Access this article online

Quick Response Code:

Website: www.ajts.org

DOI: 10.4103/ajts.ajts_192_20

Haemovigilance Programme of India: Comparative analysis of transfusion reactions reported over a 5-year period through two reporting formats and key recommendations for blood safety

Akanksha Bisht, Neelam Marwaha[1], Ravneet Kaur[2], Debasish Gupta[3], Reba Chhabra

Haemovigilance Programme of India, National Institute of Biologicals, Ministry of Health and Family Welfare, Government of India, NOIDA, Uttar Pradesh, [1]Department of Transfusion Medicine, PGIMER, [2]Department of Transfusion Medicine, Government Medical College and Hospital, Chandigarh, [3]Department of Transfusion Medicine SCTIMST, Trivandrum, Kerala, India

Address for correspondence:
Dr. Akanksha Bisht, National Institute of Biologicals, Ministry of Health and Family Welfare, Government of India, Sector 62, Noida, Uttar Pradesh, India.
E-mail: akankshabisht83@gmail.com

Submitted: 02-12-2020
Revised: 16-12-2020
Accepted: 03-12-2020
Published: 19-12-2020

Introduction

Haemovigilance Programme of India (HvPI) was launched on December 10, 2012 with the purpose to assure patient safety and promote public health through continuous monitoring of adverse reactions associated with blood/blood products transfusion to prevent their occurrence and recurrence.[1] The National Co-ordinating Centre for HvPI is a National Institute of Biologicals (NIB), NOIDA. Implementation and coordination of activities of HvPI is one of the mandates of NIB as per its bye-laws 3.4.1 as approved by the Governing Body of the Institute. The HvPI was started with the following key objectives: (i) monitor transfusion reactions, (ii) create awareness among health-care professionals, (iii) generate evidence-based recommendations, (iv) advise the Central Drugs Standard Control Organizsation for safety-related regulatory decisions, (v) communicate findings to all key stakeholders, and (vi) create national and international linkages.[1] Five expert subgroups, Core Committee, National Advisory Committee, Signal Review Panel, Quality Panel, and a Training Panel are responsible for the coordination and operationalization of HvPI.[2] A software – "Haemo-Vigil" was indigenously developed by HvPI division, NIB to collect and analyze the data related to hemovigilance all over the country.[3] From 2013 to April 2016, hemovigilance data were collected through version 1.0 of the transfusion reaction reporting form (TRRF). The new version of Haemo-Vigil software was launched in May 2016, subsequent to a key recommendation in the first report to improve the quality of hemovigilance data and the TRRF version 2.0 was used.[1]

Enrollment and Participation of Centers

HvPI started with the enrollment of 90 blood centers in the year 2012. Following inception, the enrollment of new blood centers continued throughout each successive year and the total number of enrolled centers at the end of the years 2016 and 2017 was 475 and 615, respectively. Figure 1 shows year-wise enrollment of blood centers under HvPI with the highest number of enrollment in the year 2016.

The participation of blood centers in HvPI is increasing continuously. An analysis was carried out to look for month-wise number of centers actually submitting reports that are active centers in 2016 and 2017 after the new Haemo-Vigil Software was launched on May 1, 2016.

How to cite this article: Bisht A, Marwaha N, Kaur R, Gupta D, Chhabra R. Haemovigilance Programme of India: Comparative analysis of transfusion reactions reported over a 5-year period through two reporting formats and key recommendations for blood safety. 2020;14:103-16.

It was observed that only 154 centers out of 475 enrolled centers were active in 2016 and 227 out of 615 enrolled centers were active in 2017 [Figures 2 and 3].

There is a tremendous need to increase the awareness regarding the importance of reporting in hemovigilance as a step toward safe blood transfusion and patient safety.[4]

Analysis of Adverse Transfusion Reactions Based on Various Parameters

After the launch of the first version of reporting software "Haemo-Vigil" in January 2013 and a revised second version in 2016, the number of adverse blood transfusion reaction reports submitted to HvPI is shown in Figure 4, and there is a continuously increasing trend with the highest number of reports submitted to HvPI in 2017.

A total of 8162 adverse transfusion reactions have been reported to HvPI since inception till Decemer 2017. As depicted in Figure 5, from 2013 to April 30, 2016, a total of 3903 transfusion reactions were reported to HvPI which had occurred in 3807 patients and 96 patients had more than one reaction.[1] A total of 1279 transfusion reactions were reported to HvPI from May 1, 2016, to December 2016, which had occurred in 1169 patients; thus, 108 patients had suffered more than one reaction and 2980 transfusion reactions were reported in 2017 to HvPI which had occurred in 2768 patients; thus, 212 patients had suffered more than one adverse reaction during transfusion. A report does not always correspond to a single adverse reaction, some reports contain more than one reaction in the same patient; hence, a total of 4259 transfusion reactions of the year 2016 and 2017 were reviewed and included in the analysis. Thirty-eight reports were excluded from the analysis, 14 reports from 2016 data, and 24 reports from 2017 data due to the following three main reasons after review:

(i) Incomplete information, (ii) not a transfusion reaction, and (iii) discrepancy in symptoms and investigations data. Hence, these reports did not meet the validation criteria.

The transfusion reactions as reported through the TRRF version 2.0, from May 1, 2016, to December 31, 2017 were analyzed as per International Society of Blood Transfusion definitions of adverse transfusion reactions[5] and compared with regard to the following parameters:

- Type of adverse transfusion reactions
- Age and gender of patients
- Frequency of blood transfusion
- Blood components implicated
- Outcome of adverse transfusion reactions
- Incidence rate of adverse transfusion reactions
- Implication rate of blood components
- Time gap of blood products from time of issue to time of transfusion

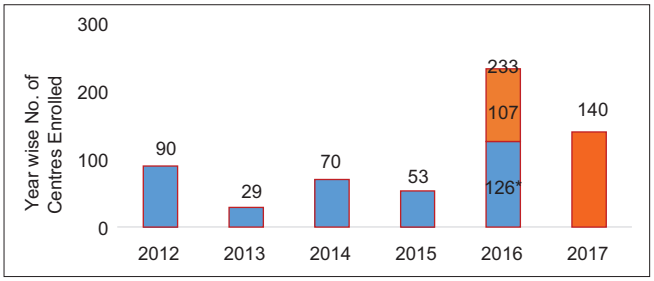

Figure 1: Year-wise new Centres Enrolled under HvPI. 126* centers were enrolled in 2016 from January 1 to April 30 and were included in 2013–2016 report published in 2018 before the new version of Haemo-Vigil software was launched on May 1, 2016

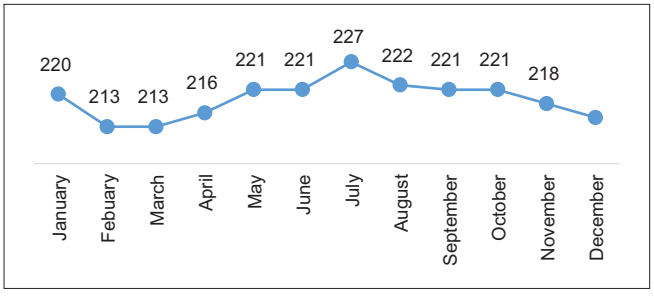

Figure 3: Month-wise active centers in 2017

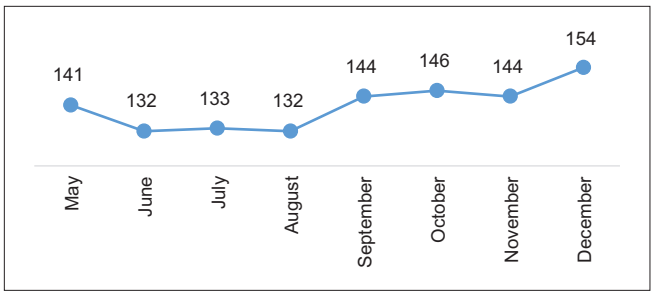

Figure 2: Month-wise active centers in 2016

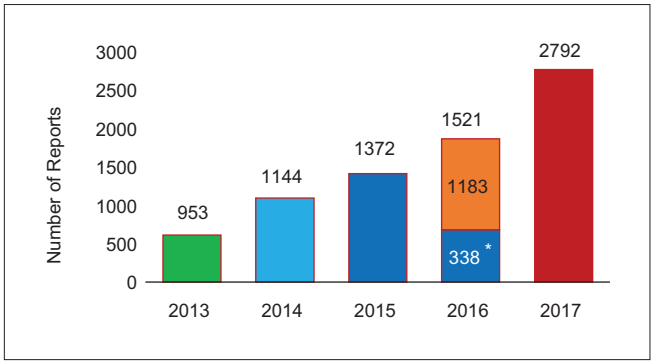

Figure 4: Year-wise number of reports submitted to Haemovigilance Programme of India. *338 reports of 2016 reported via transfusion reaction reporting form 1.0 from January 1, 2016, to April 30, 2016, were analyzed and published in 2013–2016 report

Observations

Mortalities reported to Haemovigilance Programme of India

A total of 28 death cases has been reported to HvPI since inception, with 17 cases reported from 2013 to April 30, 2016,[1] 3 cases reported from May 1, 2016, to December 30, 2016, and 8 cases in the year 2017. The underlying adverse reactions with corresponding imputabilities are shown in Figure 6. Among 28 death cases, 14 cases were unlikely related to transfusion and only 14 were due to possible/probable imputability.

Rates of Adverse Transfusion Reactions Reported to Haemovigilance Programme of India from May 2016 to December 2017

The overall incidence of adverse reactions reported to HvPI from May 1, 2016, to December 31, 2017 was 8.4 per 10,000 of blood products transfused with a rate of 8.5 in 2016 and 8.3 in 2017. The incidence of various transfusion reactions per 10,000 blood products transfused is shown in Figure 7.

Age Group wise Distribution of Males and Females

Total number of males and females with age groups reported to HvPI in 2016-2017 is shown in Table 1.

Implicated Blood Products

A total of 1204 blood products were implicated in causing adverse reactions in 1169 patients, 17 patients were transfused more than one blood product from May 1, 2016, to December 31, 2016. A total of 2823 blood products were implicated in causing adverse reactions in 2768 patients, 30 patients were transfused more than one blood product in 2017. Details of blood products transfused are shown in Figure 8. Any other products included washed packed red blood cells (PRBCs), cryosupernatant plasma, and platelet-rich plasma.

Implication Rates of Blood Products in Adverse Transfusion Reactions

From the denominator data reported by enrolled centers for

Table 1: Total number of males and females with age groups reported to HvPI 2016-2017

Age Category	Males		Females		Total
	2016	2017	2016	2017	
Pediatric (<=12 Years)	46	142	35	66	289
Adolescent (12-<=18)	35	69	40	65	209
Adult (>18)	463	1156	550	1270	3,439
Total	544	1,367	625	1,401	3,937

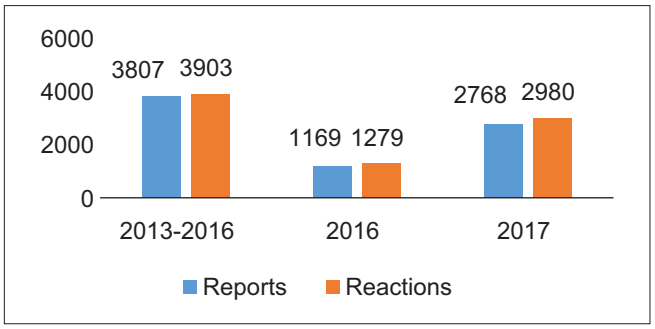

Figure 5: Distribution of *reactions and reports from* 2013 to 2017

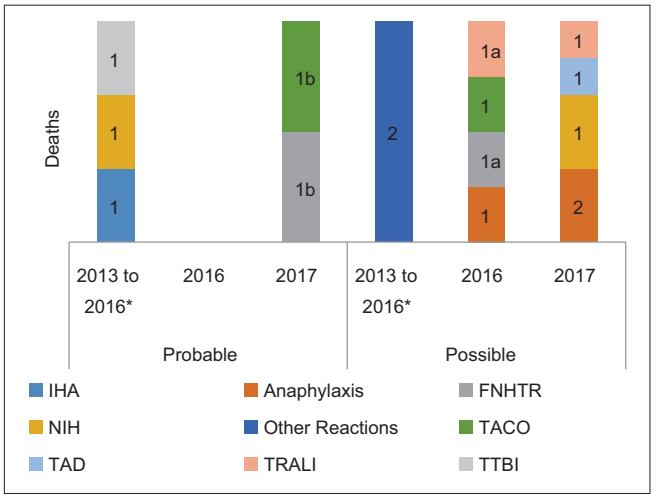

Figure 6: Mortality, transfusion reaction, and Imputability. IHA = Immunological Hemolysis due to other AlloAntibodies; FNHTR = Febrile Non*h*emolytic Transfusion Reactions; HyTR = Hypotensive Transfusion Reaction; IHABO = Immunological Hemolysis due to ABO Incompatibility; NIH = Non*i*mmunological Hemolysis; TACO = Transfusion-Associated Circulatory Overload; TAD = Transfusion-Associated Dyspnea; TRALI = Transfusion-Related Acute Lung Injury; TTBI = Transfusion-Transmitted Bacterial Infection; TAH = Transfusion-associated hypertension. a and b denotes two reactions in one report respectively

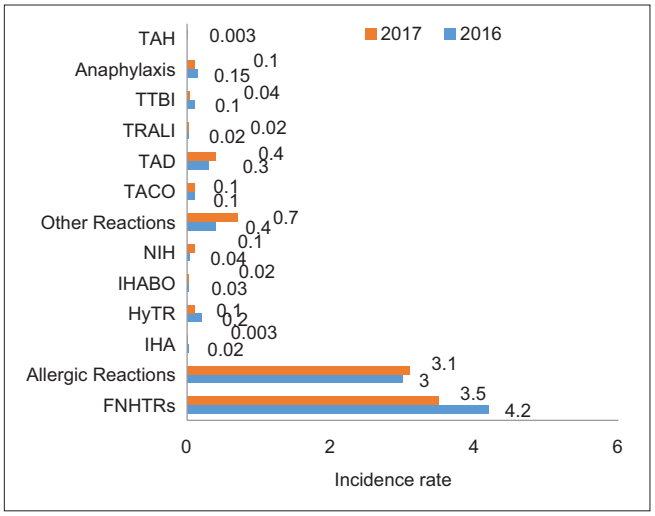

Figure 7: Incidence of adverse transfusion reactions per 10,000 of blood products transfused in 2016–2017

the year 2016 and 2017, the implication rate of blood/blood components was determined, as shown in Figure 9 which shows that the implication rate was maximum with PRBCs followed by apheresis platelets in 2016, whereas in 2017, the implication rate of adverse transfusion reactions was maximum with apheresis platelets followed by PRBCs and rest of the blood components.

Distribution of adverse transfusion reactions year wise from 2013 to 2017

Table 2 and Figure 10 shows the overall distribution of adverse transfusion reactions.

Febrile nonhemolytic transfusion reactions (FNHTRs) and allergic reactions continue to remain the most frequently reported adverse transfusion reactions.

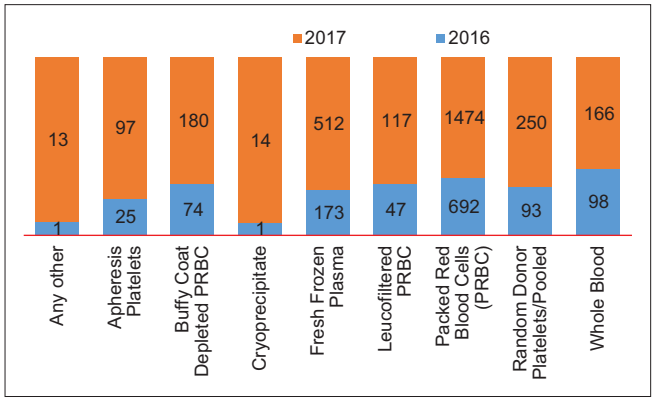

Figure 8: Details of blood products transfused (2016–2017)

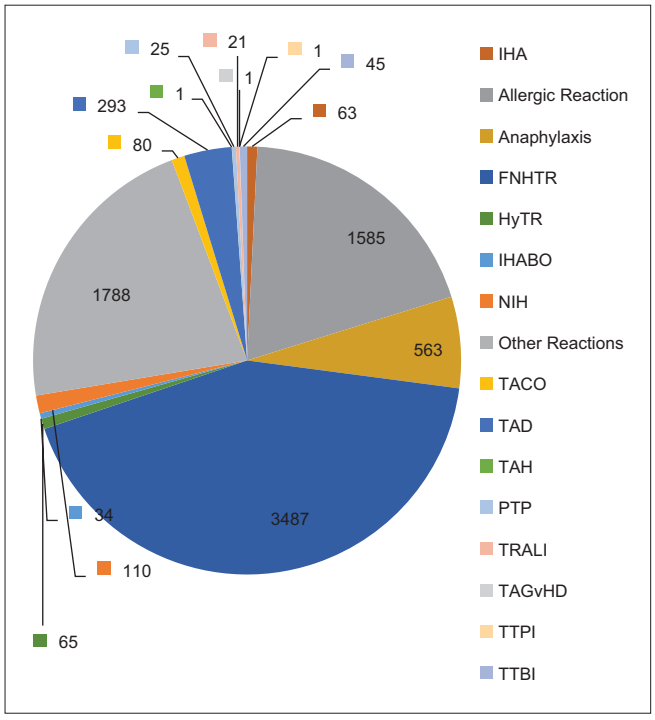

Figure 10: Overall distribution of reactions reported to Haemovigilance Programme of India from 2013 to 2017

Outcome of Adverse Transfusion Reactions Reported to Haemovigilance Programme of India from 2013 to 2017

Majority of the patients had recovered, as shown in Figure 11; mortality was seen in 17 patients from 2013 to 2016,[1] of which imputability was probable in three cases, possible in two cases and unlikely in 12 cases, three death cases were reported in 2016 with possible imputability and eight death cases were reported in 2017, of which imputability was probable in one case, possible in five cases, and unlikely in two cases with severe transfusion reactions and an underlying comorbid condition such as malignancy, post bone marrow transplant, head injury, polytrauma, chronic liver disease, acute pancreatitis, and kidney disease. The transfusion reactions which occurred in these patients were transfusion-associated circulatory Overload (TACO), transfusion-related acute lung injury (TRALI), non-immunological haemolysis (NIH), and anaphylaxis.

Observations of Special Interest

Time Gap of Blood Products from time of issue to time of transfusion

The gap between time of issue of blood from the blood

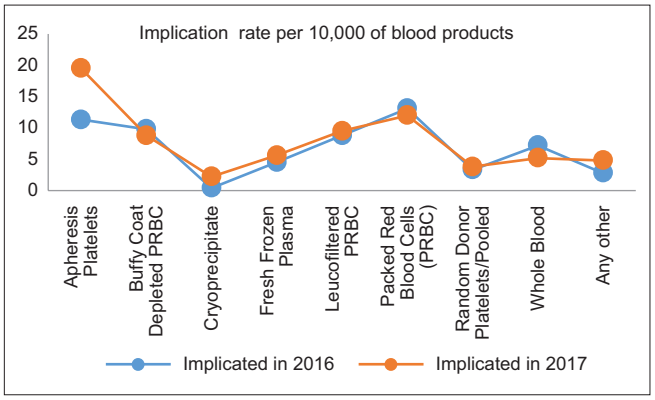

Figure 9: Implication rate in 2016 and 2017

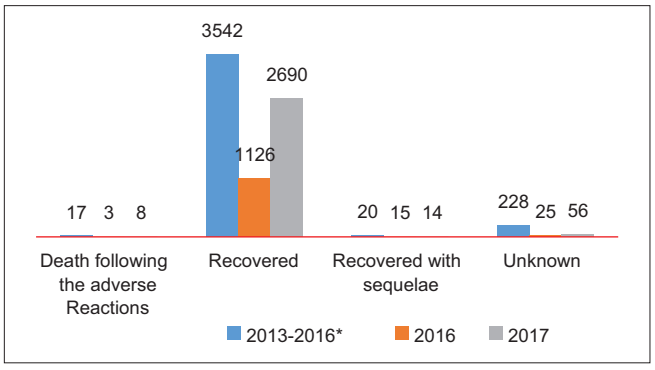

Figure 11: Outcome of adverse transfusion reactions year wise

Table 2: Distribution of adverse transfusion reactions year wise from 2013 to 2017

Adverse Reaction	2013-16*	2016	2017
Immunological Haemolysis due to other Allo-Antibodies	58 (1.49)	4 (0.31)	1 (0.03)
Allergic Reaction	N/A**	456 (35.66)	1129 (37.89)
Anaphylaxis/Hypersensitivity	495 (12.68)	22 (1.72)	46 (1.54)
FNHTR	1594 (40.84)	627 (49)	1266 (42.5)
Hypotensive Transfusion Reaction	0	25 (1.95)	40 (1.34)
Immunological Haemolysis due to ABO Incompatibility	22 (0.56)	5 (0.4)	7 (0.23)
Non Immunological Haemolysis	84 (2.15)	6 (0.47)	20 (0.67)
Other Reactions	1476 (37.82)	57 (4.46)	255 (8.56)
TACO	26 (0.67)	14 (1.1)	40 (1.34)
TAD	93 (2.38)	47 (3.7)	153 (5.13)
Transfusion associated hypertension	0	0	1 (0.03)
PTP	25 (0.64)	0	0
TRALI	10 (0.25)	3 (0.23)	8 (0.27)
TAGvHD	1 (0.03)	0	0
Transfusion Transmitted Parasitical Infection (malaria)	1 (0.03)	0	0
TTBI	18 (0.46)	13 (1.00)	14 (0.47)
Total	3903	1279	2980

*Up to 30th April, 2016 before new Haemo-Vigil Software was launched. **Covered under Anaphylaxis/Hypersensitivity Category till 30th April, 2016 before new Haemo-Vigil Software was launched

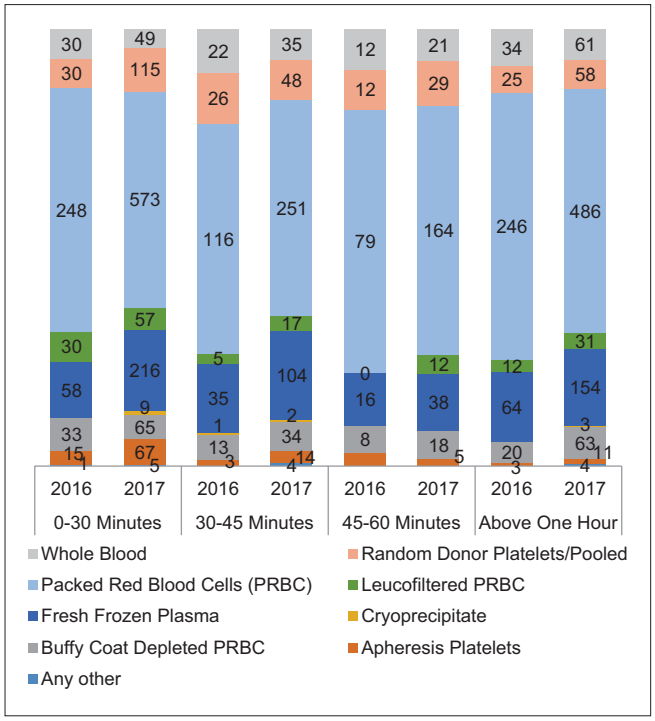

Figure 12: Time gap of blood products

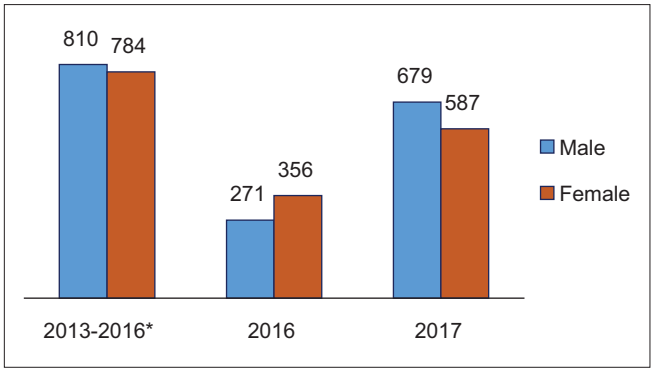

Figure 13: Febrile nonhemolytic transfusion reactions cases reported

center to the time of transfusion to patient at bedside was recorded in the transfusion reaction reports. In 2016, out of 1204 blood components transfused, the time gap was reported in 1201 components, and in 2017, the time gap was reported with all blood products issued by the blood center. The time gap reported varied from very low extremes to very high extremes (0.00 h [no gap] to more than 1 day). However, for the purpose of the analysis, the time gap was categorized into four categories, as shown in Figure 12.

Analysis based on nature of adverse transfusion reactions reported to Haemovigilance Programme of India from May 1, 2016, to December 31, 2017 after the launch of transfusion reaction reporting form version 2.0 and comparison with headline data reported to Haemovigilance Programme of India from 2013 to 2016

Febrile Nonhemolytic Transfusion Reactions

A total of 3487 cases of FNHTR have been reported to HvPI from 2013 to 2017, comprising the most frequently reported adverse reaction associated with blood transfusion. The male–female distribution is depicted in Figure 13. FNHTRs were categorized into three categories – FNHTR with chills and rigors, FNHTR with 1°C, and FNHTR with 2°C rise.

The frequency of FNHTR with 1°C rise in temperature was most common, followed by FNHTR with only chills and rigor and FNHTR with 2°C rise in the reporting period from May 1, 2016, to December 31, 2016, whereas in 2017, the frequency of FNHTRs with only chills and

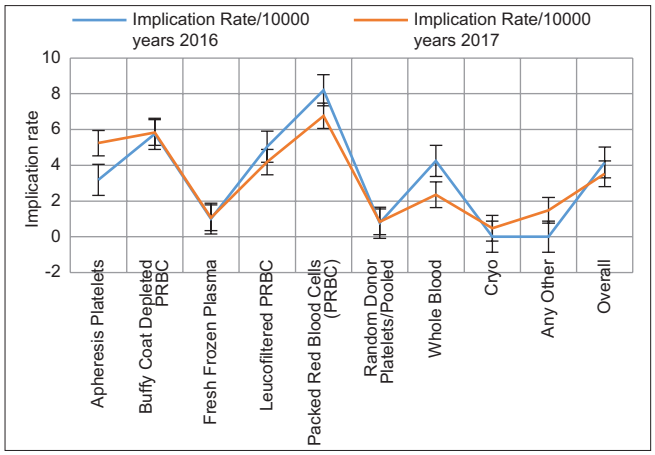

Figure 14: Year-wise implication rate of blood products

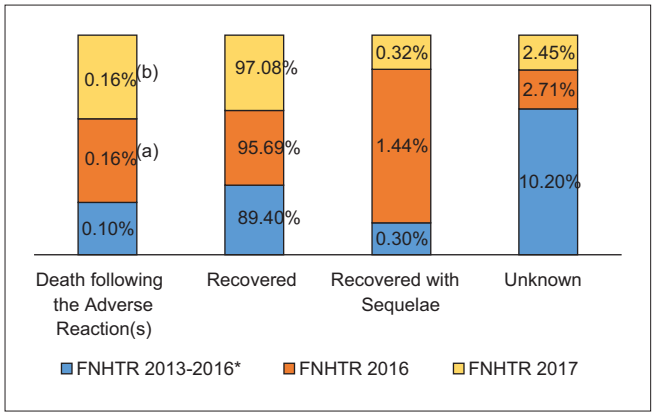

Figure 16: Distribution of outcome of febrile nonhemolytic transfusion reactions for the years 2013–2017

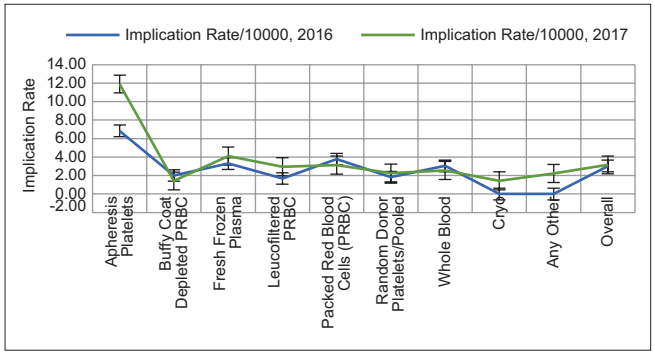

Figure 18: Year-wise implication rate of blood products

rigors was most common followed by FNHTRs with 1°C rise in temperature and FNHTR with 2°C rise. The most frequent blood component implicated in FNHTRs was PRBCs (66.88%). The age range of patients was from neonate to 96 years from 2013 to April 2016, from neonate to 96 years in 2016, and from neonate to 92 years in 2017.

As depicted in Figure 14, PRBCs have the maximum implication rate of FNHTRs both in 2016 and 2017, followed by buffy coat-depleted PRBCs, L-PRBCs, whole blood,

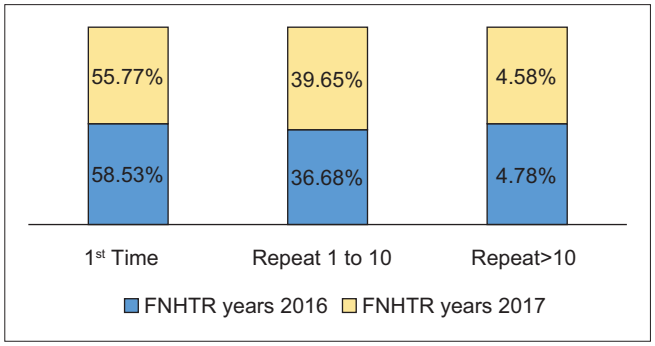

Figure 15: Transfusion frequency wise distribution of febrile nonhemolytic transfusion reactions

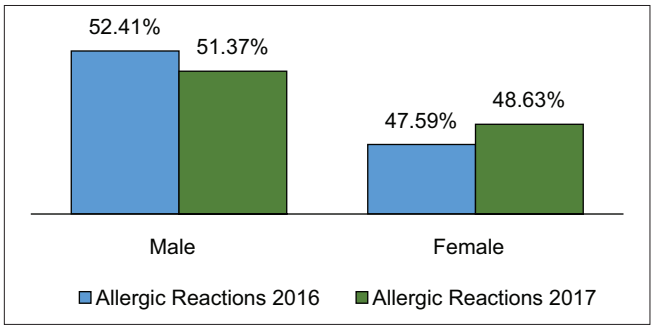

Figure 17: Allergic reaction cases reported

apheresis platelets, FFP, and RDP in 2016, and by buffy coat-depleted PRBCs, apheresis platelets, L-PRBCs, whole blood, any other, FFP, RDP, and cryoprecipitate in 2017.

The pattern of FNHTRs with respect to transfusion frequency was almost similar in 2016 and 2017, as depicted in Figure 15.

Leukofiltered PRBCs had less FNHTR rate as compared to buffy coat-reduced PRBC and nonleukoreduced PRBCs. Whole blood and plasma/platelet products had less reaction rate than PRBCs. It may be related to the age of storage of PRBCs and/or underreporting of febrile transfusion reactions with plasma/platelet products and needs further elucidation.

The clinical diagnosis of patients was varied and included both surgical and medical conditions. Anemia was the most frequent indication for transfusion, as reported from 2013 to 2017. The proportion of mortalities with FNHTRs is almost similar to slightly less from 2013 to 2016,[1] as depicted in Figure 16.

In 2016, as per the TRRF version 2, one patient (a) with an underlying clinical diagnosis of thalassemia Major and a known case of allogeneic bone marrow transplant had both FNHTR and TRALI. The patient died following transfusion; however, imputability was found to be possible.

In 2017, two death were reported associated with FNHTR. However, among the two fatalities, one was male and one female (b) with an underlying clinical diagnosis of carcinoma of the pancreas with rectal bleeding and severe anemia, respectively. Both the patients were adults aged above 50 years. The female patient had another reaction as TACO with probable imputability. Both the patients were repeat cases (repeat 1–10) of transfusion. The male patient with carcinoma of the pancreas had severe rectal bleeding, the FNHTR was mild with chills and rigors only, and hence, imputability was unlikely. As the patients had more serious additional transfusion reactions, FNHTR is not related to mortality in these cases.

Allergic Reactions

Allergic reactions constituted the second most commonly encountered acute transfusion reactions and comprised 37.2% of all the reactions reported. Allergic reactions comprised 456 (35.66%) reactions of 1279 reported reactions in 2016 and 1129 (37.89%) reactions of 2980 reported reactions in 2017. The male–female distribution is depicted in Figure 17. From 2013 to 2016*, these reactions were grouped under other reactions and anaphylaxis/hypersensitivity reactions, a report published in 2018 before new version of Haemo-Vigil software was launched on May 1, 2016.[1]

The age range of patients was from neonate to 84 years in 2016 and from neonate to 92 years in 2017, with a maximum number of patients above 18 years. The pattern of allergic reactions with respect to transfusion frequency was almost similar in 2016 and 2017.

Apheresis platelets were seen to have the highest reaction rate both in 2016 and 2017, Figure 18.

No death case was reported to HvPI associated with allergic reactions since the inception of programme, i.e., from 2013 to 2017. In 2016 and 2017, 98.25% and 98.94% of patients with allergic reaction recovered completely, 0.44% and 0.18% recovered with sequelae, and in 1.32% and 0.88%, the patient's outcome was unknown. The underlying clinical conditions of patients varied including both medical and clinical conditions. Allergic reactions were the second most frequently reported acute transfusion reactions and were better discriminated using TRRF version 2.0.

Anaphylaxis

These reactions constituted only a small proportion of all acute reactions, with 1.72% in 2016 and 1.6% in 2017. The male–female distribution is depicted in Figure 19. Reaction frequency was almost similar in the first-time and multi-transfused patients in 2016; however, it was more in multi-transfused patients in 2017, Figure 20.

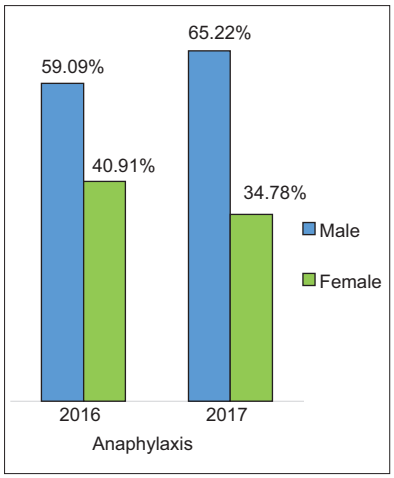

Figure 19: Anaphylaxis cases reported

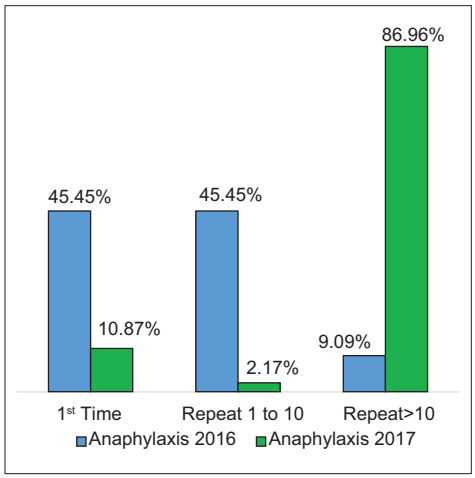

Figure 20: Transfusion frequency wise distribution of anaphylaxis

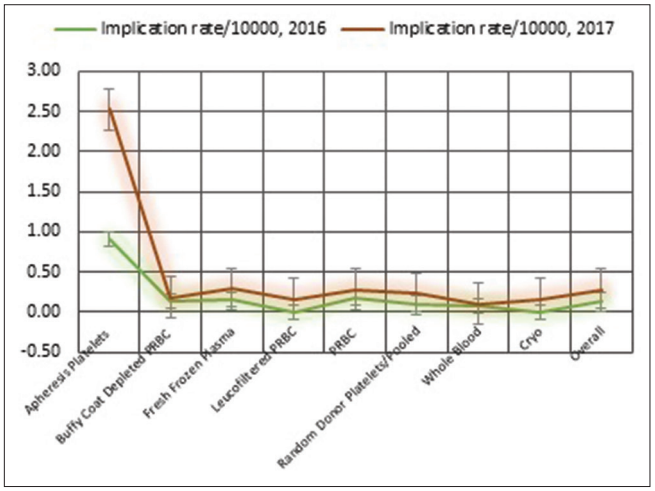

Figure 21: Implication rate of blood products

Four hundred ninety-five such reactions were reported in 2013–2016[1] under the category of anaphylaxis and hypersensitivity reactions, a report published in 2018 before the new version of Haemo-Vigil software was launched on May 1, 2016.

Of a total of 68 anaphylactic reactions reported to HvPI from 2016 to 2017, 91.2% of patients with anaphylaxis were more than 18 years of age. As depicted in Figure 21, the implication rate was maximum with apheresis platelets both in 2016 and 2017. The overall implication rate was almost similar in 2016 and 2017.

One death was reported in 2016. The patient had an underlying clinical condition of chronic kidney disease with severe anemia and the association of this mortality was found to be possible with the blood product transfused. The patient was an elderly male of 60 years, transfused for the first time, and the implicated blood product was PRBC.

Two death cases associated with anaphylaxis were reported in 2017. Among the two fatalities, both were males with an underlying clinical diagnosis of road traffic accident and decompensated chronic liver disease ethanol related, respectively. Both the patients were repeat cases (repeat 1–10) of transfusion. The corresponding imputabilities were possible in both the patients with the implicated blood products as PRBC and L-PRBC, respectively. In one case, the reaction occurred within 5 min of start of transfusion and in the other two cases, within 30 min. Most of the other patients recovered completely both in 2016 and 2017, with only 1 patient in 2016 and 2 patients in 2017 recovered with sequelae.

Hypotensive Transfusion Reaction

Hypotensive transfusion reaction was reported in 1.95% of patients in 2016 and 1.34% of the patients in 2017. The male-to-female ratio was almost similar in 2016 and 1.5:1 in 2017, as depicted in Figure 22. The reaction was found to be comparatively similar among first-time and multi-transfused patients in 2016 but comparatively more among first-time transfusion subjects in 2017, Figure 23. No hypotensive transfusion reaction was reported from 2013 to April 30, 2016.

The age range of patients was from 5 years to 80 years in 2016 and from neonate to 78 years in 2017. However, 87.7% of patients were more than 18 years of age.

The implication rate of blood products in causing hypotensive transfusion reaction was almost similar in

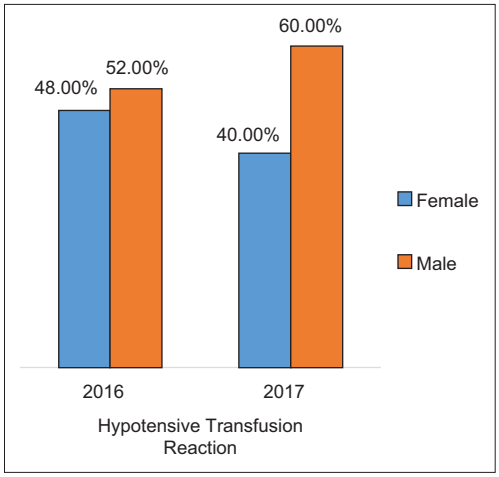

Figure 22: Hypotensive transfusion reaction cases reported

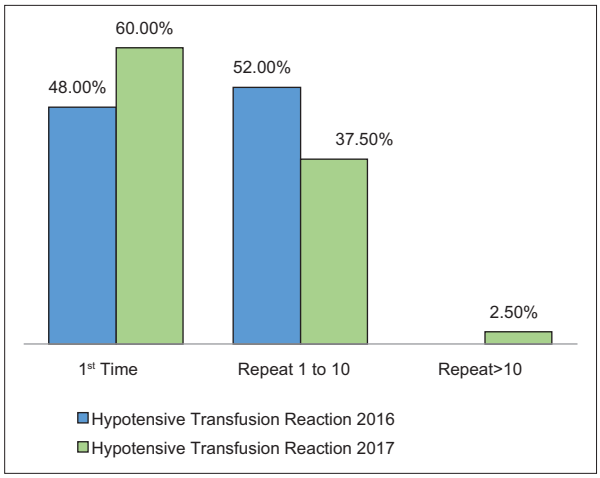

Figure 23: Transfusion frequency-wise distribution

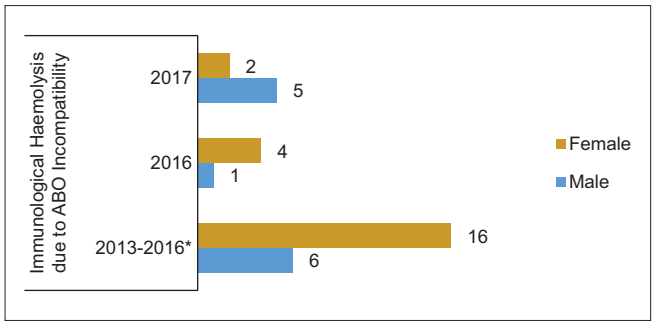

Figure 24: Immunological hemolysis due to ABO Incompatibility cases reported

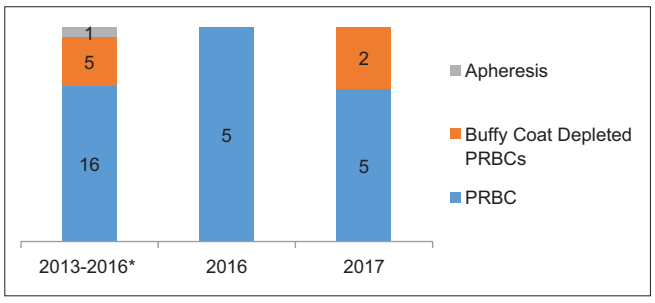

Figure 25: Immunological hemolysis due to ABO incompatibility cases reported

both 2016 and 2017. No mortality has been reported to HvPI with hypotensive transfusion reaction from 2013 to 2017.[1]

Immunological Hemolysis due to other AlloAntibodies

Sixty-three such cases have been reported to HvPI so far, with 58 reaction reported from 2013 to April 30, 2016, published in 2018.[1] Four such reactions in 2016 in two males and two females and only one such reaction in one female patient were reported to HvPI in 2017. One male patient in 2016 was transfused for the first time, the rest of the patients were multi-transfused. All the five patients in 2016–2017 were adults, i.e., more than 18 years of age. Four of five patients had recovered completely and one recovered with sequelae.

Immunological Hemolysis due to ABO Incompatibility

A total of 34 such reactions were reported to HvPI from 2013 to 2017 and constituted only 0.42% of adverse transfusion reactions reported to HvPI from 2013 to 2017.

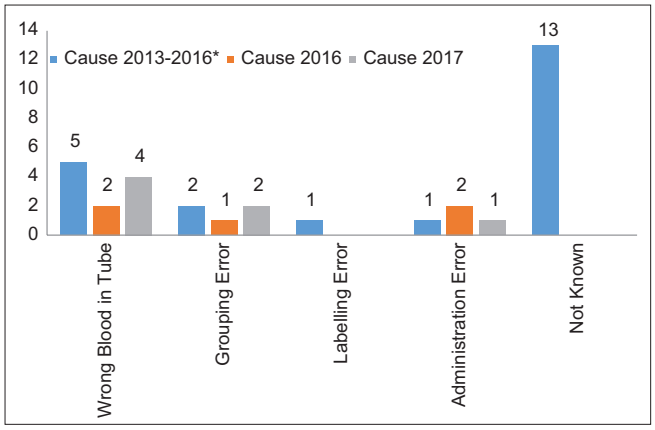

Figure 26: Cause of ABO incompatibility reported

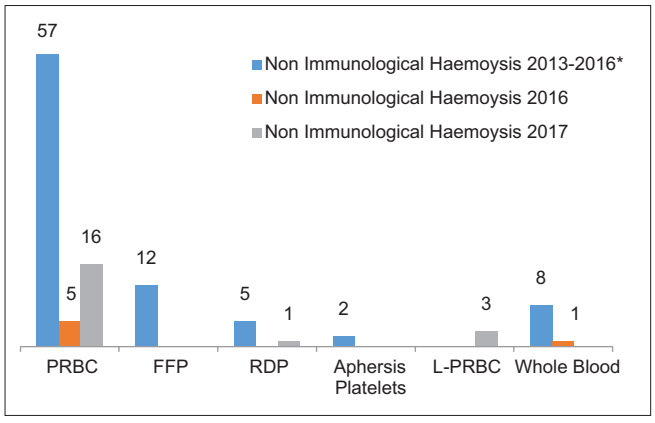

Figure 28: Implicated blood products

The year-wise male–female distribution is depicted in Figure 24. The age range was from 3 to 75 years.

In almost all ABO incompatible transfusion reactions, red cells either PRBC or Buffy Coat-depleted PRBCs were implicated blood components. In one case, only apheresis platelet which was an out-of-group transfusion was the implicated blood component, Figure 25.

Cause of ABO Incompatibility Reported to Haemovigilance Programme of India

Wrong blood in the tube (WBIT), blood grouping error, labeling, and bedside administration error were some of the causative factors recorded, Figure 26.

Nonimmunological Hemolysis

A total of 110 such reactions with 84 reactions from 2013 to April 30, 2016,[1] 6 reactions from May 1, 2016, to December 31, 2016, and 20 reactions in 2017 has been reported to HvPI and constitute 1.35% of all adverse transfusion reported to HvPI till 2017 (2.15% from 2013 to 2016*,[1] 0.47% in 2016 and 0.67% in 2017). The year-wise male–female distribution is depicted in Figure 27. The age range of patients was from neonate to 79 years.

Most of the reactions had occurred in multi-transfused patients in 2016 (1 in the first time and 5 in repeat 1–10), whereas such reactions had occurred almost equally

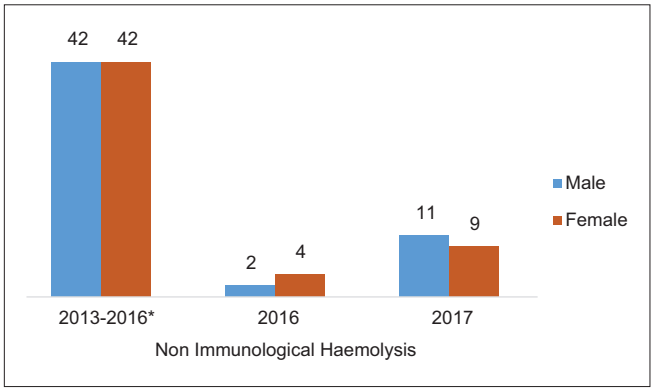

Figure 27: Immunological hemolysis due to ABO Incompatibility cases reported

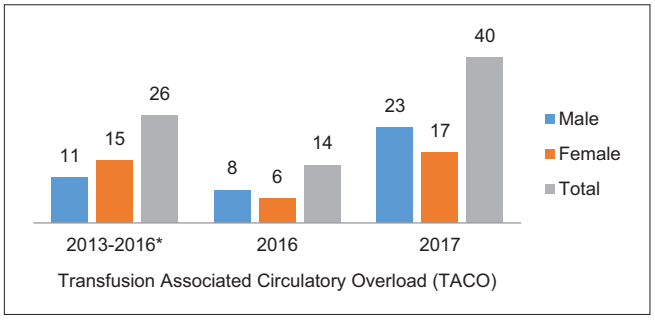

Figure 29: Transfusion-associated circulatory overload cases reported

among the first-time and multi-transfused patients (9 in the first time, 10 in repeat 1–10, and 1 in repeat >10) in the year 2017.

As depicted in Figure 28, PRBCs were the most implicated blood components in nonimmunological hemolysis.

Causes of Nonimmunological Hemolysis Reported to Haemovigilance Programme of India

Errors were recorded in only 11 reactions from 2013 to 2016* which included prolonged storage at the ward, inappropriate thawing of PRBC, warming of blood in hot water, and storage of blood in chiller tray in the ward refrigerator.[1] From May 1, 2016, to 2017, errors were recorded in all the 26 such reactions as follows:

- Hemolysis due to inappropriate warming of PRBC units –11
- Hemolysis due to infusion of any other fluid through the same BT set –2
- Hemolysis due to freezing of PRBC Units –3
- Mechanical damage –10.

Two deaths have been reported to HvPI following nonimmunological hemolysis, one from 2013 to April 30, 2016, and one in 2017. One patient who died in 2017 was an adult (45 years) male with a primary diagnosis of road traffic accident with multiple fractures. The patient had a medical history of intermittent fever since trauma. The implicated blood product was PRBCs, of which 500 ml was reported to have been transfused. The corresponding imputability was possible.

Transfusion-Associated Circulatory Overload

As depicted in Figure 29, more TACO reactions were reported in 2017. A total of 80 TACO reactions were reported to HvPI from 2013 to 2017 and constituted 0.67% of adverse transfusion reactions from 2013 to 2016*, 1.1% in 2016, and 1.34% in 2017.

Five cases of TACO had occurred in first-time recipients and the rest in multiple transfused patients in 2016. In 2017, 13 cases of TACO had occurred in first-time recipients and the rest in multi-transfused patients. The underlying clinical diagnoses were as follows: coronary artery disease, diabetes mellitus, hypertension, chronic kidney disease, severe anemia, trauma, and sepsis. All except two patients were adults. These were a 13-year male patient with acute leukemia with severe anemia and the second one was a neonate with acute dysentery and septicemia.

From 2013 to 2016, mostly red cells were implicated in TACO reactions; however, in 2017, almost all types of blood components were implicated in TACO, with red cells still retaining the highest implication rate.

A total of 3 deaths have been reported to HvPI having a temporal relationship with TACO. One death was reported in a female patient with underlying postpartum anemia from 2013 to 2016[1] and the imputability was found to be unlikely; in 2016, one death was reported in a female patient with underlying dysfunctional uterine bleeding and imputability was found to be possible; and in 2017, one death was reported in a female patient with underlying severe anemia and imputability was found to be probable. The patient had another reaction as FNHTR with probable imputability. The rest of the patients had recovered after TACO reaction.

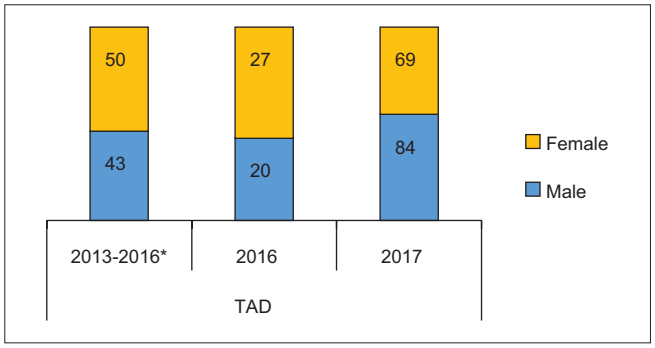

Figure 30: Transfusion-associated dyspnea cases reported

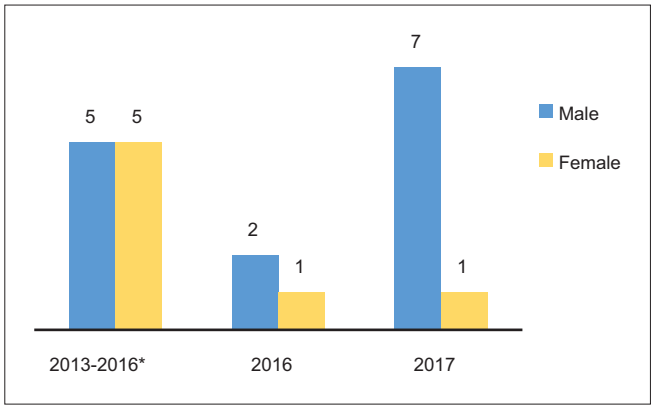

Figure 31: Transfusion-related acute lung injury cases reported

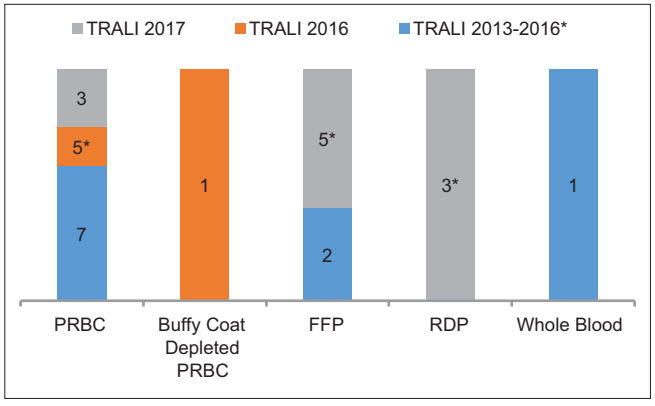

Figure 32: Implicated blood products

Transfusion-Associated Dyspnea

Transfusion-associated dyspnea (TAD) was reported in 93 patients from 2013 to 2016* with an age range of 1 to 90 years, 47 patients in 2016 with an age range of 16 to 74 years, and in 153 patients, in 2017, with an age range of neonate to 89 years. TAD constituted 2.4% of adverse transfusion reactions from 2013 to 2016*, 3.7% in 2016, and 5.13% of adverse transfusion reactions in 2017. The comparative male–female distribution is depicted in Figure 30. The patients had varied underlying conditions.

Red cells were the most commonly implicated blood products in TAD, as these are also the most frequently transfused blood products. One death was reported to HvPI from 2013 to 2016* having an unlikely causal relationship. However, in 2017, one death reported to HvPI was an adult (34 years) female with a primary diagnosis of severe anemia. The patient had a medical history of LSCS with poor chest condition and the implicated blood product was PRBCs, of which 351 ml is reported to have been transfused. The corresponding imputability was possible. The outcome was unknown in three patients in 2013–2016*, one patient in 2016, and four patients in 2017. The rest of the patients had recovered after the reaction with no significant morbid outcome reported.

Transfusion-Related Acute Lung Injury

TRALI was reported in ten patients from 2013 to 2016* with an age range of 23 to 66 years, three patients in 2016 with an age range of 6 to 51 years, and in eight patients, in 2017, with an age range of 7 months to 69 years. TRALI constituted 0.26% of adverse transfusion reactions from 2013 to 2016*, 0.23% in 2016, and 0.27% of adverse transfusion reactions in 2017.

The comparative male–female distribution is depicted in Figure 31. The patients had varied underlying conditions.

One death was reported to HvPI from 2013 to 2016* having unlikely causal relationship due an underlying condition of carcinoma colon with metastasis. One death was reported in 2016 (after the launch of TRRF version 2.0 i.e. from May 1,2016 to December 31, 2016), the patient who died was a pediatric female patient (6 Yrs. 3 Months age) with clinical diagnosis of Thalassemia major and known case of allogeneic bone marrow transplant who was transfused with Buffy Coat depleted PRBC and suffered a concurrent FNHTR and Transfusion Related Acute Lung Injury (TRALI).The Imputability was Possible in both the reactions. In 2017, again, one death was reported to HvPI, the one patient died was an adult (50 years) male with a primary diagnosis of cholelithiasis with acute pancreatitis and acute kidney injury. The implicated blood product was fresh frozen plasma, of which 30 ml was reported to have been transfused. The corresponding imputability was possible. The rest of the patients had recovered after reaction with no significant seriousness reported.

Blood Products Implicated in Transfusion-Related Acute Lung Injury

Figure 32 shows the implication rate of various blood products in TRALI.

The incidence of TRALI has remained largely unchanged, more awareness and better reporting is required.

Transfusion-transmitted bacterial infection

Transfusion-transmitted bacterial infection (TTBI) was reported in 18 patients from 2013 to 2016* with an age range of neonate to 68 years, 13 patients in 2016 with an age range of 7–56 years, and in 14 patients, in 2017, with an age range of 16–66 years. TTBI constituted 0.46% of adverse transfusion reactions from 2013 to 2016*, 1.02% in 2016, and 0.47% of adverse transfusion reactions in 2017. The comparative male–female distribution is depicted in Figure 33. The patients had varied underlying conditions.

From 2013 to 2016*, blood bag culture was positive in 9 cases of reported TTBI reaction, a report published in

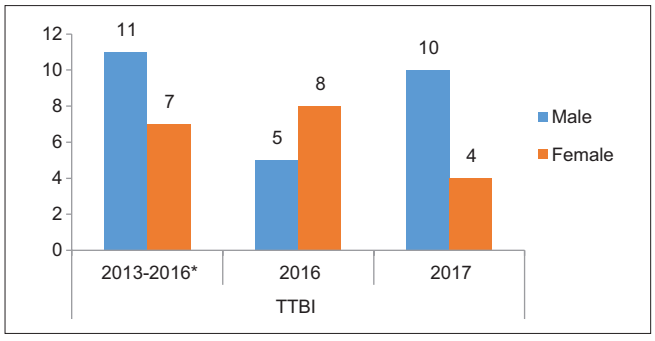

Figure 33: Transfusion-transmitted bacterial infection cases reported

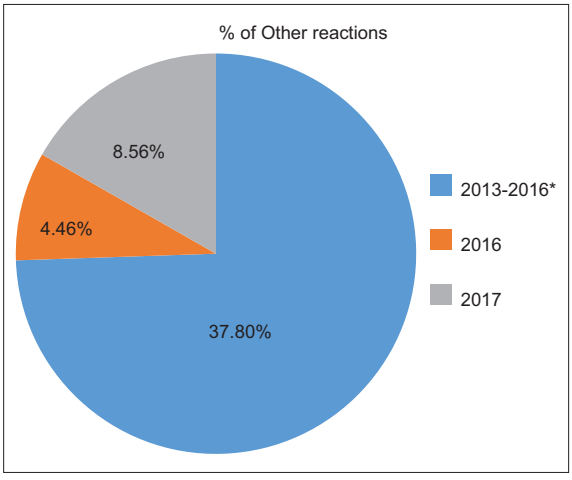

Figure 34: Year-wise distribution of other reactions

2018 before the new version of Haemo-Vigil software was launched on May 1, 2016.[1]

Blood bag culture was positive in all cases of reported TTBI reaction both in 2016 and 2017, and the bacteria grown are shown in Tables 3 and 4.

In 2016 reports, blood culture was reported in only two patients of TTBI. In one patient, both the cultures from blood bag and patient's posttransfusion blood sample had grown *Shewanella putrefaciens*. In the second patient, both the cultures from blood bag and patient's posttransfusion blood sample had grown *Staphylococcus.* In 2017, blood culture of the patient after the transfusion was done in only three patients and was negative in all the three. One death was reported to HvPI from 2013 to 2017. The patient who died was a neonate, in which the blood bag had grown coagulase-negative Staphylococci, thus having a probable causal relationship. TTBI was reported with all types of blood products. Both Gram-negative and Gram-positive bacteria have been implicated. However, posttransfusion patient samples were scant; diagnosis was suspected on the basis of symptoms and culture of blood bag.

Transfusion-associated hypertension

In 2017 only, one case of transfusion-associated hypertension was found (first reported as another reaction). The patient was an adult (75 years) male with a primary diagnosis of chronic obstructive pulmonary disease. The implicated blood product was PRBCs with an indication as surgery, of which 270 ml were transfused. The patient however recovered, and corresponding immpuability was possible; the blood pressure of the patient elevated from 86/150 to 99/180. Hypertension was the only symptom in the patient.

Other Reactions

Adverse reactions to transfusion of blood products which could not be categorized under any of the existing classes of adverse transfusion reactions are covered under other reactions under HvPI. In TRRF version 1.0, many mild allergic reactions were categorized as other reactions, also data validation could not be done. In TRRF version 2, there were better discrimination and validation of transfusion reactions.

Figure 34 shows year wise distribution of other reactions.

A total of 1476 other reactions were reported to HvPI from 2013–2016* which had occurred in 786 males and 690 females, constituting 37.8% of all adverse reactions reported to HvPI.[1]

A total of 57 other reactions were reported to HvPI in 2016 (May 1, 2016, to December 31, 2016) which had occurred in 20 males and 37 females with an age range of neonate to 86 years, constituting 4.46% of all adverse reactions reported to HvPI in 2016.

A total of 255 other reactions were reported to HvPI in 2017 which had occurred in 109 males and 146 females with an age range of neonate to 91 years, constituting 8.56% of all adverse reactions reported to HvPI in 2017.

No death with other reactions was reported in 2016; however, the outcome was unknown in two patients. One death was reported in 2017, the one patient who died was a pediatric (1 month 4 days old) female patient with a primary diagnosis of sepsis with low hemoglobin. The patient already had hypotension prior to transfusion and was a case of septic shock with positive blood culture. The implicated blood product was PRBCs, of which 16 ml was reported to have been transfused. The corresponding imputability was unlikely (doubtful), the outcome was unknown in 14 patients, and the rest of the patients had reportedly recovered.

The details of "Other reactions" were varied; these include signs and symptoms, not meeting the criteria of defined transfusion reaction diagnoses.

Table 3: 2016

Bacteria Grown	*n*
Shewanella putrefaciens	1
Klebsiella pnaemoniae	1
Staphylococcus aureus	4
Micrococcus lutues	1
E. coli	1
Acinetobacter iwaffi	1
Gram+ tive *Bacilli*	1
Gram - tive *bacteria*	1
Staph. Capitis	1
Coagulase - tive *Staph. Aureus*	1
Total	13

Table 4: 2017

Bacteria Grown	*n*
Acinetoobacter Iwoffii	1
Aeromonas	1
Bacillus Species.	1
Bacillus Subtilis	1
Coagulase Negative *Staphylococcus* Spp.	1
E. Coli	1
Enterobacter Sp.	3
Micrococcus luteus	1
Pseudomonas Sp.	1
Serratia Sp.	1
Staphlococcus bacteria	1
Streptococcus Sp.	1
Total	14

No cases of transfusion-associated graft versus host disease, post-transfusion purpura, transfusion-transmitted parasitic infection were reported to HvPI from May 1, 2016, to December 31, 2017. However, such reactions were reported from 2013 to 2016*, a report published in 2018 before the new version of Haemo-Vigil software was launched on May 1, 2016.[1] However, in TRRF version 1, adequate data were not captured for diagnosis or validation.

Summary and Key Recommendations

The participation of blood centers in HvPI is increasing continuously. A total number of reports submitted to HvPI were 1183 in 2016 (May 1, 2016, to December 31, 2016) plus 338 (January 1, 2016, to April 30, 2016, included in the TRRF version 1 report) and 2792 in 2017. A total of 4259 transfusion reactions of the year 2016 and 2017 were included and reviewed. These were based on the new Haemo-Vigil software incorporating TRRF version 2. Thirty-eight reports were excluded from the analysis, 14 reports from 2016 data, and 24 reports from 2017 data due to three main reasons after review: incomplete data for analysis 17 reports, absence of a transfusion reaction 12 reports, and discrepant data 9 reports.

The overall incidence of adverse reactions reported to HvPI from May 1, 2016, to December 31, 2017, was 8.4 per 10,000 of blood products transfused with a rate of 8.5 in 2016 and 8.3 in 2017. FNHTRS and allergic reactions continue to remain the most frequently reported adverse transfusion reactions. Better discrimination between mild-to-moderate allergic reactions and anaphylaxis was achieved with the TRRF version 2. Transfusion reactions with respiratory complications such as TRALI, TACO, and TAD were better defined. The broad group of "other reactions" narrowed to more specific diagnoses.

About 88%–89% apheresis platelets and almost 70% RDPs were transfused within 1 h of issue. Plasma components were also largely transfused (70%) within 1 h. Two-third of platelets and one-third of FFPs were transfused within 30 min. However, only one-third of red cell components were transfused within 30 min of issue. Awareness of good bedside transfusion practices needs to be increased.

FNHTRs constituted 49% of all transfusion reactions reported in 2016 (May 1 to December 31) and 42.5% in 2017. These were defined into three categories, and it was noted that milder reactions were more common, characterized by either chills and rigors alone or 1°C rise in temperature. The most frequently implicated blood component was PRBC. This reflects the fact that the most commonly transfused blood component in clinical settings are red cells. Leukofiltered PRBCs had less FNHTR rate as compared to buffy coat-reduced PRBC and nonleukoreduced PRBCs. Whole blood and plasma/platelet products had less reaction rate than PRBCs. It may be related to the age of storage of PRBCs and/or underreporting of febrile transfusion reactions with plasma/platelet products and needs further elucidation.

Allergic reactions constituted the second most commonly encountered acute transfusion reactions. Allergic reactions comprised 456 (35.66%) reactions of 1279 reported reactions in 2016 and 1129 (37.89%) reactions of 2980 reported reactions. Apheresis platelets were seen to have the highest reaction rate. Anaphylactic reactions constituted only a small proportion of all acute reactions, with 1.72% in 2016 and 1.6% in 2017. The implication rate was maximum with apheresis platelets both in 2016 and 2017. One death due to the reaction was reported in 2016, the imputability was possible. Two death cases associated with anaphylaxis were reported in 2017 with a possible imputability.

The TRRF version 2 has captured the anaphylactic reactions with better clarity and accuracy. It is a reaction with a potential fatal outcome, and close monitoring and immediate management of the recipient is essential.

Hemolysis due to other alloantibodies was reported in 1.49% of patients in 2013–2016[1] reports via TRRF version 1. It was 0.31% in 2016 and 0.03% in 2017 through TRRF version 2. From the new software reports, it seems underreported since more investigations are necessary to diagnose this reaction. Alloantibody screening and identification technologies need to be upgraded in blood centers, as this might not reflect the true incidence in view of significant multi-transfused thalassemia major patients in the country.

Hemolysis due to ABO incompatibility was seen with a frequency of 0.56% in the 2013–2016 reports, 0.4% in 2016 new software, and 0.23% in 2017. All reactions were due to red cell products except in one O blood group apheresis platelets were transfused out of group. WBIT, blood grouping error, labeling, and bedside administration error were some of the causative factors recorded. These errors are preventable and can be minimized by adhering to standard operating procedures in blood centers and implementation of good bedside clinical practices. Need for education and training in both these areas is required.

Nonimmunological hemolysis was observed with a frequency of 2.15% in 2013–2016 reports, 0.47% in 2016 new software, and 0.67% in 2017. The causative factors were as follows: hemolysis due to inappropriate warming of PRBC units, hemolysis due to infusion of any

other fluid through the same BT set, and hemolysis due to freezing of PRBC units and mechanical damage. One patient death was reported in 2017 and imputability was possible. Education and training for bedside handling, storage, and administration of blood are recommended.

TACO constituted 0.67% of adverse transfusion reactions from 2013 to 2016*, 1.1% in 2016, and 1.34% in 2017. The incidence of reported TACO is increasing with comparatively lower incidence from 2013 to 2016 and higher in 2017. This indicates better awareness and more accuracy of data in the current format. Almost two-third of patients had received repeat transfusions. A total of 3 deaths have been reported to HvPI having a temporal relationship with TACO, imputabilty was unlikely in one case and probable in two cases.

TAD constituted 2.4% of adverse transfusion reactions from 2013 to 2016*, 3.7% in 2016, and 5.13% of adverse transfusion reactions in 2017. Increasing frequency of TAD could reflect better awareness of knowledge and diagnosis of transfusion reactions with a progressive increase in the reach of HvPI.

TRALI constituted 0.26% of adverse transfusion reactions from 2013 to 2016*, 0.23% in 2016, and 0.27% of adverse transfusion reactions in 2017. The incidence of TRALI has remained largely unchanged, more awareness and better reporting is required. All blood products have been implicated It was also causally related to mortality in view of a possible imputability.

TTBI constituted 0.46% of adverse transfusion reactions from 2013 to 2016*, 1.02% in 2016, and 0.47% of adverse transfusion reactions in 2017. TTBI was reported with all types of blood products. Both Gram-negative and Gram-positive bacteria have been implicated. However, posttransfusion patient samples were scant; diagnosis was suspected on the basis of symptoms and culture of the blood bag. Mortality has been observed in one neonatal patient only. It needs to be emphasized to the reporting centers for taking posttransfusion samples of patients for confirmation of the diagnosis of TTBI.

Conclusion

The report on version 2.0 TRRF is based on 4259 adverse transfusion reactions reported from May 1, 2016, to December 31, 2017, from 218 centers of the 615 enrolled centers with a comparison with a previous 2013–2016 report. Better discrimination among reported transfusion reactions was obtained after the launch of TRRF 2.0 on May 1,2016, along with increased awareness among health-care professionals and only 7.32% of total reactions were reported unclassified in another reaction category which is contrary to 2013–2016 report, in which 37.82% transfusion reactions were reported unclassified as other reactions. Regular Continuing Medical Education programs and outreach workshops conducted by HvPI have significantly build up the confidence among stakeholders in hemovigilance which is reflected from increasing participation of blood centers in HvPI. With the launch of TRRF 2.0 having a separate denominator data form, determination of adverse transfusion reaction rate was made possible, and an overall adverse transfusion reaction rate from May 1, 2016, to December 31, 2017, was found to be 8.4 per 10,000 of blood components transfused, with FNHTRs being the most commonly reported adverse transfusion reactions followed by allergic reactions, and the most commonly implicated blood components are PRBCs and apheresis platelets. Promoting rational use of blood components, use of leukoreduced PRBCs, and better bedside transfusion practices could play a significant role in reducing the rates of such adverse reactions. Active participation of all blood centers of the country in HvPI will yield a true incidence rate of adverse transfusion reactions and associated morbidity and mortality in the country which could provide an opportunity for timely corrective action along with early detection of emerging pathogens and the implementation of measures to mitigate the associated risks.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Acknowledgment

HvPI acknowledges the contribution of Dr. R J Yadav, Consultant Statistician, NIB for providing the statistical inputs. HvPI is thankful to all the blood centers for their active participation in HvPI and reporting of adverse transfusion reactions to the central database.

References

1. Bisht A, Marwaha N, Kaur R, Gupta D, Singh S. Haemovigilance Programme of India: Analysis of transfusion reactions reported from January 2013 to April 2016 and key recommendations for blood safety. Asian J Transfus Sci 2018;12:1-7.
2. Marwaha N, Singh S, Bisht A. Setting up haemovigilance from the very first step. The Indian perspective. Voxs 2014;9;178-83.
3. Mukherjee S, Maiti R. Haemovigilance: A current update in Indian perspective. JCDR 2016;10;EE05-9.
4. Shivgunde P, Besekar S, Bhojwani K, Bhojwani D. Knowledge, attitude and practice of haemovigilance amongst healthcare professionals in Nashik, Maharashtra, India. IJBCP 2018;7:986-91.
5. International Society of Blood Transfusiion Working Party on Haemovigilance. Proposed Standard Definitions for Surveillance of Non-Infectious Adverse Transfusion Reactions; 2011. Available from: http//www.isbtweb.org/Haemovigilance/ISBT_definitions_final_2011. [Last accessed on 2020 Oct 16].