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IDENTIFYING CONTRIBUTING VARIABLES AND DELAYED ADVERSE RESPONSES IN WHOLE BLOOD DONORS

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ABSTRACT

Background: There is a dearth of information in the literature on blood donors' unfavorable delayed donor responses (D-ADR).

Aim: The purpose of this study was to determine the kind and prevalence of unfavorable delayed donor responses (D-ADRs) in whole blood donors as well as the variables that contribute to them.

Methods: All eligible blood donors were evaluated in this prospective observational research. They were questioned about their overall health and asked specific questions about adverse donor responses (ADRs) during two follow-up interviews, one 24 hours following the donation and one two weeks later. The International Society of Blood Transfusion's established procedures were followed in classifying ADRs.

Results: Compared to immediate delayed adverse donor responses, delayed ADRs were more frequent ($p < 0.001$). Among ADRs, 5%, 4.2%, and 2.25 percent of participants had bruising, generalized weakness, and painful arms, respectively. Compared to repeat donors, first-time donors reported much more delayed-adverse donor responses ($p = 0.002$). Higher D-ADR was reported by females. Systemic D-ADRs were more prevalent among repeat donors, and localized D-ADRs were more prevalent than systemic D-ADRs ($p < 0.001$).

Conclusions: Compared to acute adverse donor responses (ADRs) with distinct patterns, delayed ADRs are more frequent in whole blood donors. First-time donors, females, and young patients are particularly vulnerable to delayed adverse drug reactions (ADRs) and require extra caution while donating whole blood. To guarantee the safety of whole blood donors, active follow-up should occasionally be conducted.

Keywords: Adverse donor reactions, blood donors, delayed reactions, hematoma, safety, vasovagal reaction

INTRODUCTION

It is permissible for a healthy person to donate 350-450ml of the blood considering the body weight of the blood donor. This amount is permissible as it is the well-tolerated amount of the blood loss in the donors which is tolerated well in the donors

without causing any ADRs (adverse donor reactions). Sometimes, adverse donor reactions of varying severity might be encountered either during or after the blood donation.¹ Majority of the adverse donor reactions are seen within 30 minutes of starting with the blood donation and are generally managed by adopting simple measures of management. ADRs lead to negative experiences in the blood donors despite them being usually transient and mild.²

Given the blood donor's body weight, 350–450 ml of blood can be donated by a healthy individual. This quantity is acceptable as it represents the donors' well-tolerated blood loss, which they may bear without experiencing any adverse donor responses (ADRs). Adverse donor responses can occasionally occur during or after the blood donation, and they might range in severity. One The majority of negative donor responses occur within 30 minutes of the blood donation beginning and are often controlled with basic management techniques. Despite the fact that ADRs are often moderate and temporary, they cause unfavorable experiences for blood donors.^{2,3}

Significant evidence and studies about donor features and related risk factors for I-ADRs (immediate adverse donor reactions) can be found in the existing literature. However, there is a dearth of information in the literature currently available on delayed-adverse donor reactions. The fact that most delayed-adverse donor reactions are minor and go unreported to blood transfusion units may be the cause.⁴ In order to determine the kind and frequency of unfavorable delayed donor responses (D-ADR) in whole blood donors as well as the contributing variables, the current study was conducted. Additionally, the study sought to compare the characteristics of immediate-adverse donor reactions, donors at risk, and contributing variables between immediate-adverse and delayed-adverse donor reactions.

MATERIALS AND METHODS

Assessing the kind and prevalence of adverse delayed donor responses (D-ADR) in whole blood donors as well as the contributing variables was the goal of the current prospective observational investigation. Additionally, the study sought to compare the characteristics of immediate-adverse donor reactions, donors at risk, and contributing variables between immediate-adverse and delayed-adverse donor reactions. Prior to their involvement in the study, all individuals gave their written and verbal informed consent.

Following an explanation of the comprehensive research protocol, all subsequent whole blood donor individuals who were willing to participate were enrolled in the study. The criteria were taken from the International Society of Blood Transfusion working party on hemovigilance's working group on donor vigilance's standard for monitoring blood donation-related consequences. Any negative donor reaction that occurred right away was recorded in accordance with the Department's normal operating practice. The blood donors were then evaluated again in order to identify any delayed adverse donor responses.

While the second recall and evaluation was conducted two weeks after the blood donation, the initial assessment was completed 24 hours after the blood donation. Non-specific questions on the donor's overall health and well-being as well as any discomfort or unpleasant experiences during or after the blood donation were asked at the beginning of the interview.

Then, using a pre-made structured proforma created especially for this study, blood donors were questioned about any potential delayed-adverse donor responses that these participants could have had. The self-validation of the questionnaire was completed. In addition to any pertinent medical advice given to the research participants, donors were questioned about delayed adverse donor responses and counseled if there were any.

First-time and repeat donors, male and female donors, blood donation durations of ≤ 8 or ≥ 9 minutes, weight groups of ≤ 60 , 61-75, 76-90, and ≥ 91 kg, hemoglobin groups of 12.5-14, 14.1-16, and ≥ 16.1 gm/dl, and age groups of 18-24, 25-35, 36-50, and ≥ 51 years were all assigned to blood donors prior to their evaluation.

The data gathered were analyzed statistically using SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk, NY, USA) for assessment of descriptive measures, chi-square test, Fisher's exact test, and Mann Whitney U test. The results were expressed as mean and standard deviation and frequency and percentages. The p-value of < 0.05 was considered statistically significant.

RESULTS

Assessing the kind and prevalence of adverse delayed donor responses (D-ADR) in whole blood donors as well as the contributing variables was the goal of the current prospective observational investigation. Additionally, the study sought to compare the characteristics of immediate-adverse donor reactions, donors at risk, and contributing variables between immediate-adverse and delayed-adverse donor reactions. ADRs in 7028 whole blood donors were evaluated in the research. The research participants were 30.64 ± 7.84 years old on average. There were 6828 men and 200 females in the current study,

with mean ages of 30.63 ± 7.79 and 31.16 ± 9.54 years, respectively. First-time donors were 28.17 ± 7.31 years old, whereas repeat donors were 31.88 ± 7.78 years old (Table 1).

The research participants weighed 75.73 ± 12.22 kg on average. Males and females weighed 76.01 ± 12.11 and 66.11 ± 10.73 kg on average, respectively. First-time donors weighed 72.03 ± 11.35 years, whereas repeat donors weighed 77.62 ± 12.16 years (Table 2). The donors' hemoglobin levels were 14.85 ± 1.24 gm/dl. Male, female, first-time, and repeat donors had mean hemoglobin levels of 14.94 ± 1.26 , 13.33 ± 0.74 , 14.92 ± 1.26 , and 14.83 ± 1.22 gm/dl, respectively (Table 3).

When the research participants' initial vasovagal responses (VVRs) were evaluated, it was found that, in terms of gender, a considerably higher number of females reported VVR without losing consciousness ($p=0.005$). With $p=0.97$, VVR with convulsions and loss of consciousness was statistically similar in males and girls. Overall, females had considerably greater VVRs than males ($p=0.01$).

With $p=0.36$, 0.44 , 0.65 , and 0.14 for first-time and repeat donors, respectively, the VVRs were statistically equivalent without loss of consciousness, with loss of consciousness, with convulsions, and overall. Subjects with $EBV \leq 4500$ ml and $EBV > 4500$ ml without convulsions, without loss of consciousness, and overall had statistically similar VVRs ($p=0.81$, 0.97 , and 0.13 , respectively). Subjects with $EBV > 4500$ ml had substantially greater VVRs ($p=0.03$) (Table 4).

In terms of the kind of delayed VVRs, females had substantially greater overall and VVRs without awareness loss ($p=0.02$ and 0.03 , respectively). On the other hand, VVRs with convulsions and loss of consciousness were statistically equivalent ($p=0.97$). None of the research participants had a history of VVRs associated with convulsions. Regarding both new and returning contributors,

Compared to repeat donors, first-time donors had greater VVRs without loss of consciousness ($p=0.001$), equivalent loss of consciousness ($p=0.08$), and much higher overall evaluation ($p<0.001$) for first-time donors. With $p=0.15$, 0.97 , and 0.24 for $EBV \leq 4500$ ml and $EBV > 4500$ ml, respectively, the VVRs without loss of consciousness, with loss of consciousness, and overall were statistically equivalent (Table 5).

Overall D-ADRs, bruise, sore arms, hematoma, allergy, delayed bleeding, and overall localized D-ADRs were shown to be statistically equal in men and females for delayed adverse donor responses in blood donors (localized) ($p=0.34$, 0.85 , 0.76 , 0.97 , 0.72 , 0.97 , and 0.55 , respectively). While bruises, sore arms, hematomas, allergies, delayed bleeding, and overall localized D-ADRs were statistically comparable in first-time and repeat donors ($p=0.95$, 0.17 , 0.63 , 0.95 , 0.95 , and 0.73 , respectively), overall D-ADRs were higher in first-time donors ($p=0.003$).

The findings of the study demonstrated that weakness/fatigue was statistically similar in males and females with $p=0.47$ for delayed systemic unfavorable donor responses in blood donors. Females had considerably greater VVRs ($p=0.02$). Overall, females experienced substantially more systemic adverse donor responses than men ($p=0.01$). VVRs, total systemic delayed ADRs, and weakness/fatigue were substantially greater in first-time donors than in repeat donors ($p=0.007$, <0.001 , and <0.001 , respectively) (Table 7).

DISCUSSION

In this study, 7028 whole blood donors' ADRs were evaluated. The research participants were 30.64 ± 7.84 years old on average. There were 6828 men and 200 females in the current study, with mean ages of 30.63 ± 7.79 and 31.16 ± 9.54 years, respectively. First-time donors were 28.17 ± 7.31 years old, whereas repeat donors were 31.88 ± 7.78 years old. The research participants weighed 75.73 ± 12.22 kg on average. Males and females weighed 76.01 ± 12.11 and 66.11 ± 10.73 kg on average, respectively. First-time and repeat donors had mean weights of 72.03 ± 11.35 and 77.62 ± 12.16 years, respectively. The donors' hemoglobin levels were 14.85 ± 1.24 gm/dl. Male, female, first-time, and repeat donors had mean hemoglobin levels of 14.94 ± 1.26 , 13.33 ± 0.74 , 14.92 ± 1.26 , and 14.83 ± 1.22 gm/dl, respectively.

These findings were similar to those of studies conducted by Gupta AM et al. in 2021 and 2020, in which the authors evaluated blood donors using demographic information similar to that of the current study. When evaluating the forms of acute vasovagal responses (VVRs) in research participants, the current investigation revealed that, with regard to gender, a substantially higher number of females reported VVR without losing consciousness ($p=0.005$). With $p=0.97$, VVR with convulsions and loss of consciousness was statistically similar in males and girls. Overall, females had considerably greater VVRs than males ($p=0.01$). With $p=0.36$, 0.44 , 0.65 , and 0.14 for first-time and repeat donors, respectively, the VVRs were statistically equivalent without loss of consciousness, with loss of consciousness, with convulsions, and overall.

Subjects with EBV ≤ 4500 ml and EBV >4500 ml without convulsions, without loss of consciousness, and overall had statistically similar VVRs ($p=0.81$, 0.97 , and 0.13 , respectively). Subjects with EBV >4500 ml had substantially greater VVRs ($p=0.03$). These findings were in line with research by Bajpai M et al. (2009) and Kamel H et al. (2009), who both found immediate vasovagal responses that were comparable to the current study.

VVRs without awareness loss and total VVRs were considerably higher in females ($p=0.02$ and 0.03) when evaluating the kind of delayed VVRs. On the other hand, VVRs with convulsions and loss of consciousness were statistically equivalent ($p=0.97$). None of the research participants had a history of VVRs associated with convulsions. Regarding both new and returning contributors,

Compared to repeat donors, first-time donors had greater VVRs without loss of consciousness ($p=0.001$), equivalent loss of consciousness ($p=0.08$), and much higher overall evaluation ($p<0.001$) for first-time donors. VVRs without loss of consciousness, with loss of consciousness, and overall were statistically equivalent for EBV ≤ 4500 ml and EBV >4500 ml, with respective $p=0.15$, 0.97 , and 0.24 . These results were consistent with those of the 2009 study by Symvoulakis EK et al. and the 2017 study by Tiwari AK et al., both of which revealed delayed VVRs comparable to the current investigation.

Overall D-ADRs, bruising, aching arms, hematoma, allergies, and delayed bleeding were among the study's findings for localized delayed adverse donor responses in blood donors, and overall localized D-ADRs were statistically comparable in males and females with $p=0.34$, 0.85 , 0.76 , 0.97 , 0.72 , 0.97 , and 0.55 respectively. While bruises, sore arms, hematomas, allergies, delayed bleeding, and overall localized D-ADRs were statistically comparable in first-time and repeat donors ($p=0.95$, 0.17 , 0.63 , 0.95 , 0.95 , and 0.73 , respectively), overall D-ADRs were higher in first-time donors ($p=0.003$). These findings were consistent with those of Sojka P et al. (2004) and Custer B et al. (2012), who proposed that delayed and localized adverse donor responses in blood donors were comparable to those seen in the current study.

It was shown that weakness/fatigue was statistically similar in males and females with $p=0.47$ for delayed systemic unfavorable donor responses in blood donors. Females had considerably greater VVRs ($p=0.02$). Overall, females experienced substantially more systemic adverse donor responses than men ($p=0.01$). VVRs, total systemic delayed ADRs, and weakness/fatigue were substantially greater in first-time donors than in repeat donors ($p=0.007$, <0.001 , and <0.001 , respectively). The results were consistent with the research conducted by Newman BH et al. in 2003 and Desai PD et al. in 2009, both of which documented delayed systemic unfavorable donor responses in blood donors.

CONCLUSIONS

Whole blood donors are more likely to experience delayed adverse donor responses (ADRs) than acute ADRs with distinct characteristics. First-time donors, females, and young patients are particularly vulnerable to delayed adverse drug reactions (ADRs) and require extra caution while donating whole blood.

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S. No	Characteristics	Age (years)				Mean $\pm$ S. D
		18-24	22-35	36-50	≥ 51	
1.	Overall donors (n=7028)	1642 (23.4)	3730 (53.1)	1524 (21.7)	132 (1.9)	30.64 $\pm$ 7.84
2.	Males (n=6828)	1584 (22.5)	3650 (51.9)	1474 (21)	120 (1.7)	30.63 $\pm$ 7.79
3.	Females (n=200)	58 (0.8)	80 (1.1)	50 (0.7)	12 (0.2)	31.16 $\pm$ 9.54
4.	First-time (n=2362)	844 (12)	1154 (16.4)	338 (4.8)	26 (0.4)	28.17 $\pm$ 7.31
5.	Repeat (n=4666)	798 (11.4)	2576 (36.7)	1186 (16.9)	106 (1.5)	31.88 $\pm$ 7.78

Table 1: Age range of blood donors

S. No	Characteristics	Weight (kg)				Mean $\pm$ S. D
		≤ 60	61-75	76-90	≥ 91	
1.	Overall donors (n=7028)	678 (9.7)	3174 (45.2)	2424 (34.5)	752 (10.7)	75.73 $\pm$ 12.22
2.	Males (n=6828)	606 (8.6)	3076 (43.8)	2400 (34.2)	746 (10.6)	76.01 $\pm$ 12.11
3.	Females (n=200)	72 (1)	98 (1.4)	24 (0.3)	6 (0.1)	66.11 $\pm$ 10.73
4.	First-time (n=2362)	386 (5.5)	1186 (16.9)	644 (9.2)	146 (2.1)	72.03 $\pm$ 11.35
5.	Repeat (n=4666)	292 (4.2)	1988 (28.3)	1780 (25.3)	606 (8.6)	77.62 $\pm$ 12.16

Table 2: Distribution of blood donors based on the weight

S. No	Characteristics	Hemoglobin (gm/dl)			Mean $\pm$ S. D
		12.5-14	14.1-16	16.1-18	
1.	Overall donors (n=7028)	1942	3748	132	14.85 $\pm$ 1.24
2.	Males (n=6828)	1766	3728	1334	14.94 $\pm$ 1.26
3.	Females (n=200)	176	20	4	13.33 $\pm$ 0.74
4.	First-time (n=2362)	646	1250	466	14.92 $\pm$ 1.26
5.	Repeat (n=4666)	1296	2498	872	14.83 $\pm$ 1.22

Table 3: Distribution of blood donors based on their hemoglobin levels

S. No	Type of VVR	Without consciousness loss	With consciousness loss	With convulsions	Overall n (%)
1.	Males (6828)	58	10	2	70 (1.03)
2.	Females (200)	10	0	0	10 (5)

3.	p-value	0.005	0.97	0.97	0.01
4.	First-time donors (2362)	28	6	2	36 (1.52)
5.	Repeat donors (4666)	40	4	0	44 (0.94)
6.	p-value	0.36	0.44	0.65	0.14
7.	EBV ≤4500 ml (11222)	20	0	0	20 (1.78)
8.	EBV >4500 ml (5906)	48	10	2	60 (1.02)
9.	p-value	0.03	0.81	0.97	0.13

Table 4: Incidence of immediate VVRs (vasovagal reactions) in study subjects

S. No	Type of VVR	Without consciousness loss	With consciousness loss	Overall n (%)
1.	Males (6828)	54	6	60 (0.88)
2.	Females (200)	8	0	8 (4)
3.	p-value	0.02	0.97	0.03
4.	First-time donors (2362)	38	6	44 (1.86)
5.	Repeat donors (4666)	24	0	24 (0.51)
6.	p-value	0.001	0.08	<0.001
7.	EBV ≤4500 ml (11222)	16	0	16 (1.42)
8.	EBV >4500 ml (5906)	46	6	52 (0.88)
9.	p-value	0.15	0.97	0.24

Table 5: Incidence of delayed VVRs (vasovagal reactions) in study subjects

S. No	Type of donors	Overall D-ADRs	Bruise	Sore arms	Hematoma	Allergy	Delayed bleeding	Overall
1.	Males (6828)	928	342	152	84	72	48	588 (8.6)
2.	Females (200)	34	8	6	1	0	0	14 (7)
3.	p-value	0.34	0.85	0.76	0.97	0.72	0.97	0.55
4.	First-time donors (2362)	280	118	64	32	24	16	208 (8.81)
5.	Repeat donors (4666)	582	232	94	54	48	32	394 (8.44)
6.	p-value	0.003	0.95	0.17	0.63	0.95	0.95	0.73
7.	Overall n=7028 (%)	962 (13.69)	350 (4.98)	158 (2.25)	86 (1.22)	72 (1.02)	48 (0.68)	602 (8.57)

Table 6: Delayed adverse donor reactions in blood donors (localized)

S. No	Type of donors	Weakness/fatigue	VVRs	Overall n (%)
1.	Males (6828)	286	60	346 (5.07)
2.	Females (200)	12	8	20 (10)
3.	p-value	0.47	0.02	0.01
4.	First-time donors (2362)	130	44	174 (7.37)
5.	Repeat donors (4666)	168	24	192 (4.11)
6.	p-value	0.007	<0.001	<0.001
7.	Overall n=7028 (%)	298 (4.24)	68 (0.97)	366 (5.21)

Table 7: Delayed adverse donor reactions in blood donors (systemic)