions including 8.7% of local and 1.5% of systemic reactions. In this study, women and first donors made up 2.9% and 31.8% of all donors, respectively [12].

In Nigeria, as an African country, a study was conducted in 2017 on 459 blood donations, 5% of which caused adverse reactions. Moreover, 2.2% of the reactions were local and 2.8% were systemic [13].

Table 1 shows more details about all studies included in the systematic review.

Discussion

The results of current study showed that the incidence of adverse reactions in blood donation can be very different from one country to another. Besides, this difference even exists in the studies conducted in a same country. For example, it did also exist in the results of studies conducted in two consecutive years (2011 and 2012) in India. The reported incidence rate of adverse reactions in blood donation was 0.59% in the earlier study [4], while it was 2.35% in the other one [14].

The difference in these numbers could be due to the wide range of reactions that have been investigated, as well as the population being studied. This differences seems to be inevitable as it did exist in all reactions as well as systemic and local ones in different countries.

The highest and lowest reported incidence rate for total adverse reactions was in Japan at 6% and India at 0.03%, respectively.

On the other hand, most of the reported reactions were systemic but there was significant differences between the numbers, since, in Iran, it was 13%, while it was 0.88% in Greece.

There are many factors that can cause systemic reactions, the most important of which are age, sex, biological features, stress, fluid intake, as well as proper nutrition and adequate sleep before donating blood [6-8, 15, 16].

The incidence of local reactions differs across the countries due to their direct relationship with the quantity of human resources, the quality of infrastructure and the number of donors. However, the results of this study showed that local reactions were less common than systemic ones.

Limitations of the study

Given the heterogeneity across the studies, it was not possible to perform meta-analysis and as a result, it was not possible to calculate a total number for adverse reactions in blood donation.

Table 1. The incidence of adverse reactions in blood donation in different countries around the world

Country (Year)	Sample Size	% of Blood Donation in women	% of Blood Donation in first Donors	Incidence of Adverse Reaction			Document Quality
				local	Systemic	total	
Iran (2005) [8]	554	6	13	-	0.13	-	Medium
Saudi Arabia (2017) [15]	18936	1.4	47	-	0.11	-	High
Nigeria (2017) [13]	459	10	-	0.022	0.028	0.05	Medium
USA (2009) [17]	4348686	49	19	0.015	0.029	0.044	High
India (2015) [18]	29524	17.5	26.4	0.0017	0.0019	0.0036	High
USA (2005) [19]	89544	52	29	-	0.086	-	High
Italy (2002) [20]	94522	8.6	19.5	0.004	0.013	0.017	High
Brazil (2009) [21]	724861	30	32	-	0.022	-	High
USA (2009) [22]	793293	48	21	-	-	0.004	High
India (2014) [23]	88201	39	35	-	0.012	-	High
India (2012) [14]	22587	0.57	29.8	0.008	0.014	0.022	High
USA (1982) [6]	16424	-	14.5	-	-	0.03	Medium
India (2017) [7]	1000	15	53	-	0.025	-	Medium
Japan (2012) [24]	43984	14.8	10.5	-	-	0.06	High
Pakistan (2016) [25]	41579	0.02	-	0.0002	0.0127	0.0129	High
USA (2009) [26]	422231	57.8	24.6	-	0.014	-	High
India (2008) [27]	30370	3.1	87.2	-	0.016	-	High
Germany (2015) [11]	928411	47.8	82	-	-	0.007	High
India (2017) [12]	1095	2.9	31.8	0.087	0.015	0.103	High
Greece (2005) [28]	12198	24	19.2	-	0.008	-	High
Italy (2007) [29]	4906	24.2	-	-	0.012	-	High
India (2011) [4]	19045	23.1	87.9	0.001	0.005	0.006	High
Iran (2010) [30]	5285	26.5	18	-	0.02	-	Medium
Iran (2018) [31]	25891	7	21	-	0.007	-	High
Netherland (2012) [32]	12051	46	-	0.047	0.037	0.084	High
USA (2008) [33]	6014472	-	-	0.01	0.026	0.03	High
Japan (2017) [34]	4105	71	-	-	0.02	-	High
USA (2015) [35]	1865544	47.5	15.2	0.003	0.019	0.022	High
USA (2016) [9]	30868	46	-	-	0.0034	-	High
Italy (2010) [36]	893323	30	-	0.001	0.005	0.006	High

Conclusion

The incidence of adverse reactions in blood donation vary from one country to another, and this might be related to the characteristics of their donors. This difference even existed in different studies conducted in a same country and a same year since many factors can cause adverse reactions in blood donation and also wide range of them are investigated in one study. Moreover, it should be noted that most reported adverse reactions in blood donation were systemic.

Acknowledgements

This Article is a result of PhD thesis and has been ethically approved by the ethic committee of the Kerman University of Medical Sciences, Iran (Ethical Code: IR.KMU.REC.1397.401).

Disclosure of conflict of interest

None.

Address correspondence to: Seyyed Mohammad Tabatabaei, Department of Medical Informatics, School of Medicine, Mashhad University of Medical

Sciences, Mashhad, Iran. Tel: +989153082261; E-mail: moh.taba@gmail.com

References

[1] Taheri Soodejani M, Haghdoost AA, Sedaghat A, Baneshi MR and Zolala F. The increasing trend of blood donation in Iran. Blood Res 2019; 54: 269-273.

[2] Soodejani MT, Haghdoost AA, Sedaghat A, Baneshi MR and Zolala F. The trends of viral hepatitis B and C and HIV infections in donated bloods in iran between 2003 and 2017. J Blood Med 2019; 10: 435-441.

[3] Ghafari S, Majlessi F, Rahimi Foroushani A and Maghsudlu M. Frequency of local complications of blood transfusion and relevant risk factors among blood donor citizens. Sci J Iran Blood Transfus Organ 2007; 3: 317-324.

[4] Pathak C, Pujani M, Pahuja S and Jain M. Adverse reactions in whole blood donors: an Indian scenario. Blood Transfus 2011; 9: 46.

[5] Custer B, Rios JA, Schlumpf K, Kakaiya RM, Gottschall JL and Wright DJ; NHLBI Retrovirus Epidemiology Donor Study-II (REDS-II). Adverse reactions and other factors that impact subsequent blood donation visits. Transfusion (Paris) 2012; 52: 118-126.

[6] Pisciotto P, Sataro P and Blumberg N. Incidence of adverse reactions in blood donors taking antihypertensive medications. Transfusion 1982; 22: 530-531.

[7] Sachdev S, Singh L, Sharma RR and Marwaha N. A study on the effect of pre-donation salt loading on vasovagal reactions in young college going whole blood donors. Indian J Hematol Blo 2017; 33: 592-597.

[8] Majlessi F, Ghafari S and Maghsoodlou AR-FM. Systemic complications and their risk factors among Tehranian blood donor, 2005. Acta Med Iran 2008; 253-257.

[9] Seheult JN, Lund ME, Yazer MH and Titlestad K. Factors associated with vasovagal reactions in apheresis plasma and whole blood donors: a statistical-epidemiological study in a European donor cohort. Blood Res 2016; 51: 293-296.

[10] Munn Z, Moola S, Lisy K and Riitano D. The Joanna Briggs Institute reviewers' manual 2014 the systematic review of prevalence and incidence data. The Joanna Briggs Institute Reviewers 2014.

[11] Burkhardt T, Dimanski B, Karl R, Sievert U, Karl A, Hübler C, Tonn T, Sopvinik I, Ertl H and Moog R. Donor vigilance data of a blood transfusion service: a multicenter analysis. Transfus Apher Sci 2015; 53: 180-184.

[12] Tiwari AK, Aggarwal G, Dara RC, Arora D, Srivastava K and Raina V. Post-donation telephonic interview of blood donors providing an insight into delayed adverse reactions: first attempt in India. Transfus Apher Sci 2017; 56: 141-146.

[13] Eluke BC, Okonji CU, Ukaejiofo E, Eluke CC, Uchendu KI and Ibeagha I. Prevalence of adverse reaction to whole blood donation among voluntary donors in Asaba, Nigeria. Afr J Biomed Res 2017; 20: 261-265.

[14] Agnihotri N, Marwaha N and Sharma RR. Analysis of adverse events and predisposing factors in voluntary and replacement whole blood donors: a study from north India. Asian J Transfus Sci 2012; 6: 155.

[15] Almutairi H, Salam M, Alajlan A, Wani F, Al-Shammari B and Al-Surimi K. Incidence, predictors and severity of adverse events among whole blood donors. PLoS One 2017; 12: e0179831.

[16] Ando Si, Kawamura N, Matsumoto M, Dan E, Takeshita A, Murakami K, Kashiwagi S and Kiyokawa H. Simple standing test predicts and water ingestion prevents vasovagal reaction in the high-risk blood donors. Transfusion 2009; 49: 1630-1636.

[17] Benjamin RJ, Dy BA, Kennedy JM, Notari EP 4th and Eder AF. The relative safety of automated two-unit red blood cell procedures and manual whole-blood collection in young donors. Transfusion (Paris) 2009; 49: 1874-1883.

[18] Dogra A, Sidhu M, Dogra M and Raina TR. Study of adverse whole blood donor reactions in normal healthy blood donors: experience of tertiary health care centre in jammu region. Indian J Hematol Blood Transfus 2015; 31: 142-5.

[19] France CR, Rader A and Carlson B. Donors who react may not come back: analysis of repeat donation as a function of phlebotomist ratings of vasovagal reactions. Transfus Apher Sci 2005; 33: 99-106.

[20] Franchini M, Gandini G, Gandini A, Crocco I, De Gironcoli M, Bertuzzo D, Giuffrida A, Lippi G, Vassanelli A and Bressan F. Frequency of adverse events during blood and apheresis donations: a single-center study. Transfus Med Hemother 2002; 29: 200-205.

[21] Gonçalez TT, Sabino EC, Schlumpf KS, Wright DJ, Leao S, Sampaio D, Takecian PL, Proietti AB, Murphy E, Busch M and Custer B; NHLBI Retrovirus Epidemiology Donor Study-II (REDS-II), International Component. Vasovagal reactions in whole blood donors at three REDS-II blood centers in Brazil. Transfusion 2012; 52: 1070-8.

[22] Kamel H, Tomasulo P, Bravo M, Wiltbank T, Cusick R, James RC and Custer B. Blood donors and blood collection: delayed adverse reac-

tions to blood donation. Transfusion (Paris) 2010; 50: 556-565.
[23] Philip J, Sarkar R and Jain N. A single-centre study of vasovagal reaction in blood donors: Influence of age, sex, donation status, weight, total blood volume and volume of blood collected. Asian J Transfus Sci 2014; 8: 43.
[24] Takanashi M, Odajima T, Aota S, Sudoh M, Yamaga Y, Ono Y, Yoshinaga K, Motoji T, Matsuzaki K and Satake M. Risk factor analysis of vasovagal reaction from blood donation. Transfus Apher Sci 2012; 47: 319-325.
[25] Sultan S, Baig MA, Irfan SM, Ahmed SI and Hasan SF. Adverse reactions in allogeneic blood donors: a tertiary care experience from a developing country. Oman Med J 2016; 31: 124.
[26] Wiltbank TB, Giordano GF, Kamel H, Tomasulo P and Custer B. Faint and prefaint reactions in whole-blood donors: an analysis of predonation measurements and their predictive value. Transfusion (Paris) 2008; 48: 1799-1808.
[27] Tondon R, Pandey P and Chaudhary R. Vasovagal reactions in 'at risk' donors: a univariate analysis of effect of age and weight on the grade of donor reactions. Transfus Apher Sci 2008; 39: 95-99.
[28] Zervou E, Ziciadis K, Karabini F, Xanthi E, Chrisostomou E and Tzolou A. Vasovagal reactions in blood donors during or immediately after blood donation. Transfus Med 2005; 15: 389-394.
[29] Crocco A and D'Elia D. Adverse reactions during voluntary donation of blood and/or blood components. A statistical-epidemiological study. Blood Transfus 2007; 5: 143.
[30] Assarian Z, ABED HB, Javadi I, Fotouhi A, Seighali F and Akbari N. Risk factors for vasovagal reactions during blood donation. Sci J Iran Blood Transfus Organ 2011; 7: 221-6.
[31] Babahajian S, Khaledian K, Bigleh H, Karimian MS, Abbasian S and Ferdowsi S. The prevalence of vasovagal reactions among blood donors in Kurdistan province and its effect on blood donor return rates. Ci J Iran Blood Transfus Organ 2018; 15: 189-194.
[32] Veldhuizen I, Atsma F, van Dongen A and de Kort W. Adverse reactions, psychological factors, and their effect on donor retention in men and women. Transfusion (Paris) 2012; 52: 1871-1879.
[33] Eder AF, Dy BA, Kennedy JM, Notari IV EP, Strupp A, Wissel ME, Reddy R, Gibble J, Haimowitz MD and Newman BH. The American Red Cross donor hemovigilance program: complications of blood donation reported in 2006. Transfusion (Paris) 2008; 48: 1809-1819.
[34] Nishimori H, Fujii N, Fujii K, Ikeda T, Asano N, Ogo H, Yamakawa M, Takagi N, Otsuka F and Ikeda K. Predictors of vasovagal reactions during preoperative autologous blood donation: a single-institution analysis. Int J Hematol 2017; 105: 812-818.
[35] Rajbhandary S, Stubbs J, Land K and Whitaker B. The 2012-2014 AABB Donor Hemovigilance Report 2014 [Available from: https://www.aabb.org/research/hemovigilance/Documents/2012-2014-AABB-Donor-Hemovigilance-Report.pdf].
[36] Garozzo G, Crocco I, Giussani B, Martinucci A, Monacelli S and Randi V. Adverse reactions to blood donations: the READ project. Blood Transfus 2010; 8: 49.