

Adverse Reactions in Allogeneic Blood Donors: A Tertiary Care Experience from a Developing Country

Sadia Sultan^{1*}, Mohammad Amjad Baig¹, Syed Mohammed Irfan¹, Syed Ijlal Ahmed² and Syeda Faiza Hasan²

¹Department of Hematology and Blood Bank, Liaquat National Hospital and Medical College, Karachi, Pakistan

²Liaquat National Medical College, Karachi, Pakistan

ARTICLE INFO

Article history:

Received: 28 May 2015

Accepted: 19 October 2015

Online:

DOI 10.5001/omj.2016.24

Keywords:

Adverse Effects; Vasovagal Reaction; Blood Donors; Syncope, Vasovagal.

ABSTRACT

Objectives: Fragmented blood transfusion services along with an unmotivated blood donation culture often leads to blood shortage. Donor retention is crucial to meet the increasing blood demand, and adverse donor reactions have a negative impact on donor return. The aim of this study was to estimate adverse donor reactions and identify any demographic association. **Methods:** We conducted a prospective study between January 2011 and December 2013. A total of 41,759 healthy donors were enrolled. Professionally trained donor attendants drew blood and all donors were observed during and following donation for possible adverse events for 20 minutes. Blood donors were asked to report if they suffered from any delayed adverse consequences. **Results:** Out of 41,759 blood donors, 537 (1.3%) experienced adverse reactions. The incidence was one in every 78 donations. The mean age of donors who experienced adverse events was 26.0 ± 6.8 years, and all were male. Out of 537 donors, 429 (80%) developed vasovagal reaction (VVR), 133 (25%) had nausea, 63 (12%) fainted, 35 (6%) developed hyperventilation, 9 (2%) had delayed syncope, and 9 (2%) developed hematoma. Arterial prick, nerve injury, cardiac arrest, and seizures were not observed. Donors aged less than < 30 years and weighing < 70 kg were significantly associated with VVR, hyperventilation, and nausea ($p < 0.005$). Undergraduates and Urdu speaking donors also had a significant association with fainting and nausea, respectively ($p < 0.05$). **Conclusion:** The prevalence of adverse events was low at our tertiary center. A VVR was the predominant adverse reaction and was associated with age and weight. Our study highlights the importance of these parameters in the donation process. A well-trained and experienced phlebotomist and pre-evaluation counseling of blood donors could further minimize the adverse reactions.

Blood cannot be produced synthetically and, therefore, donation is required. The procedure is voluntary and is carried out by phlebotomists. Most blood donations are safe especially in tertiary care centers where the phlebotomists are trained and the staff are skilled and well equipped. Developing countries like Pakistan, often face blood shortages owing to lack of awareness and unmotivated community support and are mainly reliant on family/replacement donors. Replacement donors can be retained as future regular voluntary donors. However, adverse events can negatively affect donor retention and recruitment.¹ Donor retention is directly linked with donor satisfaction. An adverse reaction has a negative impact on donor's revisiting.²

Generally, blood donors do not experience adverse symptoms and tolerate the donation

process very well, but adverse reactions of variable severity occasionally occur during or at the end of the blood collection.³ Usually, these are minor symptoms related to the donation process. However, rarely, serious adverse symptoms may occur. These symptoms range from a mild vasovagal reaction (VVR), nausea, vomiting, and hyperventilation to hematoma, incontinence, nerve injury, arterial prick, and may culminate in delayed syncope, cardiac arrest, and seizures.

Adverse reactions have been observed in various ethnic backgrounds in 0.6–36% of cases.^{4,5} From South Asia, data about adverse donor reactions is available from India and Bangladesh, but there is little data available from Pakistan. To the best of our knowledge, the single study reported looked merely for adverse VVR in healthy blood donors.⁶

The aim of our study was to assess the frequency of these adverse reactions at a tertiary care hospital in Karachi, and also to determine the entire spectrum of different adverse events. We also wanted to determine any association with age, gender, weight, race, and educational status. Thus, our study sought to identify a vulnerable donors group who are at risk of developing various adverse reactions.

METHODS

This prospective study was conducted over three years, between January 2011 to December 2013. We used the non-probability, feasibility-sampling method and recruited a total of 41,759 allogeneic blood donors. The study was approved by the ethical and research committee of Liaquat National Hospital, Karachi, Pakistan.

Demographic data obtained via a structural questionnaire included the donor's name, age, gender, contact number, donor type (replacement or voluntary), linguistic background, and educational status. All donors were selected according to pre-established inclusion criteria considering age (≥ 18 years), body weight (> 50 kg), hemoglobin levels (≥ 12.5 g/dl), hematocrit levels (HCT) $\geq 38\%$, pulse (50–100 beats/min), and blood pressure (120/80 mmHg). All subjects were asked about their medical and donation history. Donors with a history of jaundice, intravenous drug abuse, non-marital sexual contact, tattoos, and recent blood transfusion or surgery were deferred and excluded from the study. All donors were interviewed and provided written informed consent.

Approximately 500 ml of whole blood was drawn by trained phlebotomists. All donors were observed for any possible adverse events during donation and were detained subsequently for 20 minutes after blood donation. All donors were asked to report back in the case of any delayed adverse events within 24 hours.

Donors were divided into groups based on their age (< 30 and ≥ 30 years), gender, linguistic background (Urdu or non-Urdu speaking), weight (< 70 , 71–90 and > 90 kg), and education (undergraduate, graduate or postgraduate). Non-Urdu speaking languages included Sindhi, Pashto, Punjabi, Balochi, and Hindko.

The frequencies of different adverse reactions in blood donors were calculated. Association

Table 1: Distribution of adverse donor reactions (n = 537).

Adverse reactions	Number of positive adverse reactions	Percentage of positive reactions
Vasovagal reaction	429	79.9
Weakness	429	79.9
Sweating	404	75.2
Low pulse	393	73.2
Pallor	330	61.5
Dizziness	225	41.9
Nausea	133	24.8
Fainting	63	11.8
Hyperventilation	35	6.5
Delayed syncope	9	1.7
Hematoma	9	1.7

between blood donor adverse reactions and age, race, education, and weight was calculated using the chi-square test. A p -value < 0.050 was considered significant. The data was analyzed using SPSS Statistics (SPSS Inc., Chicago, US) version 21.

RESULTS

A total of 41,759 blood donors were enrolled over a period of three years. Of these, 41,511 (99.5%) were replacement donors and 248 (0.5%) were voluntary donors. Almost all donors (41,645; 99.8%) were male. One-hundred and fourteen (0.2%) were female. The mean age was 26.0 ± 6.8 years and their mean weight was 66.5 ± 9.4 kg. Of the total number of donors, 537 developed adverse reactions; of these, 429 (79.9%) developed VVR. Donors with VVR showed various signs and symptoms as shown in Table 1. The overall frequency of adverse donor reactions was 1.3% with an estimated incidence of one in every 78 blood donations.

The second most common adverse reaction was nausea in 133 (24.8%) donors followed by fainting (n = 63; 11.8%). Thirty-five (6.5%) donors developed hyperventilation, nine (1.7%) developed delayed syncope, and nine (1.7%) developed hematoma. Arterial prick, nerve injury, cardiac arrest, incontinence, and seizures were not recorded.

An association was seen with age, weight, linguistic background, and educational status. A significant positive association was found between age and VVR ($p = 0.000$). VVR were seen predominantly in the < 30 years age group. A

Table 2: Correlation of adverse reactions with age, weight, education, language, and gender.

Parameters	Vasovagal reaction		Fainting		Nausea		Hyperventilation		Delayed syncope		Hematoma	
	n = 429	p-value	n = 63	p-value	n = 133	p-value	n = 35	p-value	n = 9	p-value	n = 9	p-value
Age (years)												
< 30	349	0.000	45	0.340	89	0.003	17	0.000	9	0.121	0	0.000
≥ 30	80		18		44		18		0		9	
Weight (kg)												
< 70	322	0.004	45	0.190	107	0.017	17	0.000	9	0.190	9	0.191
70–90	98		18		26		9		0		0	
> 90	9		0		0		9		0		0	
Education												
Undergraduate	170	0.101	45	0.000	62	0.021	17	0.351	0	0.040	9	0.001
Graduate	250		18		71		18		9		0	
Postgraduate	9		0		0		0		0		0	
Language												
Urdu	268	0.410		0.001	71	0.031	18	0.210	9	0.011	0	0.000
Non-Urdu	161		36		62		17		0		9	
Gender												
Male	429	-	63	-	133	-	35	-	9	-	9	-
Female	0		0		0		0		0		0	

significant association between age and nausea ($p = 0.003$) and hyperventilation ($p = 0.000$) was also seen [Table 2].

There was a significant positive association between VVR and weight ($p = 0.004$). Donors weighing less than 70 kg were positively associated with VVR ($p = 0.004$). Nausea ($p = 0.017$) was also significantly associated with weight. There was a positive correlation between nausea ($p = 0.031$) and delayed syncope ($p = 0.011$). Fainting ($p = 0.000$) and hematoma ($p = 0.001$) were seen more commonly in donors educated to an undergraduate level.

DISCUSSION

Blood banks have a dual responsibility: to meet the blood supply for the community and to ensure maximum blood donors safety. The donor's physical experiences have a noticeable impact on donor return, and adverse incidents dictate the donor return rate.⁷ Our study revealed adverse donor reactions in 1.3% of healthy Pakistani allogeneic donors. This is the first comprehensive report from Pakistan; a prior study addressed only VVR in replacement donors.⁶

Our results are in concurrence with an Indian study that reported adverse events in 2.5% of healthy blood donors.⁸ Another local study from Bangalore, India revealed a prevalence of 2.04%.⁹ A relatively high prevalence of 4.9% was reported in a study from

Bangladesh that assessed randomly selected whole blood donors.¹⁰

Compared to data from developed countries, our results are more or less analogous. An Italian study found an overall prevalence 1.2%.¹¹ A large study from Japan on 98,389 donors recorded a 2.8% positivity rate of adverse reactions.¹² However, a relatively low frequency of 0.63% adverse reactions was determined in a German study, conducted in elderly (66–71 years) voluntary blood donors.⁴ This difference is accredited to difference in the age groups of our studies, and the blood donor type (i.e., voluntary donations versus replacement donors) as in our study included virtually all replacement donors. Regular voluntary donors are likely to have less adverse donor reaction.

VVR were the most common adverse reaction occurring in 67–95% of all donation-related reactions and in 1–5% of blood donors.¹³ Donation-related VVR is a multifactorial response primarily determined by young age, low weight, female gender, and first-time donor status.^{14–16}

Rohra et al,⁶ conducted a study in two blood banks in Karachi, Pakistan, and reported a higher prevalence (8.2%) of VVR in 674 exchange blood donors. This difference perhaps could be explained by the majority of donors being aged < 30 years. The sample size was relatively small in their study where as our cohort was larger and is more likely to reflect the actual prevalence in our population.

However, earlier studies from India reported VVR prevalences of 63.5% and 70.0%, which are comparable to our findings of 79.9%.^{8,17} Age and weight might predict the VVR in blood donors, based on significant associations observed. Previous studies reported a significantly low frequency of VVR in those aged ≥ 36 years old.⁸ The highest prevalence was seen in the < 30 age group in our study. A study from France postulated that vasovagal reactors exhibited decreased baroreceptor sensitivity in healthy younger donors when they are physically or psychologically strained.¹⁸ With escalating age, the body becomes steadier hemodynamically.

An adverse event was frequently seen in donors who weighed less than 70 kg. Previous studies support our findings. Donors who experienced adverse reactions had a lower mean weight compared to donors without adverse events.¹⁹ Newman also showed that the VVR reaction rate was inversely proportional to the donors weight.²⁰ A cumulative report from three large US blood centers also revealed that low weight donors had high donation reaction (VVR) rates compared to other donors.¹⁴

We could not determine any association of gender with adverse reactions because virtually all blood donors were male. Female blood donors constituted 30% of blood donations reported from Italy.²¹ However, the situation in Pakistan is even more alarming, where the prevalence was $< 1\%$ as reported in prior studies.^{6,22} The reasons for the lack of blood donation include insufficient knowledge, lack of education, misconceptions, and false perceptions about blood donation. This is a limitation of our study that hinders the generalization of the results.

However, an Urdu-speaking linguistic background and undergraduate educational status were determined as significantly strong predictors of delayed syncope and fainting, respectively, in our study. In the literature, we did not find other studies that mentioned linguistic background or educational status as a risk factor associated with adverse events. Further studies are needed to validate this finding.

In our cohort, the second and third most common types of adverse events were nausea and fainting. In one European study, fainting was reported as an adverse event in 20.5% of blood donors.²³ The authors of the study concluded that the stressing experience of phlebotomy was the reason for the higher frequency of reactions. There are plausible explanations for this high prevalence compared to

our study: the divergence in donor's demographics, perceptions, awareness, and understanding.

Needle injuries can damage vasculature, may result in bruises, hematoma, arterial puncture, arteriovenous fistula, or pseudoaneurysm. Needle injuries were encountered minimally (2%), which was in agreement with a prior study from Bangladesh.¹⁰ However, Newman et al,²⁴ had disclosed very high frequency of bruises in 15.1% of donors while Agnihotri et al,⁸ determined hematoma as an adverse event in 35% of all reactions. Underlying etiology seems to be the faulty technique, untrained phlebotomists and failure to select an appropriate vein.⁸ Needle-associated nerve injuries occur in one of every 6300 donations.²⁴ Nerve injury was not observed in our donors. Additionally, serious fatal adverse reactions such as arterial prick, cardiac arrest, and seizures were not seen.

The prevalence of adverse donor reactions in our study was not high. However, to further minimize these adverse events and sustain the donor pool, we would suggest a number of strategies. These include lessening the donor-to-phlebotomist ratio, more pre-donation counseling, not allowing donors who have fasted before donating to donate, giving more individual concentration to each donor, keeping donors supine for longer, offering fluids before starting phlebotomy, and training blood donors about applying muscle tension exercises.²⁵

CONCLUSION

The prevalence of adverse reactions in allogeneic blood donors in the Pakistani population appears low. VVR is the predominant adverse event. Donation-related adverse reaction is a multifactorial process principally determined by young age, low weight, ethnic background, and undergraduate educational status. Our study strengthens the fact that donation process is a safe maneuver, which could be made further event-free by designing protective practices in the identified predisposed groups.

Disclosure

The authors declared no conflicts of interest. No funding was received for this study.

Acknowledgements

The authors are grateful to the donors who have participated in this study. We thank the staff of the Blood Bank particularly Mr. Asif Hammed for his support.

REFERENCES

1. Eder AF, Notari EP IV, Dodd RY. Do reactions after whole blood donation predict syncope on return donation? *Transfusion* 2012 Dec;52(12):2570-2576.
2. Custer B, Rios JA, Schlumpf K, Kakaiya RM, Gottschall JL, Wright DJ; NHLBI Retrovirus Epidemiology Donor Study-II (REDS-II). Adverse reactions and other factors that impact subsequent blood donation visits. *Transfusion* 2012 Jan;52(1):118-126.
3. Assarian Z, Abed Haghighi B, Javadi I, Fotouhi A, Seighali F, Akbari N. Risk factors for vasovagal reactions during blood donation. *Sci J Iran Blood Transfus Organ.* 2011;7(4):221-226.
4. Zeiler T, Lander-Kox J, Eichler H, Alt T, Bux J. The safety of blood donation by elderly blood donors. *Vox Sang* 2011 Nov;101(4):313-319.
5. Newman BH, Pichette S, Pichette D, Dzaka E. Adverse effects in blood donors after whole-blood donation: a study of 1000 blood donors interviewed 3 weeks after whole-blood donation. *Transfusion* 2003 May;43(5):598-603.
6. Rohra DK, Juriasinghani V, Rai K, Azam SI. Prevalence of immediate vasovagal reaction in blood donors visiting two blood banks of Karachi. *Transfus Med* 2010 Jun;20(3):129-133.
7. Patidar GK, Sharma RR, Marwaha N. Frequency of adverse events in plateletpheresis donors in regional transfusion centre in North India. *Transfus Apher Sci* 2013 Oct;49(2):244-248.
8. Agnihotri N, Marwaha N, 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 Jul;6(2):155-160.
9. Abhishekh B, Mayadevi S, Usha KC. Adverse reactions to blood donation. *Innovative Journal of Medical and Health Science.* 2013;3(4):158-160.
10. Mahbub-ul-Alam M, Hyder MS, Khan MB, Islam MA. Adverse donor reaction during and immediately after Venesection. *The Journal of Teachers Association RMC. Rajshahi* 2007;20(1):39-47.
11. Crocco A, D'Elia D. Adverse reactions during voluntary donation of blood and/or blood components. A statistical-epidemiological study. *Blood Transfus* 2007 Jul;5(3):143-152.
12. Inaba S, Takanashi M, Matsuzaki K, Ono Y, Nakajima K, Shibata R, et al. Analysis of a questionnaire on adverse reactions to blood donation in Japan. *Transfus Apher Sci* 2013 Feb;48(1):21-34.
13. Philip J, Sarkar RS, 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 Jan;8(1):43-46.
14. Trouern-Trend JJ, Cable RG, Badon SJ, Newman BH, Popovsky MA. A case-controlled multicenter study of vasovagal reactions in blood donors: influence of sex, age, donation status, weight, blood pressure, and pulse. *Transfusion* 1999 Mar;39(3):316-320.
15. Veldhuizen I, Atsma F, van Dongen A, de Kort W. Adverse reactions, psychological factors, and their effect on donor retention in men and women. *Transfusion* 2012 Sep;52(9):1871-1879.
16. Eder AF, Hillyer CD, Dy BA, Notari EP IV, Benjamin RJ. Adverse reactions to allogeneic whole blood donation by 16- and 17-year-olds. *JAMA* 2008 May;299(19):2279-2286.
17. Pathak C, Pujani M, Pahuja S, Jain M. Adverse reactions in whole blood donors: an Indian scenario. *Blood Transfus* 2011 Jan;9(1):46-49.
18. France C. Baroreflex sensitivity during noxious stimulation in vasovagal reactors to blood donation. *Int J Psychophysiol* 1995 Feb;19(1):13-22.
19. Kasprisin DO, Glynn SH, Taylor F, Miller KA. Moderate and severe reactions in blood donors. *Transfusion* 1992 Jan;32(1):23-26.
20. Newman BH. Vasovagal reaction rates and body weight: findings in high- and low-risk populations. *Transfusion* 2003 Aug;43(8):1084-1088.
21. Bani M, Giussani B. Gender differences in giving blood: a review of the literature. *Blood Transfus* 2010 Oct;8(4):278-287.
22. Irfan SM, Uddin J, Zaheer HA, Sultan S, Baig A. Trends in transfusion transmitted infections among replacement blood donors in Karachi, Pakistan. *Turk J Haematol* 2013 Jun;30(2):163-167.
23. Zervou EK, Ziciadis K, Karabini F, Xanthi E, Chrisostomou E, Tzolou A. Vasovagal reactions in blood donors during or immediately after blood donation. *Transfus Med* 2005 Oct;15(5):389-394.
24. Newman BH, Waxman DA. Blood donation-related neurologic needle injury: evaluation of 2 years' worth of data from a large blood center. *Transfusion* 1996 Mar;36(3):213-215.
25. Ditto B, Wilkins JA, France CR, Lavoie P, Adler PS. On-site training in applied muscle tension to reduce vasovagal reactions to blood donation. *J Behav Med* 2003 Feb;26(1):53-65.