Original Article

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Investigation of Transfusion Adverse Events Patterns in Fayoum University Hospitals, Egypt: Hemovigilance Initiative

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Abstract

Background and Objective: Hemovigilance is an adverse reaction surveillance and monitoring system to improve the safety and quality of blood transfusion in terms of corrective and preventive action. Identification of the adverse reactions and their risk factors will assist in taking appropriate steps to reduce their incidence and make blood transfusion safer. The aim of our study was to analyze the nature and incidence of transfusion related adverse events as a tool for implementation of hemovigilance system in Egypt.

Study Design and Methods: Our study included all transfusion related adverse reactions from Fayoum University Hospital reported to the Blood Bank over a period of one year from August 2021 to July 2022. All patients receiving transfusion and all blood donors according to The National Blood Transfusion Guidelines were included. All reported reactions were analyzed, categorized and evaluated.

Results: 28, 253 blood and blood components units were issued to 13, 544 patients. 273 (0.967%) transfusion related adverse reactions were reported to the blood bank. The most common reaction observed in recipients was allergic reaction 129 (47.25 %) followed by febrile non hemolytic transfusion reaction (FNHTR) 108 (39.56 %).

Conclusion: Data related to transfusion related adverse reactions in developing countries are rare in literature. A strict quality assurance measures are required to build a hemovigilance system including, appropriate use of blood, maintain blood cold chain, monitoring, documenting and reporting transfusion reactions so that, the proper hemovigilance system can be attained.

***Keywords**: Hemovigilance, Transfusion reactions, Adverse events*

Introduction

Blood transfusion is an essential component of healthcare system that saves millions of lives each year, and it will continue to be so for many years to come (1, 2). The production and transfusion of blood and its components is a process that carries risk for both donors and recipients (1, 3) but when used with caution and according to the guidelines is lifesaving (4). Blood transfusion changed from a hazardous and risky therapy to a relatively safe procedure with the discovery of blood group antigens in 1901, by Karl Landsteiner (5). Safety of blood transfusion improved further with the progress and improvement of technology. The incidence of transfusion-transmitted diseases has decreased with the recent advances and improved awareness of testing infectious diseases in testing facilities and blood banks; however, the incidence of other adverse events due to human errors, ABO incompatibility, alloimmunization, bacterial contamination, and immune modulation remain a subject of concern despite the fact that they occasionally occur and usually mild (4, 5,8).

In spite of precautions and preventive measures, transfusion related adverse reactions continue to occur which may be serious and even fatal (5). Hence the blood transfusion therapy needs a considerable degree of expertise for utmost recipient protection. Knowledge of possible adverse effects will be useful to prevent their occurrence and help in clinical management (6).

Hemovigilance deals with the safety of the blood transfusion entire process and can be summarized in one phrase “safety from vein to vein” (7). Hemovigilance aims to detect and analyze adverse effects of blood transfusion to correct their cause and prevent recurrence (7, 8).

The present study was undertaken to detect and analyze the transfusion related adverse events and their rates for benchmarking purposes in Fayoum University Hospitals as tool for implementation of the hemovigilance system, as similar data from Egypt and the developing world are rare in

the literature.

Material and methods

Recruitment

This study was conducted in Fayoum University Hospital blood bank, over a 1-year period from August 2021 to July 2021. Fayoum University Research Ethics Committee, a member of Egyptian Network Research Ethics Committee (ENREC), was informed of this study. Donors were recruited according to the national guidelines for blood donation in Egypt and were informed about the nature of the research, confidentiality of the personal information that they provided and a written consent was obtained along with the donor selection questionnaires of the Blood Bank. All patients' transfusion related adverse events reported to the blood bank were included in the study.

Fayoum University Hospital policy mandates reporting adverse events related to transfusion of blood and blood products. All reactions were recorded and analyzed as per standard operating procedures. Reactions rates are calculated as the percentage of all reported adverse events associated with transfusion, to units of all transfused blood components.

Blood bank and Laboratory investigations

Cases that developed adverse reactions were subjected to a full work up for transfusion reaction depending on symptoms, signs, clinical examination and investigations:

1. Clinical history of the patient regarding the indication of blood /blood component transfusion(s) and similar events of transfusion related adverse reactions in the past during transfusion, previous history of pregnancy and transfusions were also recorded. Signs and symptoms related to transfusion reactions were recorded.

2. Clerical records, red cell ABO and Rh D typing were rechecked. Patient's ABD grouping was repeated in both pre- and post-transfusion samples using column agglutination techniques (CAT) by DiaMed Gmbh Pra Rond 1785 Cressier FR, Switzerland.

3. Direct Antiglobulin Test (DAT) and Indirect Antiglobulin Test (IAT) were performed using latex agglutination technique by Bioscope Diagnostics. Renal function, serum LDH and examination of a Leishman-stained blood film for detection of hemolysis by presence of spherocytes or RBC's fragmentation.

4. Febrile non hemolytic transfusion reactions (FNHTR) are defined according to American Association of Blood Bank Technical manual as "A body temperature rise of >1 C° or more occurring during or within 4 hours of cessation of transfusion without any other explanation" such reactions are often associated with chills and rigors without hemolysis (12).

5. Delayed serologic transfusion reaction (DSTR) is defined with Demonstration of new, clinically significant alloantibodies against red blood cells between 24 hours and 28 days after cessation of transfusion despite an adequate, maintained hemoglobin response with no clinical signs of hemolysis (12).

6. Allergic reaction may present with only mucocutaneous signs and symptoms during or within 4 hours of cessation of transfusion (12).

7. Hypotensive transfusion reaction, occurs during or within 1 hour after cessation of transfusion. All other adverse reactions are excluded (12).

8. Transfusion associated dyspnea (TAD) occurs within 24 hours of cessation of transfusion and Allergic reaction, TACO, and TRALI definitions are not applicable (13).

9. Delayed hemolytic transfusion reaction (DHTR) occurs when recipient develops antibodies to RBC antigen(s) between 24 hours and 28 days after cessation of transfusion. Clinical signs of hemolysis are usually present. If performed, post-transfusion LDH and bilirubin levels increase and subsequently fall back to baseline in the following days (12).

10. Post transfusion purpura (PTP), a thrombocytopenia that occurs 5- 12 days following transfusion of cellular blood component and when the patient has a drop in platelet count to less than 80% of pre-transfusion count and more specific adverse reaction definitions do not apply (12).

11. Note: Patients suspected to have developed a septic reaction, a gram-stained direct film was examined for presence of any organisms and bacterial culture of the blood bag and patients' blood was done using BACTEC 9050, Becton Dickinson, Artisan technology group, USA.

12. Patients suspected to have TRALI, chest X-ray was done to detect any pulmonary infiltrate and oxygen saturation were done using Gem premier 3000, Instrumentation Laboratory Company, USA.

13. Patients suspected to have anaphylactic reaction, quantitative immunoglobulin A (Ig A) assay was done by nephelometer using BN ProSpec, Siemens Health Care, USA.

14. Patients who were suspected to have iron overload: serum ferritin results were retrospectively collected and evaluated by chemiluminescence using Access 2, Beckman coulter, USA.

15. Patients were tested for viral markers prior to transfusion and recalled after 6 months for follow up. For screening of HCV Ab, direct immunoenzymatic method by Bioelisa HCV 4.0, BioKit Spain was done. Screening HBs Ag was done using direct immunoenzymatic method by Bioelisa, HBSAg 3.0, ELISA Test, BioKit Spain and For HIV Ag-Ab, immunoenzymatic method ELISA by Genscreen Ultra

HIV Ag-Ab, Bio-rad, France was done. Patients who have undergone any interventions associated with transmission of viral infections were excluded from viral markers screening.

Statistical analysis

Data were statistically described in terms of ± mean, Standard deviation (± SD) and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student t test for independent samples. For comparing categorical data, Chi-square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5. P values less than 0.05 were considered statistically significant. All statistical calculations were done using computer program IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows. Chi-square with risks assessment was performed for identification of the risk groups.

Result

During the 1-year study period, 28, 253 blood component units were issued, the total number of (packed red blood cells) PRBCs were 13,303 units (47.1 %), fresh frozen plasma were 8,507 units (30.11 %), washed PRBC's were 4,513 units (15.97 %), random platelets (PLT) were 1697 units (6 %), cryoprecipitate units were 201 (0.71 %) and cryopoor plasma were 32 (0.11 %).

The total number of transfusion related adverse events reported to blood bank were 273 (0.967%), The most common reaction observed in recipients was allergic reaction 129 (47.25 %) followed by FNHTR 108 (39.56 %). Frequency of different adverse reactions among recipients are summarized in table 1.

Recipients who received washed PRBCs were found to develop adverse reactions significantly more than recipients who received other components ($p < 0.001$), Table 2 summarizes the Association between different transfused blood products and occurrence of adverse effects among all blood units.

There is a statistically significant difference with p-value 0.003 between recipients who develop adverse effects and who did not as regard indications of blood transfusion as high incidence of patients with ß-thalassemia and hemophilia were higher frequency to develop adverse reactions (Table 3).

By studying risk groups, pediatric patients were found to carry more risk to develop complications than adult group ($p<0.05$). Similarly, recipients with history of previous transfusion, was more likely to develop adverse reactions ($p<0.001$). Association between different risk factors and occurrence of adverse reactions among recipients' groups is summarized in table 4.

Discussion

Worldwide, hemovigilance systems are at varying levels of development and implementation and requires more attention to ensure the efficient required safe transfusion services, especially, in developing countries (1, 24). Many reasons appear to prevent and delay advances in this area, such as absence of support from authorities, limited resources and difficulty changing cultures to maintain a blame-free environment (3). The need to observe and

Table 1: The frequency of different transfusion related adverse reactions among recipients.

Adverse reaction	Number	% (AR)[1] (no=273)	% (total)[2] (no=13, 544)
Allergic reaction	129	47.25	0.952
FNHTR	108	39.56	0.80
DSTR	9	3.3	0.066
AHTR	1	0.37	0.007
TAD	5	1.83	0.037
DHTR	4	1.47	0.03
Acute hypotensive reaction	9	3.3	0.066
PTP	2	0.73	0.015
Anaphylactic reaction	2	0.73	0.015
Convulsions	3	1.1	0.022
TRALI	1	0.37	0.007
Total	**273**	**100**	**2.017**

[1]Percent among adverse reactions reported, [2]Percent among total transfused patients.

Table 2: Association between different transfused blood products and occurrence of adverse effects among all blood units.

Blood Component	# of blood units transfused (%)	Adverse reactions (%)	P- value
Washed PRBCs	4513 (15.97)	184 (4.08)	< 0.001
PRBCs	13303 (47.1)	21 (0.16)	0.2
FFP	8507 (30.11)	46 (0.54)	0.09
Random Platelets	1697 (6)	22 (1.3)	0.06
Cryoprecipitate	201(0.71)	NR	NA
CPP	32 (0.11)	NR	NA
Total	28253	273	

CPP: cryopoor plasma; FFP: fresh frozen plasma; NA: not applicable; NR: not reported; PRBC: packed red blood cells transfusion.

Table 3: Association between indication of transfusion and occurrence of adverse effects among all blood units.

Indications	Adverse reactions				p-value
	Yes (no=273)		**No** (no=27980)		
	No.	**%**	**No.**	**%**	
B-Thalassemia	166	0.59	1516	5.37	
Hemophilia	42	0.15	292	1	
Liver disease	19	0.07	3657	12.94	
Infective endocarditis (IE)	6	0.02	332	1.18	
G6PD deficiency	8	0.03	294	1.04	
Sickle cell anemia	5	0.018	168	0.6	
Chronic renal failure	5	0.018	143	0.51	
Hematological disorders	6	0.02	295	1.04	
Autoimmune hemolytic anemia	6	0.02	8	0.03	**0.003***
Pure red cell aplasia	4	0.014	13	0.05	
Pre- and post-operative anemia and bleeding	3	0.011	9866	34.92	
Immune Thrombocytopenic Purpura (ITP)	2	0.007	212	0.75	
Subdural hematoma	1	0.004	198	0.7	
Cancers	0	0.00	1910	6.76	
Hemorrhage and bleeding	0	0.00	345	1.22	
Other medical causes	0	0.00	4845	17.15	
Surgical operations	0	0.00	3886	13.75	

monitor adverse events occurring through the transfusion process is highly supported by WHO, the International Hemovigilance Network (IHN), and the International Society of Blood Transfusion (ISBT) (3). Very few information regarding the rates of adverse transfusion events and implementation of hemovigilance programs in developing countries are available in literature and it is still too early to be used effectively (11).

The adverse related transfusion reactions observed were seen in 273 recipients (0.976 % of recipients). Table 5 shows the comparison of transfusion related reaction rates in previous studies.

This incidence is similar to the reported study by Cho et al (18) with the rate of transfusion reactions reported as 1.2%. However, other studies by Pahuja et al (19), De Sousa Neto and Barbosa (20) and Bhattacharya et al (16) recorded the incidence of transfusion related adverse reactions was 0.19%, 0.24% and 0.18% respectively.

Allergic reactions (47.25%) were the most commonly observed adverse reactions. This is constant to the study by Harvey et al (20) recorded that nearly half (46.8%) of the reported adverse reactions were allergic reactions. Allergic reactions were associated with transfusion of washed PRBCs, PRBCs, FFP and platelets in our study. In a study by Cho et al (18) reported that the frequency of allergic reactions to FFPs and platelet components was significantly

Table 4: Association between different risk factors and occurrence of adverse reactions among recipients' group.

Variables	Adverse reactions				p-value
	Yes (no=273)		No (no=27,980)		
	No.	%	No.	%	
Sex					
Male	158	57.9 %	14,233	50,87 %	0.6
Female	115	42.12 %	13,747	49.13%	
Age group					
<18 years	170	62.27 %	8,672	30.99 %	**<0.05***
>18 years	103	37.73 %	19,308	69 %	
Previous transfusion					
Yes	191	69.96 %	2,302	8.23 %	**<0.001***
No	82	30.03 %	25,678	91.77 %	
Previous adverse reaction					
Yes	78	28.57 %	543	1.94 %	**<0.001***
No	195	71.43 %	27,437	98.05 %	

Table 5: Comparison of transfusion related adverse reactions rates with previous literature.

Previous study	%
Kumar et al [13]	0.05
Venkatachalapathy [14]	3.3
Haslina et al [15]	0.4
Bhattacharya et al [16]	0.18
Cho et al [18]	1.2
Pahuja et al [19]	0.19
De Sousa Neto and Barbosa [20]	0.24
Current study	0.967

higher than that to RBC components. The higher incidence of allergic reactions in our washed PRBCs could be related to technical errors during washing procedure, making this technique inefficient in our facility.

The next most frequently reported transfusion related adverse reactions were FNHTR (39.56%). In this study, patients who developed allergic reactions received PRBCs, washed PRBCs, FFP or platelets. These finding were in agreement with Bassi et al, (21) who previously reported that, these allergic reactions could be attributed to plasma proteins in FFP, and the traces of plasma kept in PRBCs.

69.96 of recipients with adverse reactions had history of previous transfusions. In a study by De Sousa Neto and Barbosa (19), 36.5 % of cases with adverse reactions, had previous history of transfusion. Other study by Bhattacharya et al (16), history of previous transfusions was present in 52.38 % of patients with adverse reactions.

In this study AHTR was seen in 0.007% of all recipients (1 case). A study by Pahuja et al (18) observed that acute hemolytic transfusion reaction was seen in 1.27%. Clerical errors are the most common cause for AHTR. We revised the records and documents for ABO and cross match of both cases, no errors were found. Although not further investigated, but AHTR in this case could be explained by errors in cross-match procedure, or in blood administration to the patients by nursing staff. This prompted the essential need to a total computerized system for grouping, cross matching and even for bedside patient identification. In our blood bank, we do not routinely perform an antibody screen for all recipients. AHTR probably due to a pre-formed alloantibody. Screening for viral transmitted infections were done by ELISA, Seroconversion occurred in 4 cases that had been equivocal for HCV Antibodies

The aim of our study was to estimate the frequency and type of transfusion related adverse events occurring in recipients, identify the types of blood products associated with these reactions and identify the risk groups so that appropriate actions can be taken through appropriate educational processes to prevent occurrence and recurrences of these incidences and sufficient and safe blood supply can be maintained by ensuring safety and well-being of the donors and recipients.

Conclusion

The study serves as a basis for risk assessment and further research to be conducted. It also sets a step for improvement of the current reporting system as well as the preventive action required to minimize transfusion-related risks in Egypt.

Our data suggests important recommendations to improve blood transfusion services at Fayoum University Hospitals,

including the use careful donor selection and screening procedures favoring voluntary blood donation, using washed PRBCs for leucodepletion should be discouraged and replaced by using filtered units, Nucleic acid testing should be applied to all negative cases to identify early infection prior to seroconversion, Establish a recording and barcoding system to facilitate recipient and donor identification, keep records of all transfusion procedures, eliminate clerical errors, in addition to developing institutional guidelines, hospital blood transfusion committee and adequate education of the staff and awareness regarding reporting of adverse events.

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