



# Adverse Events Among Plateletpheresis Donors in a Tertiary Care Hospital at Dhaka, Bangladesh

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## Key words:

Plateletpheresis donation, Citrate reactions, donor adverse events, Vascular injuries, Vasovagal reaction.

## Abstract:

**Introduction:** The rising demand for platelet transfusions among patients has increased the usage of automated blood collections. Many of the same reactions and injuries are found with pooled platelets received from whole blood donation, although notable differences exist.

**Objective:** To study the adverse events (AEs) during plateletpheresis procedures in a tertiary care hospital and plateletpheresis procedure session profiles.

**Materials and Methods:** This retrospective study was conducted from January 2021 to December 2021 by analyzing records of two-hundred and thirteen (213) plateletpheresis procedures done in transfusion medicine department. All the donors were male. All adverse effects were recorded and noted in the registrar.

**Results:** A total of 13 (Thirteen) AEs were noted, of which 08 (61.53%) events were associated with donors, 03 (23.07 %) were owed to a fault in the kit/equipment, and 02 (15.38 %) were due to technical faults. Donor-related AEs included hematoma (23.07%), vasovagal (23.07%), and perioral tingling sensation (15.38%). Technique-related AEs were 23.07%, and faulty kit/equipment-related AEs were 15.38%.

**Conclusion:** Apheresis donations performed on apheresis machines are safe. Careful donor selection, well-trained expert technical personnel, and supervision of experienced transfusion medicine specialists will make the donor's experience more pleasant.

## Introduction

Over decades, increased demand for platelet transfusions for patients with various medical and surgical conditions led to an accelerated use of technologically advanced “apheresis” for platelet concentrates.<sup>1</sup> This has resulted in an increase in the usage of single-donor platelets collected through automated blood collection. These collection

methods share many of the same reactions and injuries observed with pooled platelets obtained from whole blood donation, and there were also exceptional complications due to the collection method and the frequency at which donation can occur.<sup>2</sup> Apheresis procedures are usually nicely tolerated, but adverse events (AEs) occur in a few cases. They may arise during or after the

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procedure. The overall rate of AEs with apheresis donation is approximately ten times less than that seen with pooled random donor platelets obtained from whole blood donation, with mild events outnumbering the more severe ones.<sup>3</sup> Hospitalization is still extremely rare; it occurs in only 0.01% of donations.<sup>4</sup> AEs associated with apheresis donation can be due to anticoagulant delivery, vasovagal, allergy, venous access, or machine malfunction. These can be of variable severity. More plateletpheresis is taking place nowadays than in the past times. Knowing the adverse effects of plateletpheresis donation is essential for advancing such procedures in Bangladesh. This study aims to evaluate the adverse effects of plateletpheresis procedures done in a tertiary medical college hospital in Dhaka, Bangladesh.

#### **Materials and Methods:**

This retrospective study was done between January 2021 to December 2021 in the Department of Transfusion Medicine, Sir Salimullah Medical College Mitford Hospital, Dhaka. Two hundred thirteen plateletpheresis procedures were performed on Haemonetics MCS+ after obtaining informed written consent from the donors. All the donors were selected according to the standard operating procedure.<sup>5</sup> All the donors were between 18 and 60 years old, weighing >60 kg, and were medically fit. Complete hemogram and ABO and Rh grouping of donors were done. All the donors had hemoglobin levels  $\geq 12.5$  g/dl and platelet count  $\geq 150 \times 10^9$  /L. Tests mandatory for transfusion-transmitted infections (Hepatitis B virus, Hepatitis C virus, HIV-1 and 2, Syphilis, and Malaria) for donors were done before the procedure, and nonreactive donors were selected for the process. All the data recorded, including adverse reactions, were noted in the register. These data were analyzed using MS Excel 2000 and summarized.

The AEs were classified into donor-related, kit/equipment-related, and technique related. Donor-related adverse events were divided into local reactions and systemic reactions. AEs were classified according to severity into mild, moderate, and severe and according to etiology in a donor into hypotensive

reactions, citrate reactions, hematomas, loss of consciousness, seizures, and allergy.

**Hypotensive reaction** Hypotension during apheresis donation can result from several causes, including intravascular volume depletion, vasovagal reactions, citrate toxicity, and severe allergic reactions. Of these, the most common are vasovagal reactions and citrate toxicity. Symptoms and signs of a vasovagal reaction include light headedness, hot flashes, pallor, diaphoresis, nausea, vomiting, decreased heart rate, and decreased blood pressure. Preventive steps involve helping the donor feel comfortable and confident throughout the procedure. This reaction is significant for first-time apheresis donors, who are more likely to be anxious about the procedure.<sup>6</sup>

**Citrate reactions** are the most common adverse effects seen with apheresis procedures. They result from ionized hypocalcemia caused by the infusion of citrate anticoagulant during the procedure. The lowered ionized calcium levels allow spontaneous depolarization of neurons, and resulting symptoms include numbness and tingling in the lips and nose and sneezing. Moderate symptoms include nausea and vomiting; progression of paresthesia to the hands, feet, and chest; intense vibrating sensation throughout the body; chills; abdominal cramping; and lightheadedness or hypotension. Severe symptoms include painful muscle cramps, tetany, blurred or double vision, loss of consciousness, arrhythmia, and seizure. These symptoms are usually progressive in adult donors, so moderate and severe symptoms can generally be avoided through close monitoring and treatment of earlier signs.<sup>3,7</sup>

#### **Hematoma**

Complications of venous access can occur at any time during an apheresis donation. Hematoma formation and thrombosis are among possible acute complications. Symptoms include pain and pressure and bruising or swelling at the needle site. If venous access fails during the procedure, the procedure may not be completed, and the resulting physical discomfort may influence donor retention.<sup>6</sup> Treatment includes discontinuing the collection,

removing the needles, and applying pressure to the site. Since inexperienced phlebotomy staff are a significant risk factor for these reactions, prevention strategies include maintaining apheresis personnel competency. Preventive strategies for donors include encouraging donors to be well-hydrated before the donation and instructing them to keep the needle sites secure and stable during the donation.<sup>6</sup> Loss of consciousness and seizures is uncommon and usually occur due to a vasovagal reaction or severe citrate toxicity. Tonic-clonic seizures may accompany it; however, this does not represent true seizure activity.

### Allergic reactions

Allergic reactions occur due to reaction to ethylene oxide used to sterilize the disposable set. They occur predominantly in donors who have donated several times. There is intense itching, widespread urticaria, hives or welts, rhinitis, wheezing, tongue or facial edema, shortness of breath, hypotension, diarrhoea, laryngeal edema, and cardiopulmonary arrest.

### Kit/equipment-related adverse events

These adverse effects are secondary to improper use of disposable plateletpheresis kits. There may be hemolysis, thrombus formation, air embolism, leakage, infection, etc.<sup>7</sup>

### Technique-related adverse events

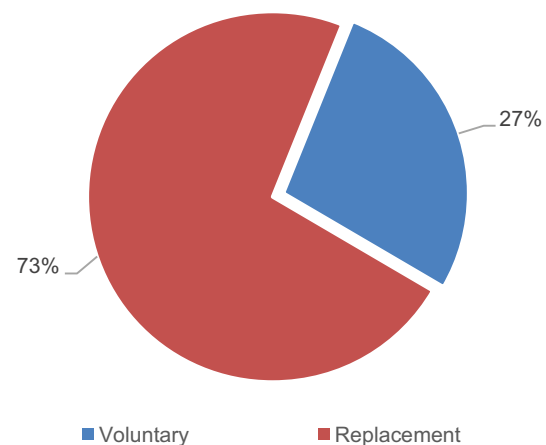
These are due to improper mounting of the set.

### Results

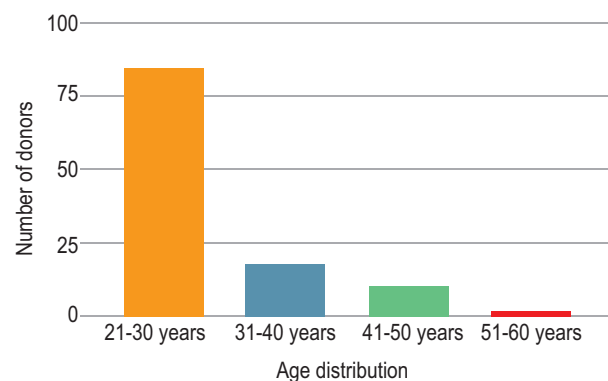
All 213 donors were male, 136 (63.84%) were voluntary, and 77 (36.15%) were replacement donors. (Figure-1) Maximum donors (68.07%) were in the age group between 21 and 30 years, minimum age being 19 and maximum being 60 years. (Figure -2) The weight of donors ranged from 60 kg to 115 kg; maximum donors (47.88%) were in the 61–70 kg category; the mean donor height was 170 cm. The prevalent blood type was O-positive, which accounted for 35.6% of the donations. The mean hemoglobin and hematocrit values were 13.76 g/dl and 41.2%, respectively. In maximum donors (31.92%), preprocedural platelet count of donors

ranged from  $200$  to  $450 \times 10^9/L$ .

According to the plateletpheresis session profiles, in 114 (53.52%), donation platelet yield was  $3 \times 10^{11}$ . In 32 (15.02%) donations, platelet yield was  $6 \times 10^{11}$ . With a mean platelet yield of  $3.83 \times 10^{11}$ , the donor's mean post-procedural platelet count reduction was  $71.09 \times 10^9/L$ . The mean volume of blood processed by the equipment was 2362 ml, and the mean volume of the product obtained was 310 ml. The mean amount of Acid Citrate Dextrose (ACD) used during the procedures was 258 ml. The mean duration of a plateletpheresis session was 51.04 minutes. With a platelet yield of  $6 \times 10^{11}$ , the mean volume of blood processed by the equipment was 2792 ml, the mean volume of the product obtained was 428 ml, and the mean amount of ACD used during the procedures was 310 ml.



**Fig.-1 :** Distribution of plateletpheresis donors according to donor category



**Fig.-2:** Distribution of plateletpheresis donors according to age groups (n=115)

Fig

**Table-I.** Distribution of the adverse reactions occurred during plateletpheresis sessions (n=7)

Main types of Adverse effects (AE)	Subtypes of AEs	Recoded Adverse effects (n=13)	Percentage
Adverse reactions linked to donors	Hematomas	03	61.3%
	Vagovagal reactions	03	
	Tingling sensations due to citrate toxicity	02	
Adverse reactions due to equipment or kit fault	Faulty kits	03	23.07%
Adverse reaction due to technical errors	Donor line clamp not open in time	02	15.38%

Regarding adverse events, a total of 13 AEs were noted; of which 8 (61.53%) events were associated with donors, 3 (23.07%) owed to a fault in kit/equipment, and 2 (15.384%) were due to technical aberrations. However, all the AEs associated with donors were mild, and none of the donors was hospitalized in the study [Table 1].

Donor-related adverse events, i.e., vascular injuries, were seen in three donors. Bruising was seen in only one donor, while hematoma formation was seen in two first-time donor cases. The vasovagal reaction was seen in three donors, out of whom one donor was a teenager. The second donor was a replacement donor and was reluctant to donate. Citrate toxicity manifested as perioral tingling sensation was seen in two donors. In these donors, platelet yield was  $6 \times 10^{11}$ , ACD infusion was more. In routine, oral mouth-dissolving calcium tablets were given to all the cases to prevent hypocalcemia.

Technique-related AEs included 2 (15.38%) events; the donor line clamp was not opened due to low inlet pressure time. Kit/equipment-related AEs included three defective kits (23.07%).

### Discussion

The potential donor should meet several requirements to be accepted as a suitable candidate for blood component donation.[8] Criteria such as hematocrit or hemoglobin levels, age, weight, and minimum platelet count are essential for the safety of the donor.[9] In this study, all the donors were male. Females did not fulfill the criteria for selection of apheresis donors. Most of the females were anemic, underweight, or had poor veins. Alloimmunization due to repeated pregnancies also makes the females unfit for donation.<sup>10</sup> Several

studies show a common profile for donation, in which a more significant number of male donors exist.<sup>11-15</sup> Some studies also show that men have lower rates of AEs than women in plateletpheresis donation. Another study also pointed out that only women were associated with venipuncture-related complications.<sup>16</sup> Weight or body mass is a criterion to maximize plateletpheresis donation because larger donors with higher blood volume can obtain higher platelet yields.<sup>11</sup> In the present study, technique and equipment-related complications were more as compared to analysis conducted by Dogra et al.<sup>1</sup> The percentage of AEs among healthy donors undergoing plateletpheresis procedures in the present study was 6.1% which was lower as compared to the survey by Dogra et al.<sup>1</sup> and Khajuria et al.<sup>17</sup> and higher than the studies conducted by Philip et al.<sup>2</sup> and McLeod et al.<sup>18</sup> This low incidence is consistent with the literature, indicating that donors tolerated the plateletpheresis procedure well.<sup>11</sup> In this study, the frequency of vascular injuries in plateletpheresis was similar to that reported in the literature.<sup>1,2,17,18</sup> These are usually due to faulty phlebotomy techniques by inexperienced technical staff, the number of prior apheresis donations, and the anatomy at the venipuncture. Unlike citrate reactions, which are more likely to occur in repeat donors, the probability of bruising reduces with the number of donations.<sup>18,19</sup> In this study, the frequency of citrate reactions was 1.4% which is almost equal in comparison to the study done by McLeod et al.<sup>18</sup> and Philip et al.<sup>2</sup> In the study conducted by Dogra et al.<sup>1</sup> and Khajuria et al.<sup>17</sup> citrate reactions were slightly more, i.e., 2.7% and 3.03%, respectively. In the present study, the mean volume of blood processed, the mean amount of ACD used, and the run duration were more in donors with low platelet

count than in donors with high platelet count with the same platelet yield. This is because the machine has to process more blood volume with more infusion of ACD to the donor to achieve the same platelet yield in donors with low platelet count, thus more AEs. These findings are consistent with the study of Mercan et al., who showed that donors who repeat the procedure several times or for an extended period are susceptible to an accumulation of citrate as levels exceed the amount that the body can metabolize.<sup>19</sup> Another study revealed that AEs occurred in apheresis procedures which took more time (mean: 77.1 min) and had a higher infusion of ACD (mean: 301.5 ml) than those without AEs.<sup>13</sup> Citrate can chelate magnesium as well as calcium.<sup>20</sup> However, magnesium supplementation has not been shown to decrease mild citrate-related symptoms. Hence, prophylactic magnesium supplementation is not recommended for plateletpheresis donation. While we did not determine preprocedural ionized calcium levels in the present study, Bolan et al.<sup>21</sup> found an average fall in ionized calcium of 33% from baseline, producing the signs and symptoms of citrate toxicity. In our study, we prescribed mouth-dissolving oral calcium tablets to all the donors during the procedure. In the study by Philip et al.<sup>2</sup> calcium supplementation was given orally as 1 g capsules of calcium carbonate. The results of oral calcium carbonate administration and its effects on citrate toxicity by Bolan et al.<sup>21</sup> stated that the administration of 2 g of calcium carbonate was associated with a statistically significant reduction in the severity of paresthesia.<sup>21,22</sup> The treatment of citrate reactions includes slowing the reinfusion rate, increasing donor blood-to-citrate ratio, oral calcium supplementation, and, if required, giving intravenous calcium.<sup>4,23-25</sup> Vasovagal reactions may be attributed to apprehension due to mechanical and psychological factors. In our study, vasovagal reactions were almost similar to that of the study done by Dogra et al.<sup>1</sup> while it was lower in the study conducted by McLeod et al.<sup>18</sup> and Philip et al.<sup>2</sup> and higher in the study done by Khajuria et al.<sup>17</sup> In a study done by Tomita et al.<sup>14</sup> examined that the incidence of vasovagal reactions among male apheresis donors and whole blood donors was 0.83% and 0.99% respectively. They also found that the incidence of vasovagal reactions increased with age among apheresis donors, unlike what has been reported with whole blood donors.

### Conclusion:

The adverse effects of plateletpheresis donation are relatively mild, occasionally occurs and can be easily treated. Thorough donor vigilance, superior technical personnel training, and experienced transfusion medicine specialist supervision will make donors' experience more pleasant, promoting and preparing a voluntary plateletpheresis donor pool in Bangladesh.

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### Conflicts of interest

There are no conflicts of interest.

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