Modeling predonation testing strategies in platelet donations - Approach from low throughput apheresis blood center from India

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Abstract:

BACKGROUND: Hospital-based blood centers in India adopt pre-donation testing for transfusion-transmitted infections (TTI) before plateletpheresis donations. However, the WHO emphasizes on TTI tests be performed on samples collected during the donation process. The study objective was to determine whether cost implications by adopting product testing along with predonation testing or only product testing strategy in platelet donation in Indian blood centers.

MATERIALS AND METHODS: Cross-sectional study on registered plateletpheresis donors, strategy-1 with predonation testing using rapid tests and product testing using chemiluminescence (CLIA) were compared with alternate models: Strategy-2 (predonation test using CLIA and product testing with rapid test) and strategy-3 (product testing). For strategy-1 and 2, donors wait for predonation test to complete or visit blood center twice, while strategy-3 donors donate plateletpheresis immediately. The cost implications of these strategies were compared among registered plateletpheresis donors.

RESULTS: Out of 560 donors registered with strategy-1, three donors were reactive in predonation tests and six platelet units were discarded at product testing. After modeling, for strategy-2, nine donors would be identified as sero-reactive at pre-donation test only, while in strategy-3, nine units would be discarded in product testing. Only 506 donations were completed in strategy 1 after donor attrition. Recoverable costs was greater for strategy-3 (INR 5,146,500) than strategy-2 (INR 5,120,000) and strategy-1 (INR 5,069,000).

CONCLUSION: Strategy-3 appears cost-effective but requires regulatory changes in the Indian setting. Testing apheresis procedures using Strategy 2 had greater cost recovery, and also prevents infectious donations and thereby enhances blood safety with the present guidelines.

Keywords: Apheresis, predonation test, plateletpheresis, transfusion transmitted infectious

Introduction

Serological assay is typically used as first-line screening strategy in detecting transfusion-transmitted infectious (TTI) testing in donated blood units. The awareness and need for platelet donations are increasing, and globally 11% of blood units collected were donated by apheresis.[¹] The Directorate General of Health Services (DGHS) Manual, India, for platelet donation mention donors be screened before apheresis for TTI markers unless the donor is undergoing repeated procedures, in such case testing for markers of disease need to be repeated at 30 days interval.[²]

Due to high apheresis procedure cost, technical skill and regulation, most blood...
centers in India issue blood after predonation screening result only. Though the risk of collecting infectious donation has been reduced through predonation screening, the WHO states predonation testing of the donor does not ascertain the infectious status of the donation and will need to be followed by tests on the blood sample collected during the blood donation process.\[^{[3,4]}\]

As predonation screening with ELISA testing for TTI requires time, most donors are required to visit blood centers twice for platelet donation. Hence, centers adopt rapid test or chemiluminescence (CLIA) assay for screening as it provides rapid turnaround time making it an effective assay system for predonation testing for TTI in apheresis donors. The donors who are sero-reactive by these assay are deferred, thereby saving costs involved in apheresis collection.

As Indian blood centers are hospital based with no unique donor identification facility, traceability of blood donors during subsequent visit remains a major concern. To overcome this, few blood centers, practice mandatory testing for the product before issue. Similarly, high-income countries perform only mandatory testing on products and such testing strategy warrant consideration for Indian setting too.\[^{[1]}\]

To best of our knowledge, this is the first study from India to generate model for evaluating the predonation testing strategy for plateletpheresis donations. Given these issues, the model will address whether there are any cost implications by adopting product testing along with predonation testing using rapid test or CLIA versus no predonation testing in platelet donation in Indian blood centers.

**Materials and Methods**

**Study population**
This was a cross-sectional study on platelet donors registered in a tertiary care cancer center blood center. Donors found eligible after medical examination, and complete blood counts between March 2018 and May 2019 were included in the study.

**Study setting**
The study was conducted in blood center of tertiary care cancer center hospital in South India. The blood center has four apheresis equipment (MCS ±1 no from Haemonetics; Trima Accel 1-no, Spectra Optia-2 no’s from Terumo BCT) for platelet donations.

**Predonation testing**
A volume of 4 ml of blood was collected into an EDTA sample bottle from each donor at registration. The blood count was done using the automated cell counter LH750 (Beckman Coulter), and infectious disease test by rapid test to determine HIV 1 and HIV 2, Hepatitis B and C (from Tulip Diagnostics), Malaria (from Zephyr Biomedicals) and by Rapid Plasma Reagin (RPR) test (from Tulip Diagnostics) for Syphilis. Donors testing positive on predonation samples were not confirmed and permanently deferred and referred to the appropriate clinic for confirmation and treatment.

**Product testing**
Donors tested negative during pre-donation were allowed to donate platelets. During the procedure, 4 ml blood was collected from sample diversion pouch for mandatory tests such as blood grouping, antibody screening and infectious disease testing as per national guidelines. The infectious disease testing was performed using CLIA equipment from Vitros ECiQ, Ortho Clinical Diagnostics equipment for HIV (4th generation), Hepatitis B and Hepatitis C. Malaria was performed using rapid test and syphilis by RPR test. Blood units that are non-reactive are released for transfusion.

**Strategy**

**Modeling calculations**
A model was developed to simulate three testing strategies for platelet donations.

- **Strategy 1**: Predonation testing using rapid tests with product test using CLIA
- **Strategy 2**: Predonation testing using CLIA and product test using rapid tests
- **Strategy 3**: Product testing using CLIA.

Figure 1 summarizes testing different testing strategies on platelet donors. The models begin with strategy 1, include:

- a. Donors nonreactive and reactive for predonation test
- b. Platelet units collected
- c. Platelet units discarded due to TTI reactive after product testing by CLIA.

Strategy 2, is assumed to be distinct from Strategy 1 in terms of assay sensitivity by cross-over the testing strategy. CLIA, when used initially, would identify donors reactive by rapid test and products reactive of strategy 1 at the predonation testing stage only, thereby avoiding any infectious unit collections.

For both Strategy 1 and 2, expenditure for:
- Number of donors screened at predonation testing
- Procedural expense for apheresis units collected (excludes donors who did not return to donate in strategy 1)
- Number of units discarded after product testing was calculated, as this has a bearing on the costs of testing strategy.
For Strategy 3, i.e., no predonation testing, the estimated number of donors available for platelet donations was determined by adding the number of donations completed and the number of donors reactive by predonation tests using strategy 1. The donors who did not donate in strategy 1 after negative predonation tests might not have donated even in this model also. The procedure cost for estimated donations and cost for units discarded after product testing was calculated.

The cost of infectious disease marker testing using rapid test and CLIA in India is at least INR-200 and INR-500 per donation. In recently published NACO guidelines, the cost a recipient pays for a unit of apheresis platelets is fixed at INR 11000 [Table 1].\[^5\] This was estimated after considering the direct cost of the consumables linked to the procedure, nonvariables fixed costs include, equipment utilization, equipment maintenance, and human resource.

To understand the cost implications of these strategies, data were applied from a model population of eligible platelet donors registered over a time horizon of one year and 3 months, and to generate and compare anticipated cost when adopting strategy-2 and strategy-3.

### Statistical methods

Descriptive statistics were used for determining frequency and proportions. Continuous variables such as previous donations were summarized in terms of mean ± standard deviation Monetary calculations was done in INR will be used to compare between the predonation testing strategies.

### Results

#### Predonation screening using strategy 1

The number of apheresis donors eligible after medical examination and blood counts were 560. Three donors...
were reactive in predonation tests using rapid tests. Among them, one donor found reactive for HIV and two donors for HBV. Only 506 donors completed platelet donations after the predonation test results. 435 (86%) donations happened on the same day, 30 (6%) donations within 2 days and 41 (8%) donations more than 2 days of predonation testing.

Six platelet units were collected as five were sero-reactive for HCV and one for HIV after product testing. Hence, the units available for transfusion were 500 out of 506 donations at the end of strategy 1.

Only 22 donors turned up for repeat donation with a mean frequency of 2.5 ± 0.9 times during the study period. The cost involved in donors who did not turn up for donation \( n = 51 \) were used for calculating only pre-donating testing expenditure and not for procedure expenditure.

**Modeling analysis**
Similarly, for strategy 2, 560 donors will be screened using CLIA initially, and 9 donors may be identified as sero-reactive. Only 500 donors might have donated platelets, after excluding donors who did not turn up for donations (51 donors as mentioned in strategy 1). No products shall be discarded in this strategy [Table 2].

For strategy 3, estimated donations and procedure costs were calculated as 509; after excluding donors who did not turn up for donations in strategy 1. This shall include 506 donations and 3 donors who were seroreactive in predonation test in strategy 1. Nine collected units may be discarded due to seroreactivity after CLIA at the product testing [Table 2].

**Cost implications**
Each testing strategy was analyzed for cost comparison using strategy 1 seroreactive data and shown in Table 2.

The most beneficial strategy based on recoverable cost from transfusable products was strategy 3 (INR 5,146,500), followed by pre-donation testing strategy using chemi (strategy 2-INR 5,120,000). Strategy 1 had least cost recovery of INR 5,069,000.

**Discussion**
The present study identified three donors reactive for TTI with predonation test using rapid tests; however, six sero-reactive donors were identified at product testing using CLIA (Strategy 1). Platelet donation differs from the whole-blood donation in many ways, where the donor may donate every 14 days and require a minimum of up to 3 h for the procedure as compared to 30 min for whole-blood donation.[6]

The cost-effectiveness in infectious disease screening varies according to underlying prevalence of disease in donor populations accepted for donation. However, there might be situations where the incremental gain from any additional intervention is so small that no health benefit is evident, yet the cost of the intervention is incurred.[7]

With predonation testing for apheresis recommended by DGHS Manual, India and majority of platelet donations being directed donations, screening donors prior to apheresis was accepted widely. The WHO mentions, use of the rapid test for blood screening is not recommended; however, it may be appropriate when specific donations need to be screened on the emergency basis provided followed up with repeat testing using an EIA if these assays are routinely used. Similarly, the WHO emphasizes on the importance of test performed on blood samples collected during the donation process i.e., product testing.[4]

### Table 2: Cost analysis with various predonation testing strategy on platelet donations from low throughput blood center from India

| Predonation Test | Strategy 1 Rapid tests (INR 200) | Strategy 2 CLIA (INR 500) | Strategy 3 No testing CLIA (INR 500) |
|------------------|---------------------------------|---------------------------|-----------------------------------|
| Predonation tests (N1) | 560 | 560 | 0 |
| Predonation TTI reactive | 3 | 9 | 0 |
| Donors available for donations | 557 | 551 | 509 |
| Apheresis collections undertaken (N2)* | 506 | 500 | 509 |
| Products TTI reactive (N3) | 6 | 0 | 9 |
| Number of transfusable products (N4) | 500 | 500 | 500 |
| Predonation test expense (N1* predonation test) | INR 112,000 | INR 280,000 | 0 |
| Product test expense (N2* product test) | INR 253,000 | INR 100,000 | INR 254,500 |
| Wastage Expense due to TTI reactivity (N3* INR 11000/product) | INR 66,000 | 0 | INR 99,000 |
| Net Expenditure | INR 431,000 | INR 380,000 | INR 353,500 |
| Cost recovery from apheresis collections ([INR 11,000/product]* N4) | INR 5,500,000 | INR 5,500,000 | INR 5,500,000 |
| Recoverable Cost from Transfusable Products | INR 5,069,000 | INR 5,120,000 | INR 5,146,500 |

*Donors registered and did not turn up for donation were excluded. Recoverable cost from transfusable product=Cost recovery from apheresis products - Net expenditure. CLIA=Chemiluminescence, TTI=Transfusion-transmitted infections, INR=Indian rupee.
Product testing remains a more robust approach than predonation testing, but most centers in India do not perform product testing of plateletpheresis units and release units based on predonation test results. As platelet donors requiring more than one visit to the blood center for donating platelets, and with no dedicated system to identify them in subsequent visits, the need for product testing in addition is essential. Hence we decided to combine the two available methodologies rapid test and CLIA in both sequences and compare the use of rapid test plus CLIA in Strategy 1 versus CLIA plus rapid test in Strategy 2 and CLIA testing on product alone in Strategy 3 as followed in most western countries.

Pre-donation testing using strategy 1 yielded INR 5,069,000; which was economically lower recovery than strategy 2 (INR 5,120,000) and strategy 3 (INR 5,146,500). When simulating strategy 2 using CLIA and rapid, the possible benefits can be identification of all high risk donors at the initial test, thereby saving the cost involved in apheresis procedure [Table 2].[1] This potential benefit in terms of avoiding reactive donations outweighs strategy 2 than strategy 1. However, when adopting CLIA as predonation test, it also increases the waiting period for the availability of test results by additional one hour and overall it also increases donor deferral due to biological false positive results.[4]

Only 86% donations happened on the same day of predonation testing, 51 (9%) eligible donors did not participate in the donation process resulting in donor attrition and wastage of resources in the form of predonation tests. The common deterrents among platelet donor are time constraints, health reasons, waiting period for donating blood, being farther away from the blood centre etc.[6] When employing strategy 3, i.e., only product testing, the wastage of resources can be minimized and seems to be better than the other two strategies.

With increasing demands for platelets by apheresis and multi-component apheresis procedures, the need for reserving the unit for the particular patient does not arise. Strategy 3 might provide an increased number of donors available for platelet donation, as donor waiting time is avoided, and also the most economical approach among all (INR 5,146,500). However, this model needs validation with data from blood centers with large donations for prospective regulatory changes in India.

Blood components discard rates due to reactivity for markers of transfusion-transmissible infection ranges between 1.1% and 5.1% for upper and lower-middle-income countries, respectively.[1] Indian National Blood Transfusion Council, decided to use Global Status Report on Blood Safety and Availability, WHO 2016, with India featuring as upper middle-Income country for acceptable levels of discard of blood and blood components, with median discard rate due to TTI being 3.9%. The overall infectious disease discard rates during the study were 1.8% well within the upper middle-income country.

The demand, as well as the cost for performing apheresis platelets, has steadily increased over the years rapidly. It is time to introspect whether a given intervention is worthwhile with respect to blood safety achieved for the cost incurred. The present study highlights the importance of product testing within strategy 1 and 2, as platelet donations require multiple visits.

Only 22 donors donated more than once during the 15 months period. A thorough understanding of donor behavior and friendly environment is necessary for the development of effective strategies for recruiting new platelet donors and inducing both existing and new donors to continue the practice of donating platelets over the long term.[6]

Our study has few limitations, first, the study is a retrospective single-center approach and this also forms the strength of the study as blood centers in India are hospital based with different volumes of apheresis donations. The reasons for donors not returning to donate was not collected. While estimating the cost implications, blood donor’s opportunity cost– the cost of the donor’s time spent for donating apheresis platelet was not taken into calculation.

The present model clearly illustrates that with predonation testing using EIA such as CLIA followed by product testing by the rapid test will be a better strategy to enhance blood safety in plateletpheresis donations with the present Indian scenario.

**Conclusion**

Strategy 3 avoids the waiting period of predonation test, thereby, more plateletpheresis donation can be obtained. Hence, strategy 3 was cost-effective but requires regulatory changes in the Indian setting. Testing apheresis procedures using CLIA and Rapid test as sequence (Strategy 2) had greater cost recovery, and also prevents infectious donations, thereby enhance blood safety with the present guidelines.

**Ethical approval**

Being retrospective study, Institutional Review Board (IRB) approved the present study without ethical approval through Ref. No: 1616/1RB-SRC/13/MCC/30-5-2019/2 dated: 2nd July 2019.
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Conflicts of interest
There are no conflicts of interest.

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