Observational Study

Medicine®

OPEN

Incidence and severity of adverse events among platelet donors

A three-year retrospective study

Hamdan Almutairi, RN, MS[a], Mahmoud Salam, RN, PhD(c)[b,c,*], Khalid Batarfi, MD[a], Dima Alharbi, RN, MS[a], Faisal Wani, MD[a], Adel Almutairi, RN, PhD[b], Bushra Al-Shammari, RN, MS[a], Khaled Al–Surimi, PhD[d]

Abstract

Adverse events (AEs) are unfortunate consequences of platelet donation. This study reports the incidence and severity of AEs and the associated risk factors in platelet donation at a major blood donation center in Riyadh, Saudi Arabia.

A review of donation records was conducted between 2014 and 2017. Eligible study participants were 5007 platelet donors who had donated 7969 times. Each donation was accounted for as a single study subject. Participants' characteristics were described and analyzed as potential contributing factors to adverse events.

The average age of platelet donors was 30.0±7.3 years. First-time donors comprised (n = 3,100, 61.9%) of the sample, and 1907 (38.1%) were multiple donors (periodic/routine). Their average BMI was 28.6 ± 4.9 kg/m^2. Most donors have blood type "O" and Rheo "positive". The range of blood volume processed was 0 to 5273 ml, while the procedure duration ranged from 0 to 90 minutes. The average platelet yield was 3.8 ± 3.5 *10^{11} platelets per unit, and the average collected volume was 257.6 ± 86.1 ml. Incidence of AEs was 4.2%, of which 91.3% were mild and 8.7% were severe. AEs were vascular injuries (65.3%), vasovagal reactions (11.6%), and citrate toxicity (5.3%). AEs were associated with first-time donation, adj.OR (95%CI) = 1.5 (1.1–1.8) and lower BMI, adj. OR (95% CI) = 1.4 (1.1–1.8). Citrate toxicity was present in severe forms, unlike vascular injuries and vasovagal reactions that tended to be milder. Donors with hemoglobin levels above 16 g/dl, adj. OR (95% CI) = 1.3 (1.1–1.7) and platelet levels below 250,000, adj. OR (95% CI) = 1.3 (1.1–1.6) were more likely to contract AEs than others.

Reporting adverse events is essential to establish a benchmark for the annual incidence rates to be compared against local and international figures. Blood donor centers should also take notice of blood donors characteristics that are associated with higher incidence and more severe forms of AEs during or after platelet donation.

Abbreviations: AABB = American Association for Blood Banks, AEs = adverse events, BMI = body mass index, DBP = diastolic blood pressure, SBP = systolic blood pressure, SD = standard deviation, TBV = total blood volume.

Keywords: apheresis, blood, citrate, donation, mild, vascular, vasovagal

Editor: Ahmet Emre Eskazan.

This study was supported by King Abdullah International Medical Research Center, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia.

All authors certify that this manuscript is a unique submission and is not being considered for publication by any other source in any medium.

The authors declare that there is no conflict of interest.

Supplemental Digital Content is available for this article.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

[a] Department of Pathology and Laboratory Medicine, [b] King Abdullah International Medical Research Center, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia, [c] Hariri School of Nursing, American University of Beirut, Beirut, Lebanon, [d] Department of Health System Management, College of Public Health and Health Informatics, King Abdullah International Medical Research Center, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia.

[*] Correspondence: Mahmoud Salam, Science and Technology Unit, King Abdullah International Medical Research Center, King Saud bin Abdulaziz University for Health Sciences, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, POB 22490, (Mail Code 1515) Riyadh 11426, Saudi Arabia (e-mail: mahmoudsalam@hotmail.com).

How to cite this article: Almutairi H, Salam M, Batarfi K, Alharbi D, Wani F, Almutairi A, Al-Shammari B, Al–Surimi K. Incidence and severity of adverse events among platelet donors: a three-year retrospective study. Medicine 2020;99:52(e23648).

Received: 2 April 2020 / Received in final form: 2 October 2020 / Accepted: 11 November 2020

http://dx.doi.org/10.1097/MD.0000000000023648

Key points

- The incidence of AEs associated with platelet donation is higher among first-time donors and those with lower BMI.
- Citrate toxicity events are mainly exhibited in severe forms, unlike vascular injuries and vasovagal reactions that tend to be milder.
- Donors with hemoglobin levels above 16 g/dl and platelet levels below 250,000 are more prone to contract adverse events.
- Vascular injuries are also more likely to be prevalent among donors with lower BMI.
- Severe events, especially citrate toxicities are more likely to occur among first-time donors.

1. Introduction

Platelet donation or plateletpheresis is an intricate procedure performed in blood donation centers. It utlizes an automated continuous centrifugation technology to collect concentrated platelets.[1] In contrast to whole blood donation, platelet donation is physically demanding and time-consuming to donors.[2] Although plateletpheresis procedures are well tolerated, adverse reactions may occur, which usually discourage eligible donors from donating again, resulting in limited platelet supplies. Blood centers make tremendous efforts to motivate, recruit, and retain healthy platelet donors besides the fact that the collected platelet units have a short shelf life.[3,4]

Platelet donation is prone to adverse events (AEs) that are usually mild, but can lessen the number of future donations. If an AE occurs during or directly after the procedure, there is a 76% chance the individual will permanently refrain from donating again.[5] In the published literature, the incidence of AEs ranged from 1.56% to 4.06%.[6–9] These AEs were classified under "vasovagal reactions", "citrate-related reactions", or "vascular injuries".[10] Other causes of adverse events can be attributed to procedure troubleshooting.[6] Most AEs are mild, with self-limiting symptoms, and only require observation or supportive care.[9] The incidence of mild adverse events in one setting was (1.5%), while moderate adverse events were (1%).[7] Findings from 1 study revealed that among mild AEs, 54% resulted from difficult venous access, 7% faulty devices, 15% hypotension, and 8% tingling. In moderate AEs, 58% were tingling, 15% urticaria, 10% hypotension, and 3% nausea. Severe AEs were rarely reported in the literature.[11] In severe forms of AEs, 32% arose from syncope/hypotension, 17% urticaria, and 4.5% arrhythmias.[11]

The risk of encountering AEs is attributed to either the procedure itself or specific donor characteristics. For instance, platelet donors are exposed to various citrate amounts, depending on the procedure type/duration and the machine type. [10] In one setting, the rate of citrate reactions was 6.8%.[10] Paresthesia, resulting from citrate toxicity, was the most common sign reported in the literature.[9] On the other hand, the rate of vasovagal reactions with or without loss of consciousness was .1% and 2.5%, respectively, which is closely linked to the physiological changes in blood volume during the procedure.[10] A number of donor-related factors can also aggravate AEs. [6,12] For example, males were at higher risk of citrate reactions, while females were at higher risk of vasovagal reactions. [10] Age was a significant predictor of vasovagal reactions, but it failed to predict citrate reactions in 1 study. [10] Blood donor centers thrive on implementing the highest standards of practice to ensure platelet donors' safety. Therefore, proper assessment of donor eligibility criteria is required to maximize donors' safety and optimize platelet transfusion outcomes.[13]

Curbing the rate of adverse events is a pressing need to encourage new and regular platelet donors to donate. The prevalence of AEs in platelet donation can negatively affect donor retention and will eventually shorten blood supplies in donation centers. Despite being reported at low rates, unfortunate incidents must be further investigated to promote donor safety and satisfaction. Although the pre-donation screening criteria are strict, adverse events still occur, which raises a debate on whether such criteria need further recommendations. Thus, the purpose of this study was to report the incidence and severity of AEs and to identify associated risk factors that may help recognize donors at risk of experiencing AEs at one of the largest blood donation centers in Saudi Arabia.

2. Materials and methods:

2.1. Study design and setting

A cross-sectional correlation study was adopted based on a review of platelet donation records archived between January 1, 2014 and August 2, 2017 at a major blood donor center in Riyadh, Saudi Arabia. The blood donor center was established in 1984, it has been accredited by the College of American Pathologists and the American Association for Blood Banks since 1986. Its current seating capacity is 16 blood donation chairs allotted to whole blood donation and apheresis. On an annual basis, the blood donation center supplies more than 35,000 blood units to medical centers across Saudi Arabia upon request.[14] Further details on the quality management system of the targeted setting are stated in Supplement A, http://links.lww.com/MD/F378.

2.2. Study participants and sampling technique

The accessible population constituted of all platelet donors who visited the targeted setting during the study period. In Saudi Arabia, blood donation is unpaid and voluntary. Females are ineligible for donating at this setting, so all participants were males. Eligible study participants signed written informed consents and fulfilled the AABB donation criteria prior to donation.[14] The platelet apheresis procedure followed the guidelines of AABB (Supplement A, http://links.lww.com/MD/F378). As the type of medical instruments and kits are likely to have a confounding effect on the relationship between exposures and AEs,[6] the apheresis kits (Trima Accel kit) were used as the standardized platelet collection kits. More details on the plateletpheresis procedure are provided in Supplement A, http://links.lww.com/MD/F378.

2.3. Data collection

The platelet donation records contained medical history, physical examination (conducted by healthcare practitioners), and laboratory blood tests. Data were uploaded from records into

a local database by a group of administrative assistants with pre-defined entry restrictions on input variables. A random check and verification of entries was performed by a quality management specialist and 2 co-investigators.

2.3.1. Exposure variables. Study exposures included age (years), gender, height (m), weight (kg), body mass index (BMI in kg/m^2), and donation pattern (single donor vs periodic/occasional donor).[15] BMI was categorized as underweight (<18.5 kg/m^2), normal weight (18.5–25 kg/m^2), overweight (26–30 kg/m^2), and obese (>30 kg/m^2). Typing cross matching (ABO), the Rho factor (+ve; -ve), the platelet count (count per mm^3), hematocrit (%), and white blood cell counts were obtained prior to donation. Blood pressure (mm Hg) was categorized as normal (SBP < 120, DBP < 80), pre-hypertension (SBP: 120–139, DBP: 80–89), stage I (SBP: 140–159, DBP: 90–99), stage II (SBP ≥ 160, DBP ≥ 100), and stage III (SBP ≥ 180, DBP ≥ 110). The total blood volume (ml) and the length of procedure were recorded. Post-donation variables consisted of the platelet counts, hemoglobin, and hematocrit levels, as well as the platelet yield (x10^{11} platelets per unit) and plasma volume (ml).[14] The recommended platelet yield is 3.0x10^{11} to 3.5x10^{11} for 1 dose, 6.0x10^{11} to 6.5x10^{11} for 2 doses, and 9.0x10^{11} for 3 therapeutic doses.

2.3.2. Outcome variables. AEs comprised a list of observed signs and/or reported symptoms that occurred during or immediately after donation. The severity of signs/symptoms were categorized as mild-to-moderate or severe. Mild-to-moderate signs/symptoms, such as sweating, pallor, dizziness, cold feeling, weakness, nausea, heart rate/blood pressure fluctuations, and/or feeling of pins/needles, were self-limited and only required observation or minor support. Severe cases were persistent and required medical interventions. These include loss of consciousness, fainting, vomiting, cramps, cardiac arrhythmia, convulsions, tetany, laryngeal edema, loss of sphincter control, and hypovolemia.[15] AEs were vascular injuries at the insertion site, vasovagal reactions due to hypovolemia, and citrate toxicity owing to citrate exposure (hypocalcaemia).[16] Vascular injuries included bleeding, hematomas, pain and discoloration at the insertion site. Vasovagal reactions included sweating, pallor, dizziness, cold feeling, and heart rate/blood pressure fluctuations with or without loss of consciousness. Citrate reactions included numbness, tingling in the lips, paresthesia to the hands, chills, abdominal cramps, muscle cramps, tetany, visual disturbances, loss of consciousness, cardiac arrhythmia, and seizures. Miscellaneous AEs were also reported, such as machine errors, blood leaks, and/or other reasons irrelevant to the procedure.[17]

2.3.3. Donor characteristics. A total of 5,007 platelet donors were enrolled in this study. First-time donors comprised 3100 (61.9%) of the studied population, while 1907 (38.1%) were regular donors (periodic/routine). Throughout the study period, donation numbers reached a total of 9343, with an average of 1.2 ± 1.4 donations per donor. Each donation was accounted as a single study subject and analyzed against the study outcomes. Figure 1 displays the excluded cases for being duplicates, global outliers, or having missing data. The total number of donations with complete data was 7969 (85.3%). Processed blood volume ranged from 0 to 5273 ml, while the procedure duration varied from 0 to 90 minutes. The average platelet yield was 3.8 ± 3.5

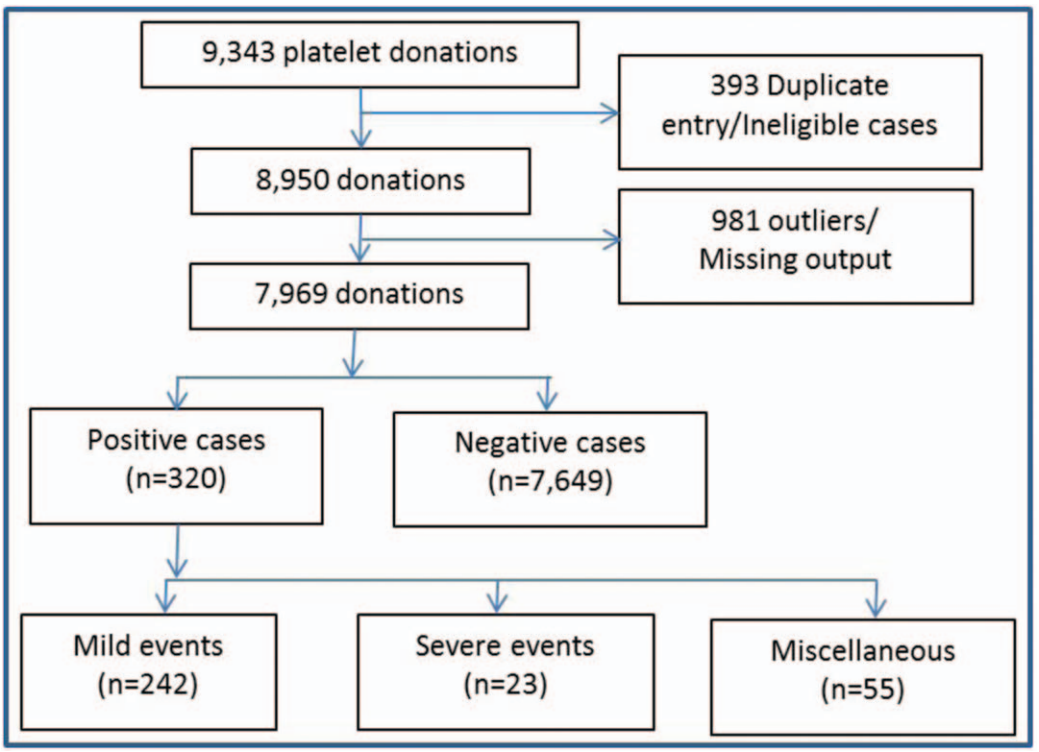

Figure 1. Inclusion and exclusion criteria.

($x10^{11}$) platelets per unit and the average collected volume was 257.6 ± 86.1 ml. It is worth noting that all first-time donors who developed reactions have refrained from future donations.

2.4. Data management and analysis

SPSS statistical software (Version 26; SPSS Inc., NY, USA) was used for data analyses. Categorical variables were presented in frequencies and percentages, while the average of continuous variables was presented in mean ± standard deviation (SD). Incidence of adverse events was calculated by dividing the number of events over the total number of participants within the study duration multiplied by 100. Bivariate analysis using Pearsons Chi-Squared test (χ^2) and binary logistic regression models were constructed to determine the factors associated with the incidence and severity of adverse events (mild/moderate vs severe). The adjusted odds ratio (OR) and 95% confidence intervals (CI) were presented, and a *P* value (P) was deemed significant at <.05.

2.5. Ethical considerations

This study was approved by the Institution Review Board at the Ministry of National Guard, Riyadh, Saudi Arabia (SP 16/147). The study was observational without the usage of experimental kits nor new machines. Confidential information about donors was stored in a secure database. Donors were also informed about using their data for other purposes, such as generating quality performance indicators, improvement projects, and research activities without revealing their identities.

3. Results

3.1. Platelet donation characteristics

Of the 7969 donations, 1713 (21.5%) were donated by individuals <25 years old, while others were donated by 6256 (78.5%) individuals of age ≥25 years, with an age average 30.8 ± 7.3 years. The average BMI was 28.6 ± 4.9 kg/m^2, and almost one quarter 2005 (25.2%) had normal weight. Almost 2 thirds 4,869 (61.1%) of donations were provided by regular donors, most of whom have blood type "O" and Rho factor "positive". Other platelet donation characteristics are presented in Table 1.

Table 1

Platelet donation and outcome characteristics.

	n (%) 7969 (100%)
Donation characteristics	
Age (years)	
<25	1713 (21.5%)
≥25	6256 (78.5%)
(Mean ± SD)	30.0 ± 7.3
BMI	
Underweight (<18.5)	19 (.2%)
Normal (18.5–24.9)	2005 (25.2%)
Overweight (25–29.9)	3026 (38.0%)
Obese (≥30)	2919 (36.6%)
(Mean ± SD)	28.6 ± 4.9
Donation history	
First time donor	3100 (38.9%)
Regular donor	4869 (61.1%)
Blood group	
A	2422 (30.4%)
B	1786 (22.4%)
AB	726 (9.1%)
O	3035 (38.1%)
Rho factor	
Positive	7534 (94.5%)
Negative	435 (5.5%)
Blood pressure	
Normal	2176 (27.3%)
Prehypertension	4179 (52.4%)
Stage I hypertension	1481 (18.6%)
Stage II hypertension	133 (1.7%)
Hemoglobin (g/dl), Mean ± SD	15.3 ± 1.0
Hematocrit (%), Mean ± SD	46.1 ± 2.8
Platelet (per micro liter), Mean ± SD	250,942 ± 47,337
Blood volume (ml), Mean ± SD	5262 ± 595
Outcome characteristics	
Adverse events	
None	7649 (95.8%)
Yes	320 (4.2%)
Vascular injuries	209 (65.3%)
Miscellaneous	55 (17.2%)
Vasovagal reactions	37 (11.6%)
Citrate toxicity	17 (5.3%)
Both (Vasovagal & Citrate toxicity)	2 (.6%)
Severity of event	
Mild-moderate	242 (91.3%)
Severe	23 (8.7%)

% = percentage, BMI = body mass index, dl = deciliter, g = gram, ml = milliliter, n = frequency, SD = standard deviation.

3.2. Outcome characteristics

The incidence of AEs was 320/7969 (4.2%), among which the leading type was vascular injuries (65.3%), vasovagal reactions (11.6%), and citrate toxicity (5.3%). The majority of AEs 242 (91.3%) were classified as mild-to-moderate, while the minority 23 (8.7%) comprised severe AEs (Table 1). Figure 2 shows the percentage distribution of severity among the 3 types of events.

3.3. Factors associated with AEs

Bivariate analyses showed that younger age, lower BMI, first-time donation, higher hemoglobin levels and lower platelet counts were all significantly associated factors with AEs, *P* = .011, *P* = .001, *P* < .001, and *P* = .0141 (Table 2). Logistic regression demonstrated that donors with lower BMI had a 40% [OR = 1.4 (1.1–1.8)] more chance to experience AEs than others, adj. *P* = .011. First-time donors were 50% [OR = 1.5 (1.2–1.9)] more likely to experience AEs than previous donors, adj. *P* < .001, respectively. Donors with hemoglobin levels (>16 g/dl) and platelet levels (≤250,000) were both 30% (OR = 1.3) more likely to complain about AEs compared to their counter groups, adj. *P* = .041 and adj. *P* = .025 (Table 3).

The rate of vascular injuries was significantly higher among donors with lower BMI, *P* = .006. Citrate toxicity was higher among first-time donors (n = 14, 8.6%, *P* = .038). The rate of vasovagal reactions was significantly higher in older adults (14.6%, *P* = .031), negative Rho factor (36.0%, *P* = .001), and Stage I /II hypertensive donors (22.0%, *P* = .01), Table 4. Regression analyses showed that those with higher BMI were 50% (95%OR = .3-.9) less likely to contract vascular events, compared to donors with lower BMI, adj. *P* = .012. The risk of citrate toxicity was three-fold higher among first-time donors,

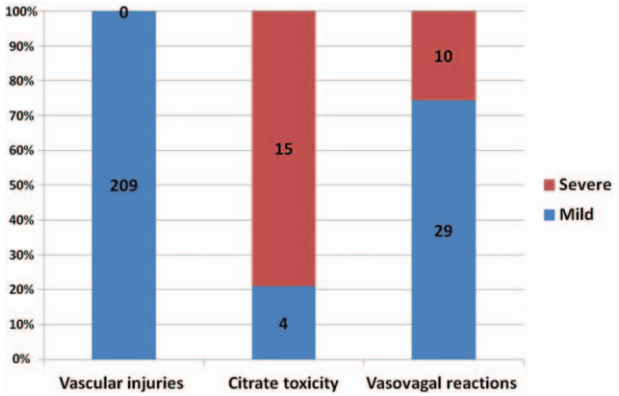

Figure 2. Mild vs severe adverse events.

adj. $P=.044$. Vasovagal reactions were 2.8 times more likely to be observed among older donors (adj. $P=.048$); 5.4 times more likely to be observed among donors with negative Rho factor (adj. $P<.001$); 2.8 times more likely among donors with abnormal blood pressure (adj. $P=.011$), compared to their counter groups (Table 5).

3.4. Factors associated with the severity AEs

Severe forms of AEs were significantly higher among first-time donors 17 (12.2%) compared to regular donors 6 (4.8%), $P=.031$ (Table 2). Severe AEs were also significantly more prevalent among donors who underwent larger volumes of processed or collected blood ($P=.001$ each), longer durations of procedure ($P=.003$), and higher yields of platelets ($P=.001$). Regression analysis showed that first-time donors were 3 times (1.1–8.1) more likely to endure severe AEs compared to regular donors, adj. $P=.032$ (Table 3).

4. Discussion

4.1. Risk factors for AEs

Identifying risk factors helps practitioners with the screening of high-risk donors. Donors with lower BMI are more likely to encounter AEs. Though one study reported no significant

Table 2

Incidence and severity of adverse events across donation characteristics.

	Incidence of Adverse Event		Severity of event		
			Mild-moderate	Severe	
	n (%)	RR[95%CI]	n (%)	n (%)	RR[95%CI]
Age (years)					
<25	87 (5.1%)	1.4[1.1–1.7]	61 (88.4%)	8 (11.6%)	1.5 [.7–1.1]
≥25	233 (3.7%)	1	181 (82.3%)	15 (7.7%)	1
	$\chi^2=6.400$, $P=.011$*		$\chi^2=1.000$, $P=.317$		
BMI					
Underweight/Normal	107 (5.3%)	1.5[1.2–1.9]	89 (80.9%)	9 (19.1%)	1.1 [.5–2.4]
Overweight/Obese	213 (3.6%)	1	153 (91.6%)	14 (8.4%)	1
	$\chi^2=11.371$, $P=.001$*		$\chi^2=.05$, $P=.823$		
Donation history					
First time donor	162 (5.2%)	1.6[1.3–2.0]	122 (87.8%)	17 (12.2%)	2.6 [1.0–6.3]
Regular donor	158 (3.2%)	1	120 (95.2%)	6 (4.8%)	1
	$\chi^2=19.281$, $P=.00001$*		$\chi^2=4.651$, $P=.031$*		
Rho factor					
Positive	295 (3.9%)	1	222 (91.4%)	21 (8.6%)	1
Negative	25 (5.7%)	1.5[.9–2.2]	20 (90.9%)	2 (9.1%)	1.1 [.3–4.2]
	$\chi^2=3.579$, $P=.059$		$\chi^2=.005$, $P=.943$		
Blood pressure					
Normal/Prehypertension	261 (4.1%)	1.1[.9–1.5]	197 (91.2%)	19 (8.8%)	1.1 [.4–3.0]
Stage I /II hypertension	59 (3.7%)	1	45 (91.8%)	4 (8.2%)	1
	$\chi^2=.681$, $P=.409$		$\chi^2=.020$, $P=.887$		
Hemoglobin (g/dl)					
12.5–14	29 (3.2%)	1	24 (92.3%)	2 (7.7%)	1.1
14.1–16	191 (3.8%)	1.2	143 (92.9%)	11 (7.1%)	1
16.1–18	100 (4.9%)	1.5	75 (88.2%)	10 (11.8%)	1.7
	$\chi^2=6.397$, df=2, $P=.041$*		$\chi^2=1.512$, df=2, $P=.470$		
Hematocrit (%)					
≤45	115 (3.5%)	1	91 (93.8%)	6 (6.2%)	1.1
46–50	184 (4.3%)	1.2	134 (89.3%)	16 (10.7%)	1.9
>50	21 (4.6%)	1.3	17 (94.4%)	1 (5.6%)	1
	$\chi^2=3.427$, df=2, $P=.180$		$\chi^2=1.730$, df=2, $P=.421$		
Platelet count					
<250,000	194 (4.5%)	1.3[1.1–1.6]	149 (92.0%)	13 (8.0%)	1
≥250,000	126 (3.4%)	1	93 (90.3%)	10 (9.7%)	1.0 [.9–1.1]
	$\chi^2=6.030$, $P=.014$*		$\chi^2=.225$, $P=.635$		

* Statistically Significant at $P<.05$.

% = percentage, χ^2 = Pearson's Chi-Squared, BMI = body mass index, CI = confidence interval, df = degree of freedom, dl = deciliter, g = gram, n = frequency, P = P value, RR = risk ratio.

Table 3

Factors associated with adverse events.

	Incidence of events		Severe adverse events	
	Adj. OR (95%CI)	Adj. *P* value	Adj. OR (95%CI)	Adj. *P* value
Age (years) (<25 vs ≥25)	1.2[.9–1.6]	.120	1.7[.7–4.3]	.253
BMI (Lower vs. Higher)	1.4[1.1–1.8]	.011*	.9[.4–2.3]	.851
History of Donation (1st time vs multiple)	1.5[1.2–1.9]	<.001*	3.0[1.1–8.1]	.032*
Rho factor (Negative vs Positive)	1.4[.9–2.2]	.089	1.0[.2–5.0]	.960
Blood pressure (Normal vs abnormal)	1.1[.8–1.5]	.539	1.2[.4–4.0]	.717
Hemoglobin (g/dl) (>16 vs ≤16)	1.3[1.1–1.7]	.041*	1.7[.7–4.1]	.262
Platelet (per micro liter) (≤250,000 vs >250,000)	1.3[1.1–1.6]	.025*	.7[.3–1.7]	.430

* Significance at $P < .05$.

BMI = body mass index, CI = confidence interval, dl = deciliter, g = gram, OR = odds ratio.

relationship between AEs and weight,[18] low weight was associated with a higher risk of adverse events after platelet[19] and whole blood donations.[14] Despite the fact that AABB has set the nadir of donors' weight at 50 kg, investigating BMI as a predictor of AEs was seldom carried out in the literature. Being a first-time platelet donor also increases the chance of encountering AEs, unlike routine/occasional donors.[14] For first-time donors, stress is inevitable due to their unfamiliarity with the donation process (immobility of arm and length of procedure) and lack of proper communication with staff or noncompliance with pre-donation instructions (hydration and nutrition). In this regard, repeated and regular platelet donors had an added advantage over first-time donors who are unlikely to return for future donations.[5,20]

Higher incidence of AEs was observed among platelet donors with higher hemoglobin levels, and beyond 16 g/dl the odds increased by 1.5 times. A study showed that elevated hemoglobin levels were associated with higher rates of AEs,[14] in particular

Table 4

Various types of adverse events across donation characteristics.

	Vascular injuries n (%)	Citrate toxicity n (%)	Vasovagal reactions n (%)
Age (years)			
<25	60 (69.0%)	5 (5.7%)	5 (5.7%)
≥25	149 (63.9%)	14 (6.0%)	34 (14.6%)
	χ^2=.704, *P*=.402	χ^2=.008, *P*=.930	χ^2=4.631, *P*=.031*
BMI			
Underweight/Normal	81 (75.7%)	7 (6.5%)	11 (10.3%)
Overweight/Obese	128 (60.1%)	12 (5.6%)	28 (13.1%)
	χ^2=7.657,*P*=.006*	χ^2=.105, *P*=.746	χ^2=.546, *P*=.460
Donation history			
First time donor	106 (65.4%)	14 (8.6%)	21 (13.0%)
Regular donor	103 (65.2%)	5 (3.2%)	18 (11.4%)
	χ^2=.002, *P*=.964	χ^2=4.297, *P*=.038*	χ^2=.184, *P*=.668
Rho factor			
Positive	196 (66.4%)	19 (6.4%)	30 (10.2%)
Negative	13 (52.0%)	0 (.0%)	8 (36.0%)
	χ^2=2.121, *P*=.145	F-exact, *P*=.203	F-exact, *P*=.001*
Blood pressure			
Normal/Prehypertension	175 (67.0%)	17 (6.5%)	26 (10.0%)
Stage I /II hypertension	34 (57.6%)	2 (3.4%)	13 (22.0%)
	χ^2=1.886, *P*=.170	F-exact, *P*=.284	χ^2=6.553, *P*=.010*
Hemoglobin (g/dl)			
12.5–16	147 (66.8%)	13 (5.9%)	22 (10.0%)
16.1-18	62 (62.0%)	6 (6.0%)	17 (17.0%)
	χ^2=.704, *P*=.401	χ^2=.001, *P*=.975	χ^2=3.148, *P*=.076
Hematocrit (%)			
≤50	194 (64.9%)	19 (6.4%)	36 (12.0%)
>50	15 (71.4%)	0 (.0%)	3 (14.3%)
	χ^2=.371, *P*=.542	χ^2=1.419, *P*=.234	χ^2=.092, *P*=.761
Platelet count			
<250,000	123 (63.4%)	13 (6.7%)	28 (14.4%)
≥250,000	86 (68.3%)	6 (4.8%)	11 (8.7%)
	χ^2=.794, *P*=.373	χ^2=.514, *P*=.473	χ^2=2.321, *P*=.128

Statistically Significant at $P < .05$.

% = percentage, χ^2 = Pearson's Chi-Squared, BMI = body mass index, dl = deciliter, F-exact = fisher exact, g = gram, n = frequency, P = P value.

Table 5

Factors associated with the type of adverse event.

	Vascular Adj. OR[95%CI] Adj. *P* value	Citrate Adj. OR [95%CI] Adj. *P* value	Vasovagal reactions Adj. OR [95%CI] Adj. *P* value
Age (years)	.8 [.5–1.5]	1.1 [.4–3.1]	2.8 [1.1–7.6]
(≥25 vs <25)	.541	.911	.048*
BMI	.5 [.3-.9]	1.1 [.4–2.9]	1.0 [.5–2.3]
(Higher vs. Lower)	.012*	.882	.927
History Donation	1.0 [.6–1.6]	3.0 [1.1–8.8]	1.0 [.49–2.1]
(1st time vs multiple)	.971	.044*	.988
Rho factor	.5 [.2–1.2]	–	5.4 [2.1–13.7]
(Negative vs positive)	.147		<.001*
Blood pressure	.7 [.4–1.4]	.4 [.1–2.0]	2.8 [1.3–6.3]
(Abnormal vs normal)	.342	.292	.011*
Hemoglobin (g/dl)	.9 [.5–1.5]	1.[.4–2.8]	1.6 [.8–3.3]
(>16 vs ≤16)	.685	.999	.209
Platelet (per micro liter)	1.2 [.7–2.0]	.8 [.3–2.1]	.6 [.3–1.4]
(≥250,000 vs <250,000)	.447	.618	.259

* Significance of $P < .05$.

BMI = body mass index, CI = confidence interval, dl = deciliter, g = gram, OR = odds ratio.

vasovagal reactions.[21] Though evidence-based literature has set a minimum safe hemoglobin level at 12.5 g/dl, a safer margin of hemoglobin needs to be reconsidered within the pre-donation criteria to maximize donors' safety. Donors with platelet levels below 250,000 were also more likely to contract AEs than their counter group. In this setting, donors with platelet counts <250,000 had higher rates of citrate toxicity and vasovagal reactions, yet without statistical significance. It should also be noted that the AABB has recommended that a platelet count >150,000 is considered safe and common. Further studies are warranted to confirm whether the minimum safe margin of platelet count needs to be elevated in the Arab Gulf population.

4.2. Vascular adverse events

Vascular AEs have been observed among platelet donors with lower BMI (7.4%).[22] Study investigators reported that hematomas occurred among 33/11,712 (.28%) of whole blood donors with BMI < 25 compared to their counter group 44/8,890 (.43%) with BMI ≥ 25.[23] Vascular adverse events can be attributed to vein conditions, stability of the underlying subcutaneous tissue, or arm muscularity [24]. Vascular injuries can also result from traumatic needle insertion and/or be aggravated by the anticoagulant solution infused into the system. The practitioners, manual dexterity to perform venipuncture might have had a confounding effect,[14] yet authors believe that measuring their performance is a challenge. The tendency to ascribe pre-calculated dosage of anticoagulants to hematomas or bleeding at insertion sites necessitates a research interventional approach.

4.3. Vasovagal adverse events

Vasovagal events have been observed among platelet donors (0.8%) and manifested in the form of pre-syncope/syncope.[22] Similar to previous studies, elevated hemoglobin levels in this setting was associated with these types of events.[21,25] Vasovagal events are mainly caused by the loss of blood volume. One meta-analysis study reported that plateletpheresis negatively affected the erythrogram parameters due to blood loss in the kits used for the procedure and cell lyses.[26] Such type of events were in particular higher among older adults, donors with Rho negative and hypertensive donors at this setting. One of the key preventive measures to avoid vasovagal events is hydration before, during and after donation to compensate for fluid loss. Although pre-donation education on this aspect plays a great role,[22] authors speculate that it might fail to secure compliance on the donors' part. Blood pressure is expected to drop due to the physiological changes in the plasma volume withdrawn from the donor. One study reported that the mean predicted change in BP (pre/post donation) will be higher in stage I and II hypertensive donors than those with normal BP.[27] Authors infer that the extent of deviation from the donors own baseline blood pressure may have resulted in higher or lower rates of pre-syncope events.

4.4. Citrate toxicity

Citrate toxicity is also expected during or after plateletpheresis (9%).[22] In this setting, first-time donors were significantly at a higher risk of encountering AEs. The anticoagulant dosage and the pre-calculated yield are standardized among all donors as per the AABB criteria and donor parameters.[16] The longer the plateletpheresis duration, the greater the volume of anticoagulants infused.[18] However, the longer the plateletpheresis, the higher the citrate exposure and the risk of contracting citrate toxicity. Citrate toxicity signs might have been under-reported because some donors perceive these signs as trivial or inherent in plateletpheresis. Therefore, staff at donation centers should be extremely vigilant when performing plateletpheresis on first-time donors.

4.5. Severity of adverse events

The severity of AEs during or after plateletpherisis is a great concern to any blood donor center. The rate of moderate-to-severe AEs in one setting was 37% among 15,763 platelet donations.[28] In this study, AEs were 3 fold more severe among first-time donors than regular donors. Authors believe that the psychological stress of first-time donors might have played a significant role in exaggerating some self-reported symptoms.

More severe events were observed in higher processed blood volumes, longer procedures and higher platelet yields. Authors also agree that some donors might have experienced - at a certain stage of the procedure - milder forms of AEs (nausea, light headiness, and cold feeling), yet ignored early warning signs and failed to report back on time.

4.6. Limitations

Delayed adverse events like hematomas might have occurred after leaving the donation center, but these were not followed up. Further, the incidence and severity of AEs were not assessed among female platelet donors, which restricted the generalizability of the study findings in both genders. Authors suspect that there could be an under reporting of some AEs by some practitioners who might have perceived them as an indicator of malpractice or incompetence. Other risk factors of AEs might have been pre-existing, such as lack of sleep, insufficient intake of meals/fluids prior donation, needle phobia or hemophobia. These were missed in this study since it was a retrospective analysis of previously collected data.

5. Conclusion

Blood banks ,mission entails that platelets storage capacity must always meet blood transfusion demands in medical centers. Blood donation is a valuable, humane, voluntary contribution, where donors, safety is of paramount importance. An unsatisfied donor is unlikely to return for donation, and such refrainment may eventually reinforce a negative risk perception of blood donations within the community.

Blood donation centers should anticipate that AEs will be higher among first-time donors and those with lower BMI. Citrate toxicity events are mainly exhibited in severe forms, unlike vascular and vasovagal events that tend to be milder. Donors with hemoglobin levels above 16 g/dl and platelet levels below 250,000 are expected to be at higher risk of contracting adverse events. Vascular injuries are also believed to be more prevalent among donors with lower BMI, while severe events, such as citrate toxicities, are more prevalent among first-time donors. Vasovagal reactions are associated with older age, negative Rho blood types, and hypertension. Overall, meticulous donor-vigilance, risk factor screening prior to donation, and extensive training of practitioners can contribute to the prevention of adverse events.

Acknowledgments

Special thanks to the team of nurses, technicians and laboratory staff at the blood donor center and King Abdulaziz Medical City.

Author contributions

Conceptualization: Hamdan Almutairi, Mahmoud Salam, Khalid Batarfi, Dima Alharbi, Faisal Wani, Adel Almutairi, Bushra Al-Shammari, Khaled Al–Surimi.
Data curation: Hamdan Almutairi, Mahmoud Salam, Khalid Batarfi, Dima Alharbi, Adel Almutairi, Bushra Al-Shammari, Khaled Al–Surimi.
Formal analysis: Mahmoud Salam, Adel Almutairi.
Investigation: Hamdan Almutairi, Mahmoud Salam, Khalid Batarfi, Dima Alharbi, Faisal Wani, Khaled Al–Surimi.
Methodology: Hamdan Almutairi, Mahmoud Salam, Khalid Batarfi, Dima Alharbi, Faisal Wani, Adel Almutairi, Bushra Al-Shammari, Khaled Al–Surimi.
Project administration: Hamdan Almutairi.
Supervision: Hamdan Almutairi, Khalid Batarfi, Dima Alharbi, Faisal Wani, Adel Almutairi, Bushra Al-Shammari.
Validation: Hamdan Almutairi, Mahmoud Salam, Adel Almutairi, Bushra Al-Shammari.
Visualization: Mahmoud Salam.
Writing – original draft: Hamdan Almutairi, Mahmoud Salam, Khalid Batarfi, Dima Alharbi, Faisal Wani, Adel Almutairi, Bushra Al-Shammari, Khaled Al–Surimi.
Writing – review & editing: Hamdan Almutairi, Mahmoud Salam, Khalid Batarfi, Dima Alharbi, Faisal Wani, Adel Almutairi, Bushra Al-Shammari, Khaled Al–Surimi.

References

[1] Van der Meer PF. Platelet concentrates, from whole blood or collected by apheresis. Transfus Apher Sci 2013;48:129–31.
[2] Charbonneau J, Cloutier M-S, Carrier É. Why do blood donors lapse or reduce their donation's frequency? Transfus Med Rev 2016;30:1–5.
[3] Lambert MP, Sullivan SK, Fuentes R, et al. Challenges and promises for the development of donor-independent platelet transfusions. Blood 2013;121:3319–24.
[4] Tendulkar A, Shah S, Patil D, et al. Platelet donation drives: a novel initiative to recruit platelet donors. Transfus Apher Sci 2014;50:407–10.
[5] Riga A, Sapey T, Bacanu M, et al. Blood donors-Serious adverse reactions (SAR) 2010-2014 EFS Châteauroux, France. Transfus Clini Biolo 2015;22:62–5.
[6] Yin G, Xu J, Shen Z, et al. The relationship of platelet yield, donor's characteristic and apheresis instruments in China. Transfus Apher Sci 2013;49:608–12.
[7] Amanat ST, Shakoor HA, Raza M, et al. Clinical indications and adverse reactions of platelet apheresis. J Coll Physicians Surg Pak 2015;25: 403–6.
[8] Arora D, Garg K, Kaushik A, et al. A retrospective analysis of apheresis donor deferral and adverse reactions at a tertiary care centre in India. J Clin Diagn Res 2016;10:EC22.
[9] Das SS, Sen S, Chakrabarty R. Machine and man individualities in apheresis adverse events. Global J Transfu Med 2018;3:30.
[10] Robillard P, Grégoire Y. Comparison of vasovagal and citrate reaction rates in donors according to type of apheresis procedure. Paper presented at: 2017 AABB Annual Meeting 2017.
[11] Henriksson MM, Newman E, Witt V, et al. Adverse events in apheresis: an update of the WAA registry data. Transfus Apher Sci 2016;54:2–15.
[12] Woodall WJ, Nguyen VQ, Tran MH. Evaluation of donor factors contributing to plateletpheresis yields among apheresis platelet donors. J Clin Apher 2014;29:139–47.
[13] Das SS, Zaman R, Biswas D. Era of blood component therapy: time for mandatory pre-donation platelet count for maximizing donor safety and optimizing quality of platelets. Transfus Apher Sci 2013;49:640–3.
[14] Almutairi H, Salam M, Alajlan A, et al. Incidence, predictors and severity of adverse events among whole blood donors. PloS one 2017;12: e0179831.
[15] Crocco A, D'Elia D. Adverse reactions during voluntary donation of blood and/or blood components. A statistical-epidemiological study. Blood Transfus 2007;5:143.
[16] Philip J, Sarkar RS, Pathak A. Adverse events associated with apheresis procedures: incidence and relative frequency. Asian J Transfus Sci 2013;7:37.
[17] Bassi R, Thakur KK, Bhardwaj K. Plateletpheresis adverse events in relation to donor and Plateletpheresis session profile. Iraqi J Hematol 2017;6:38.
[18] Barbosa MH, Silva KFNd, Coelho DQ, et al. Risk factors associated with the occurrence of adverse events in plateletpheresis donation. Rev Bras Hematol Hemoter 2014;36:191–5.
[19] Eder AF, Kiss JE. Adverse reactions and iron deficiency after blood donation. Rossi's Principles of Transfusion Medicine. 5th ed. Oxford, England: John Wiley & Sons Ltd. 2016:43-57.
[20] Custer B, Rios JA, Schlumpf K, et al. Adverse reactions and other factors that impact subsequent blood donation visits. Transfusion 2012;52: 118–26.

[21] Odajima T, Takanashi M, Sugimori H, et al. Impact of elevated hemoglobin and serum protein on vasovagal reaction from blood donation. PloS one 2016;11:e0148854.
[22] Patidar GK, Sharma RR, Marwaha N. Frequency of adverse events in plateletpheresis donors in regional transfusion centre in North India. Transfus Apher Sci 2013;49:244–8.
[23] Meena M, Jindal T. Complications associated with blood donations in a blood bank at an Indian tertiary care hospital. J Clin Diagn Res 2014;8: JC05.
[24] WHO . WHO guidelines on drawing blood: best practices in phlebotomy 2010.
[25] Gonçalez TT, Sabino EC, Schlumpf KS, et al. Vasovagal reactions in whole blood donors at three REDS-II blood centers in Brazil. Transfusion 2012;52:1070–8.
[26] Gil-Betacur A, Mantilla-Gutiérrez CY, Cardona-Arias JA. Effect of plateletpheresis on hematocrit, hemoglobin and erythrocyte count: meta-analysis 1980–2018. Sci Rep 2019;9:1–8.
[27] Rosa-Bray M, Wisdom C, Marier J, et al. The effect of plasmapheresis on blood pressure in voluntary plasma donors. Vox Sang 2015;108:11–7.
[28] Yuan S, Ziman A, Smeltzer B, et al. Moderate and severe adverse events associated with apheresis donations: incidences and risk factors. Transfusion 2010;50:478–86.