HAEMOVIGILANCE STUDY OF ACUTE TRANSFUSION REACTIONS AT HOSPITAL SULTANAH BAHIYAH

By

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MASTER OF MEDICINE (TRANSFUSION MEDICINE)

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DISCLAIMER

I declare that this dissertation records the results of the study performed by me and that it is my own composition.

Dr. Firdaus bin Che Ros
16th November 2020

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LIST OF ABBREVIATIONS

ATR	Acute Transfusion Reaction
AHTR	Acute Haemolytic Transfusion Reaction
FNHTR	Febrile Non Haemolytic Transfusion Reaction
TRALI	Transfusion Related Acute Lung Injury
TACO	Transfusion-Associated Circulatory Overload
TAD	Transfusion-Associated Dypsnoea
RBC	Red Blood Cell
SPSS	Statistical Package For The Social Sciences
SD	Standard Deviation
CI	Confidence Interval
OR	Odds Ratio
GSH	Group, Screen and Hold
GXM	Group and Crossmatch
CME	Continuous Medical Education
PBM	Patient Blood Management
HTC	Hospital Transfusion Committee
STC	State Transfusion Committee
HIV	Human Immunodeficiency Virus

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ABSTRAK

Pengenalan : Reaksi transfusi akut (RTA) kerap dilaporkan dalam amalan transfusi klinikal dan boleh menyebabkan morbiditi yang signifikan dan mortaliti. Sistem "haemovigilance" memainkan peranan penting untuk memantau RTA bagi pencegahan dan juga meningkatkan penjagaan dan keselamatan pesakit. Kajian ini bertujuan untuk mengetahui ciri-ciri dan faktor-faktor berkaitan RTA di Hospital Sultanah Bahiyah, Kedah, Malaysia.

Kaedah : Ini adalah kajian retrospektif yang menggunakan rekod daripada borang-borang "haemovigilance" untuk laporan reaksi transfusi, E-Delphyn (sistem tabung darah berkomputer) dan E-His (sistem informasi hospital). Sejumlah 118 kes RTA sejak 1 Januari 2015 sehingga 31 Disember 2017 telah dipilih dan dianalisa. Untuk setiap kes, satu kes daripada pesakit yang tidak mengalami RTA telah dipilih sebagai kawalan.

Keputusan : Sejumlah 122,215 unit darah utuh dan komponen darah telah ditransfusi sepanjang tempoh kajian dan sebanyak 415 RTA kes telah dilaporkan. Prevalensi RTA adalah 0.34% atau satu dalam 294 unit darah ditransfusi. Reaksi alergik adalah RTA yang paling banyak dilaporkan iaitu sebanyak 62 kes (52.5%), diikuti "febrile non-haemolytic transfusion reactions" 45 kes (38.1%), "transfusion-associated circulatory overload" 4 kes (3.4%) dan "transfusion-associated dyspnoea" 4 kes (3.4%). Reaksi alergik mempunyai hubungan yang signifikan dengan pesakit wanita ($p = 0.038$) dan pesakit pediatrik ($p = 0.038$). Terdapat hubungan yang signifikan antara "febrile non-haemolytic transfusion reaction" dan tempoh sel darah merah disimpan > 14 hari ($p = 0.002$).

Kesimpulan : Prevalensi RTA di Hospital Sultanah Bahiyah adalah rendah dan berhubungkait dengan pesakit wanita, pesakit pediatrik dan tempoh masa penyimpanan sel darah merah.

(239 patah perkataan)

Kata kunci : *Reaksi transfusi akut, "haemovigilance", prevalensi*

ABSTRACT

Introduction: Acute transfusion reactions (ATRs) are commonly reported in clinical transfusion practice, and they may result in significant morbidity and mortality. Haemovigilance system plays a major role in the monitoring of ATRs for prevention, as well to promote patient care and safety. This study aims to explore the characteristics and associated factors of ATRs at Hospital Sultanah Bahiyah, Kedah, Malaysia.

Methods: This was a retrospective study using records from haemovigilance forms of reported transfusion reactions, E-Delphyn (blood bank system) and E-His (hospital information system). A total of 118 cases of ATRs from January 1st 2015, until December 31st 2017, were selected and analysed. For each case, a control was selected from a patient who did not develop ATR.

Results: A total of 122,215 units of whole blood and blood component transfusions were performed and 415 ATRs were reported. The prevalence of ATR was 0.34% or one in 294 units transfused. The most common ATR is allergic reactions with 62 cases (52.5%), followed by febrile non-haemolytic transfusion reactions with 45 cases (38.1%), transfusion-associated circulatory overload with four cases (3.4%), and transfusion-associated dyspnoea with four cases (3.4%). Allergic reaction was significantly associated with female patients ($p = 0.038$) and the paediatrics age group ($p = 0.038$). There was a significant association between febrile non-haemolytic transfusion reaction and red blood cells (RBCs) stored >14 days ($p = 0.002$).

Conclusion: The prevalence of ATRs at Hospital Sultanah Bahiyah was low and are associated with female patients, paediatric age group, and RBC's storage duration.

(249 words)

Keywords *: Acute transfusion reaction, haemovigilance, prevalence*

Chapter 1 :

INTRODUCTION

Chapter 1

INTRODUCTION

1.1 Overview

This chapter covers some brief introduction on haemovigilance, acute transfusion reactions and the study location, which is Hospital Sultanah Bahiyah. This chapter also highlights the problem statements and objectives of the study.

1.2 Background of Study

Haemovigilance consists of surveillance procedures during the process of blood transfusion, from the donation and blood component preparation, through to their provision and transfusion to recipients, and including their follow-up. It involves the monitoring, reporting, investigation and analysis of adverse events occurred during blood donation, processing and transfusion of blood, taking measures to prevent their occurrence or recurrence (WHO., 2016). In Malaysia, all adverse events that happen during blood donation, processing, testing, transfusion procedures and outcome of the transfusion including near misses must be reported to Hospital Transfusion Committee (HTC), the State Transfusion Committee (STC) and National Haemovigilance Coordinating Centre (NHCC). Transfusion processes in the clinical area are monitored by a surveillance system which is patient haemovigilance (Transfusion Practice Guidelines for Clinical and Laboratory Personnel 2016).

This study focused on acute transfusion reaction cases reported at Hospital Sultanah Bahiyah, a tertiary hospital in Kedah, Malaysia. All reported cases of acute transfusion reactions (ATRs) from January 1st 2015, until December 31st 2017, were collected and analysed. Given this is a case-control study, a control was selected from each patient who did not develop acute

transfusion reaction at that time. Department of Transfusion Medicine, Hospital Sultanah Bahiyah, Alor Setar was chosen to be study location in which this is a collaborative study between the Ministry of Health (MOH) and Universiti Sains Malaysia (USM). Hospital Sultanah Bahiyah is the largest government tertiary hospital in Kedah. This hospital consists of 15 departments with 1084 beds. Besides performing various transfusion-related laboratory tests and supplying blood for clinical transfusion activities, Department of Transfusion Medicine in this hospital plays a role as the regional blood centre for collecting, screening, processing and supplying blood products to hospitals in Kedah and Perlis.

1.3 Acute Transfusion Reactions (ATRs)

An acute transfusion reaction is a reaction in which signs and symptoms occur within 24 hours of a blood transfusion (Harmening 2015). The ATR types that were analysed in this study were acute haemolytic transfusion reaction (AHTR), febrile non haemolytic transfusion reaction (FNHTR), allergic reaction, transfusion related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO) and transfusion-associated dypsnoea (TAD).

Febrile non haemolytic transfusion reaction (FNHTR) is defined as one or more of fever ($\geq$38°C oral or equivalent and change of $\geq$1°C from pre transfusion temperature) or chills/rigors, which occurs during or within 4 hours following transfusion without any cause such as haemolytic transfusion reaction, bacterial contamination or underlying illness (International Society of Blood Transfusion.,2011).

An allergic reaction is characterised with mucocutaneous signs/symptoms, which are morbiliform rash with pruritus, urticaria, localized angioedema, edema of lips/tongue/ uvula, periorbital pruritus/erythema/edema and conjunctival edema which present during or within 4 hours of transfusion (International Society of Blood Transfusion.,2011).

Transfusion-related acute lung injury (TRALI) consists of 5 indicators which are acute onset, hypoxemia (PaO2/FiO2<300 mmHg / oxygen saturation is < 90% on room air or other clinical evidence), bilateral infiltrates on chest X-ray, left arterial hypertension is not present, no temporal relationship to an alternative risk factor for acute lung injury during or within 6 hours of completion of transfusion (International Society of Blood Transfusion.,2011).

Transfusion-associated circulatory overload (TACO) is the presence of any 4 of these signs/symptoms which are acute respiratory distress, tachycardia, increased blood pressure, acute or worsening pulmonary edema on frontal chest X-ray and positive fluid balance that occur within 6 hours of completion of transfusion is categorised as transfusion associated circulatory overload (TACO) (International Society of Blood Transfusion.,2011).

Transfusion-associated dypsnoea (TAD) is a respiratory distress which occurs within 24 hours of transfusion that does not fulfill the criteria of TRALI, TACO or allergic reaction (International Society of Blood Transfusion.,2011).

1.4 Factors Associated with ATRs

A study of acute transfusion reactions was conducted by Sharma et al. (2015) in a teaching hospital of Sikkim, India enabled them to develop insight into ATR patterns. It was a retrospective observational study in which all ATRs reported to the blood bank over a period of 20 months were reviewed and analysed. They found that 32 ATRs (0.92%) were reported from a total of 3455 transfused blood products. Adverse reactions were most commonly associated with packed red blood cell transfusions (p=0.06), followed by whole blood transfusion (p=0.83) and allergic reaction (65.6%) was the most often reported, which was most frequently seen with packed red blood cells (Sharma *et al.*, 2015).

An audit on acute transfusion reaction in Hospital Universiti Sains Malaysia found that the incidence of transfusion reaction was 0.23% of total blood components transfused (Haslina *et*

al., 2012). They reported that allergic reactions were the commonest symptom (50.2%) and followed by febrile non haemolytic transfusion reaction (38%). They found that red cell transfusion was the most commonly associated with acute transfusion reactions, followed by fresh frozen plasma and platelet concentrates.

A study in Uganda reported that 9.6% of the 507 transfusions were concluded as ATRs whereby the febrile non haemolytic transfusion reaction (FNHTR) was the most common ATR (49%) and followed by allergic reaction (14.3%) with no significant associated factors were found (Waiswa *et al.*, 2014).

An effective strategy to reduce the rate of febrile non haemolytic transfusion reaction is to provide random platelets which are stored equal or less than 3 days (Kelley *et al.*,2000). Kato et al. (2014) reported that there are risks of acute transfusion reactions on the first transfusion as well as transfusions of those with history of transfusion. Allergic reactions may be contributed by blood component factors and patient factors such as history of pregnancy (Kato *et al.*, 2014).

Harvey et al. (2015) reported allergic reaction was the highest rate for transfusion reaction (112.2/100 000), followed by febrile non haemolytic reactions (86.4/100 000). Platelet was the blood component type that showed the highest rate of adverse reactions (421.7 per 100 000) (Harvey *et. al.*, 2015). The reaction incidence was similar between genders in adults, while in paediatric patients, reactions were more common in male patients (7.9/1000 paediatric males vs 4.3/1000 paediatric females, $p<0.01$). It also was discovered that transfusion of plasma and platelets were significantly associated with allergic reaction compared to red blood cells ($p<0.0001$) and there were no association between ATRs with blood groups (Oakley *et al.*, 2015). Transfusion of blood components that were in more than 14 days of storage (>14 days) showed a higher percentage of ATR cases, (69.23%) and there was significant difference in

patients with allergic reactions had history of prior sensitization, which were transfusion and pregnancy (Vasudev *et al.*,2016).

A haemovigilance study of red cell transfusion was performed across 17 countries in United States of America in which FHNTRs and delayed serologic transfusion reactions were the most frequent adverse events reported. It was concluded that the higher rate of some adverse transfusion reactions in the United Stated was may be contributed by the lack of universal leukoreduction of RBC units (Rogers *et al.*, 2015).

Most common types of ATR reported which are allergic reaction and febrile non haemolytic transfusion reaction (FNHTR) often result in little or no morbidity, however early detection and management are crucial (Tinegate *et al.*, 2012). Other type of ATR such as acute haemolytic transfusion reaction (AHTR) may lead to severe morbidity and mortality even though after early recognition (Yahalom *et al.*, 2015). Most ATR cases are preventable whereby haemovigilance system is essential to appropriately monitor transfusion safety, to identify areas for enhanced patient safety, and to evaluate the impact of future interventions (Harvey *et al.*, 2015). This will give clue to clinicians such as to give pre-medications or not for transfusion especially patients who have ATR risk factors.

1.5 Problem Statement and Study Justification

Acute transfusion reactions (ATRs) are more common nowadays and more likely will cause severe morbidity and mortality due to blood transfusion (Haslina *et al.*, 2012). Even though most of the ATRs are not severe, ATRs can result in hospital admission for outpatients or prolonged admission for inpatient (H. Kato *et al.*,2014). Some severe ATRs can cause significant patient morbidity and mortality and can be avoided (Harvey *et al.*, 2015). It has been shown that more than 90% of total adverse transfusion reactions reported at Hospital

Sultanah Bahiyah were acute transfusion reactions. Thus continuous monitoring of acute transfusion reactions is essential to promote patient care and safety.

It was reported by Vasudev *et al.*, (2016) that their haemovigilance study on transfusion-related adverse reactions was useful to minimise the adverse reactions related to transfusion. In term of severity, blood transfusion is related with risks varying from minor to life-threatening. In order to reduce transfusion-related adverse events, prudent patient selection with practical pre-transfusion assessments of risk versus benefit together with strict quality control is an effective method to implement (Sharma *et al.*, 2015).

This study was aimed to reduce the number of ATRs at Hospital Sultanah Bahiyah by identifying the characteristics and associated factors of ATRs in order to implement appropriate interventions.

Chapter 2 :

OBJECTIVES

Chapter 2

OBJECTIVES

2.1 General Objective

To analyse the prevalence and study the characteristics of acute transfusion reactions at Hospital Sultanah Bahiyah.

2.2 Specific Objectives

i. To determine the prevalence of acute transfusion reactions (ATRs).

ii. To determine the association between ATRs with patients' demographics (age, gender, blood group, history of the previous transfusion, history of pregnancy).

iii. To determine the association between ATRs with the characteristics of blood components (days of storage, blood group).

2.3 Null Hypotheses

H_{01}: There is no significant association between ATRs with patients' demographics.

H_{02}: There is no significant association between ATRs with the characteristics of blood components.

2.4 Alternative Hypotheses

H_{A1}: There is a significant association between ATRs with patients' demographics.

H_{A2}: There is a significant association between ATRs with the characteristics of blood components.

Chapter 3:

STUDY MANUSCRIPT

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	Subtotal Posi ve[a]			Subtotal Nega ve[a]			Subtotal General[a]			Total PANSS[a]		
*CYP2D6*1*	9.	7	(3.52)	8.	9	(3.86)	20.	2	(4.46)	38.	7	(10. 11)
*CYP2D6*4*	9.	8	(2.75)	7.	3	(0.50)	22.	3	(5.32)	39.	3	(8. 42)
*CYP2D6*5*	10.	9	(2.78)	9.	2	(3.74)	22.	5	(6.26)	42.	6	(11. 13)
*CYP2D6*10*	9.	4	(2.63)	8.	8	(3.77)	20.	6	(4.27)	38.	9	(8. 96)
Duplica on	11.	2	(5.01)	14.	1	(7.67)	24.	5	(8.76)	49.	8	(19. 31)
F sta s c (*df*)	1.	29	(4, 289)	4.	44	(4, 289)	2.	67	(4, 289)	3.	22	(4, 289)
P value[b]	0.	276		0.	002		0.	033		0.	013	
NA	8.	1	(2.19)	7.	2	(0.65)	18.	8	(2.90)	34.	1	(4. 86)
Total	9.	6	(3.12)	8.	9	(3.97)	20.	5	(4.65)	39.	1	(10. 02)

[a]Mean (SD). [b]Analysis of variance (ANOVA). NA represents samples that were ampli able during rst PCR, but genotypes were not determined during the second PCR. Samples were screened for *CYP2D6*3, *4, *5, *6, *9, *10, *14, *17,* and duplica on gene.

Source: Zahari et al. *Malays J Med Sci.* 2009;**16(3)**:13–21.

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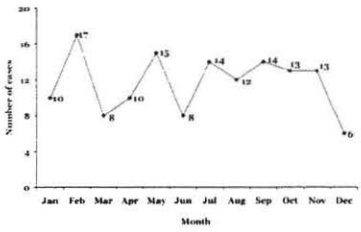
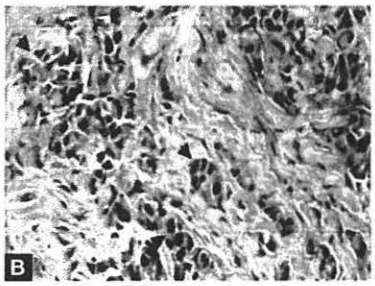
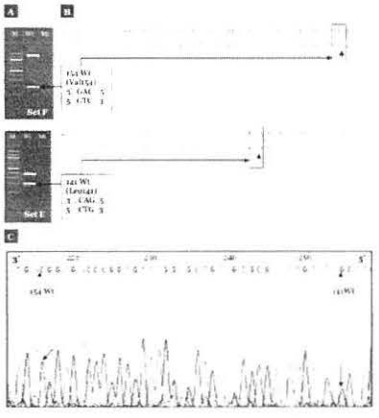
Line Art Lines and texts (without tonal or shaded area)		TIFF or EPS	1000 dpi Half page = 8 cm Full page = 16 cm	RGB
Hal one Con nuous tone photograph (without text)		TIFF	300 dpi Half page = 8 cm Full page = 16 cm	RGB
Combina on Hal one and line art elements		TIFF or EPS	600 dpi Half page = 8 cm Full page = 16 cm	RGB

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3.2 Draft Manuscript

Haemovigilance Study of Acute Transfusion Reactions at Hospital Sultanah Bahiyah

Running head : Acute transfusion reactions and haemovigilance

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Abstract

Introduction: Acute transfusion reactions (ATRs) are commonly reported in clinical transfusion practice, and they may result in significant morbidity and mortality. Haemovigilance system plays a major role in the monitoring of ATRs for prevention, as well to promote patient care and safety. This study aims to explore the characteristics and associated factors of ATRs at Hospital Sultanah Bahiyah, Kedah, Malaysia.

Methods: This was a retrospective study using records from haemovigilance forms of reported transfusion reactions, E-Delphyn (blood bank system) and E-His (hospital information system). A total of 118 cases of ATRs from January 1st 2015, until December 31st 2017, were selected and analysed. For each case, a control was selected from a patient who did not develop ATR.

Results: A total of 122,215 units of whole blood and blood component transfusions were performed and 415 ATRs were reported. The prevalence of ATR was 0.34% or one in 294 units transfused. The most common ATR is allergic reactions with 62 cases (52.5%), followed by febrile non-haemolytic transfusion reactions with 45 cases (38.1%), transfusion-associated circulatory overload with four cases (3.4%), and transfusion-associated dyspnoea with four cases (3.4%). Allergic reaction was significantly associated with female patients ($p = 0.038$) and the paediatrics age group ($p = 0.038$). There was a significant association between febrile non-haemolytic transfusion reaction and red blood cells (RBCs) stored >14 days ($p = 0.002$).

Conclusion: The prevalence of ATRs at Hospital Sultanah Bahiyah was low and are associated with female patients, paediatric age group, and RBC's storage duration.

(249 words)

Keywords *: Acute transfusion reaction, haemovigilance, prevalence*

Introduction

Haemovigilance was first developed in France and Japan in 1993 as a reaction to the risks of blood transfusion following the emergence of Human Immunodeficiency Virus (HIV) during that time (1). Haemovigilance consists of procedures during the blood transfusion process, from blood donation and blood component preparation, through to their provision and transfusion to recipients, as well as their follow up. It also involves the monitoring, reporting, investigation, and analysis of adverse events that occurred during blood donation, processing and transfusion, which prompted the need to prevent their occurrence or recurrence (2). Quality aspects of blood transfusion, such as appropriate use of blood, can be improved by adhering to haemovigilance systems (3). In Malaysia, all adverse events that happened during blood collection, processing, testing, transfusion procedures, and the outcome of the transfusion (including near misses) must be reported to the Hospital Transfusion Committee (HTC), the State Transfusion Committee (STC), and the National Haemovigilance Coordinating Centre (NHCC). This study is focused on acute transfusion reaction cases reported from 2015 to 2017 at Hospital Sultanah Bahiyah, which is a tertiary hospital in Kedah, Malaysia. The Department of Transfusion Medicine of this hospital supplies blood and blood components to various speciality and sub-speciality services. An acute transfusion reaction (ATR) is a reaction in which signs and symptoms occur within 24 hours of a blood transfusion (4). Acute transfusion reactions (ATRs) are more common nowadays and they are more likely to lead to severe morbidity and mortality following transfusion (5). Studies done before revealed that ATRs were associated with red blood cell transfusion (9), paediatric patients (12), red blood cells stored > 14 days (13), history of transfusion and history of pregnancy (13). Continuous quality enhancement of the transfusion process through corrective and preventive actions to boost donor and patient safety, improve transfusion appropriateness, and decrease wastage are the

goals of haemovigilance (2). ATRs can result in hospital admission for outpatients or prolonged admission for inpatients, even though most ATR cases are not severe (6). Severe transfusion reactions can lead to significant patient morbidity and mortality, which can be avoided. (7). At the Hospital Sultanah Bahiyah (HSB), most of the reported adverse transfusion reactions were acute transfusion reactions. These ATRs included allergic reactions and febrile non-haemolytic transfusion reactions (FNHTR). Prompt recognition and management are crucial, even though both types of ATRs often result in little or no morbidity (8). Hence, continuous monitoring of ATRs are essential to promote patient care and safety. This study (Ethical Approval No. : USM/JEPeM/17120692) was conducted at Immunohaematology Laboratory, Department of Transfusion Medicine, Hospital Sultanah Bahiyah. The study population were focused on all the patients who being transfused from January 1st 2015 until 31st December 2017. This study was designed to determine the prevalence, the characteristics and associated factors of ATRs in order to develop appropriate interventions to reduce ATR incidence at Hospital Sultanah Bahiyah.

Materials and Methods

i. Sampling Method

Systematic random sampling was used to select 118 cases of acute transfusion reactions (ATRs) from January 1st 2015, until December 31st 2017 from total of 415 cases. Given that this was a matched case-control study (matched by the type of blood component transfused), control for each case was selected from patients who did not develop ATR during the study period with ratio of 1 : 1. A subject was taken from every three samples while control was taken from every fifth sample until a match for the type of blood component transfused was found.

For ATR cases, the inclusion criterion was transfused patients who developed acute transfusion reactions and the reports were sent to the laboratory during the study period. The exclusion criteria were reported transfusion reaction cases that were not concluded as acute transfusion reactions and uncomplete reporting forms.

For non-ATR cases (control), the inclusion criterion was transfused patients who did not develop acute transfusion reactions during the study period, while the exclusion criteria were patients who requested the Group, Screen and Hold (GSH) test, and patients who requested the Group and Crossmatch (GXM) test, but were not transfused.

ii. Research Tool

Data were collected from the adverse transfusion event reporting form, the report of reaction to blood or plasma form, and the worksheet for investigation of transfusion reaction which are kept at the Immunohematology Laboratory, Department of Transfusion Medicine, Hospital Sultanah Bahiyah.

The E-His system was used to collect patients' clinical information. The E-His system is a computerised hospital information system at Hospital Sultanah Bahiyah that stores medical records for easy assessments. Additional information related to the patient such as blood group, transfusion history and blood component characteristics were traced from the E-Delphyn system, which is a computerised blood bank information system used at Hospital Sultanah Bahiyah.

iii. Data Analysis

Descriptive statistics were analysed for their frequencies and percentage distributions for categorical variables, while continuous data were presented as means and standard deviation (SD). The conditional regression analysis for matched data for both univariate and multivariate

analyses was performed using the Cox proportional hazard model. The interaction was checked and adjusted for confounding factors. The final model was selected based on the principle of parsimony and best fit using the Hosmer Lemeshow approach of using -2 log-likelihood ratios. A p-value of < 0.05 was considered statistically significant. Data were analysed using the IBM SPSS Statistics V24 under IBM Corporation, New York.

Results

i. Prevalence

During the study duration, which was from 2015 to 2017, a total of 122, 215 units of whole blood and blood component transfusions were performed. Clinicians reported a total of 415 ATRs during the study period. A total of 118 ATR cases were selected using systematic random sampling.

Prevalence of ATR (%) = number of ATRs/number of blood components transfused

= 415/122, 215

= 0.34%

ii. Types of ATRs

Out of 415 acute transfusion reaction (ATR) cases identified during the period of the year 2015 to 2017, 118 acute transfusion reaction cases were randomly selected by using systematic random sampling. Descriptively, the most frequently reported ATR type throughout the study period was allergic reaction (52.5%), followed by febrile non-haemolytic transfusion reaction (FNHTR) (38.1%), transfusion-associated circulatory overload (TACO) (3.4%), transfusion-associated dyspnoea (3.4%), suspected transfusion-related acute lung injury (TRALI) (1.7%) and anaphylactic (0.8%) as shown in Table I.

Table I: Types of Reported Acute Transfusion Reactions (n=118)

Type of Acute Transfusion Reaction	n (%)
a) Allergic reaction	62 (52.5)
b) Febrile non-haemolytic transfusion reaction (FNHTR)	45 (38.1)
c) Transfusion-related circulatory overload (TACO)	4 (3.4)
d) Transfusion-associated dyspnoea (TAD)	4 (3.4)
e) Suspected transfusion-related acute lung injury (TRALI)	2 (1.7)
f) Anaphylactic	1 (0.8)

iii. Association between Patients' Demographics and Characteristics of Blood Components with ATR

The recipients were categorised as adults (≥18 years old) and paediatrics (<18 years old). The adult group showed a higher percentage for ATR at 83.9%, while the percentage of ATR among the paediatrics group was 16.1% (Table II). In the univariate analysis, a significant association was found between the occurrence of ATR and the paediatrics group ($p = 0.005$) (Table III). The risk of developing ATR was five times higher in the paediatrics patients compared to the adults (crude OR 4.74, 95% CI 1.62-13.96).

As for gender, female patients showed a higher percentage of ATR at 65.3%, while for male patients, the percentage was 34.7%, with the odds of 3.13 (crude OR = 3.13, 95% CI 1.75-5.60) times higher in females compared to males ($p < 0.001$). Patients with blood group O showed the highest percentage of 42.2%, followed by blood group B (28.8%), blood group A (23.7%), and blood group AB (5.1%). However, no significant difference was observed between each blood group.

The most common signs or symptoms reported for ATR were fever only (21.2%), followed by fever with chills and rigors (17.8%), urticaria (45.8%), rashes (5.9%), dyspnoea (8.5%), and dyspnoea/urticarial/periorbital oedema (0.8%). Next, the univariate analysis showed that ATR cases were more commonly presented with the history of transfusion compared to non-ATR cases ($p=0.038$). On the other hand, a significant difference in the occurrence of ATR was also observed among patients with a history of pregnancy (50.8%) compared to those without this

attribute in the univariate analysis, with the odds of 3.00 (crude OR=3.00, 95% CI 1.55-5.79, p = 0.038).

ATRs were mostly seen after the transfusion of red cells (70.3%), followed by whole blood (14.4%), fresh frozen plasma (11.0%), and platelets (4.2%). During this study period, no ATR case were reported from the transfusion of cryoprecipitate and cryosupernatant. Transfusion of blood components that were in more than 14 days of storage (>14 days) showed a higher percentage of ATR cases, (74.6 %), while blood components that were in less than 14 days of storage (0-14), 25.4% of ATR cases were reported, and this difference was significant ($p < 0.001$). As for the blood groups of the blood components transfused, the O blood group was the most reported (43.2%), followed by the B blood group (28.0%), the A blood group (23.7%) and the AB blood group (5.1%), with no significant difference.

However, in the multivariable analysis, age, gender, the history of transfusion and history of pregnancy are no longer contribute to the occurrence of ATR. The only blood characteristic factor that independently associated with the occurrence of ATR in this study is days of blood storage. It shows that patients transfused with blood components stored more than 14 days were 65 times higher possibility of experiencing ATR compared to those transfused with blood components stored $\leq$ 14 days (adj OR=65.29, 95% CI 9.29-458.85). The results mentioned above are shown in Table II and III.

Given both allergic reaction and febrile non-haemolytic transfusion reaction (FNHTR) were the most commonly reported ATR in this study, both types of ATR were selected for the specific analysis to determine the association between febrile non-haemolytic transfusion reaction (FNHTR) and allergic reaction with patients' demographics and characteristics of blood components.

Table II: Patients' Demographics and Characteristics of Blood Components Among ATR Cases (n=118)

Variables	n (%)
Patients' Demographics	
Adult	99 (83.9)
Paediatrics	19 (16.1)
Gender;	
-Male	41 (34.7)
-Female	77 (65.3)
Blood group ;	
-A	28 (23.7)
-B	34 (28.8)
-O	50 (42.4)
-AB	6 (5.1)
Signs and symptoms ;	
-Fever only	25 (21.2)
-Fever with chills and rigors	20 (17.8)
-Urticaria	54 (45.8)
-Rashes	8 (5.9)
-Dyspnoea	10 (8.5)
-Dyspnoea,urticaria,periorbital edema	1 (0.8)
History of transfusion	58 (49.2)
History of pregnancy	60 (50.8)
Characteristics of Blood Components	
Type of Blood Component ;	
-Whole blood	17 (14.4)
-Red cell	83 (70.3)
-Fresh frozen plasma	13 (11.0)
-Platelet	5 (4.2)
-Cryoprecipitate	0 (0)
Days of storage ;	
-0-14	30 (25.4)
->14	88 (74.6)
Blood groups ;	
-A	28 (23.7%)
-B	33 (28.0%)
-O	51 (43.2%)
-AB	6 (5.1%)

Table III: Association between ATRs with Patients' Demographics and Characteristics of Blood Components

Variables	ATR Group (n=118) n (%)	Non-ATR Group (n=118) n (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Age group ;				
Adult	99(83.9)	114(96.6)	Reference	
Paediatrics	19(16.1)	4(3.4)	4.75(1.62-13.96)*	
Gender ;				
Male	41(34.7)	73(61.9)	Reference	
Female	77(65.3)	45(38.1)	3.13(1.75-5.60)*	
Blood group ;				
A	28(23.7)	35(30.0)	0.93(0.29-3.00)	
B	34(28.8)	27(22.9)	1.37(0.44-4.32)	
O	50(42.4)	49(41.5)	1.14(0.37-3.56)	
AB	6(5.1)	7(5.9)	Reference	
History of transfusion	58(49.2)	42(35.6)	1.76(1.03-3.01)*	
History of pregnancy	60(50.8)	26(22.0)	3.00(1.55-5.79)*	
Days of storage ;				
0-14	30(25.4)	98(83.1)	Reference	
>14	88(74.6)	20(16.9)	65.29(9.29-458.85)*	65.29 (9.29-458.85)
Blood groups ;				
A	28(23.7)	38(32.20	1.04(0.31-3.52)	
B	33(28.0)	24(20.3)	1.77(0.52-6.00)	
O	51(43.2)	48(40.7)	1.40(0.42-4.61)	
AB	6(5.1)	8(6.8)	Reference	

*significant with $p<0.05$

iv. Association between Allergic Reaction with Patients' Demographics and Characteristics of Blood Components

The analysis results of allergic reactions, showed that allergic reaction was significantly associated with female patients (p = 0.038) and the paediatrics age group (p = 0.038) (Table IV). There was no significant difference with other variables which were blood group, history of transfusion, history of pregnancy. Allergic reaction was also significantly associated with days of storage > 14 days (p = 0.011) in the univariate analysis, but the effect was no longer observed after controlling for patients' age and gender.

Table IV: Association between Allergic Reaction with Patients' Demographics and Characteristics of Blood Components

Variables	Allergic group (n=62) n(%)	Non allergic group (n=62) n(%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Age ;				
Adults	45(72.5)	61(98.4)	Reference	
Paediatrics	17(27.5)	1(1.6)	17.00 (2.26-127.74)*	9.351(1.14-76.94)*
Gender ;				
Male	24(38.7)	37(59.7)	Reference	
Female	38(61.3)	25(40.3)	2.44(1.13-5.31)*	3.484(1.07-11.32)*
Blood group ;				
A	13(21.0)	19(30.6)	0.61(0.15-2.52)	
B	20(32.3)	16(25.8)	0.98(0.24-4.01)	
O	24(38.7)	23(37.1)	0.85(0.21-3.45)	
AB	5(8.1)	4(6.5)	Reference	
History of transfusion	28(45.2)	19(30.6)	1.90(0.88-4.09)	
History of pregnancy	19(30.6)	15(24.2)	2.09(0.87-5.00)	
Days of storage ;				
0-14	21(33.9)	46(74.2)	Reference	
>14	41(66.1)	16(25.8)	65.289(2.62-1627.33)*	
Blood groups ;				
A	13(21.0)	23(37.1)	0.676(0.16-2.95)	
B	19(30.6)	14(22.6)	1.304(0.29-5.96)	
O	25(40.3)	20(32.3)	1.236(0.28-5.40)	
AB	5(8.1)	5(8.1)	Reference	

*significant with p<0.05

v. Association between Febrile Non-Haemolytic Transfusion Reaction (FNHTR) with Patients' Demographics and Characteristics of Blood Components

The analysis of FNHTR showed that it was significantly associated with days of blood storage > 14 days (adj OR=65.29 95% CI 4.64-918.05, p = 0.002) (Table V). There was no significant difference in other variables which were age, gender, patient's blood group, history of transfusion, history of pregnancy, and blood component's blood group.

Table V: Association between Febrile Non-haemolytic Transfusion Reaction (FNHTR) with Patients' Demographics and Characteristics of Blood Components

Variables	FNHTR group (n=45) n(%)	Non FNHTR group (n=45) n(%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Age ;				
Adults	43(95.6)	43(95.6)	Reference	
Paediatrics	2(4.4)	2(4.4)	1.00(0.14-7.10)	
Gender ;				
Male	13(28.9)	29(64.4)	Reference	
Female	32(71.1)	16(35.6)	4.20 (1.58-11.14)*	
Blood group ;				
A	11(24.4)	15(33.3)	Reference	
B	10(22.2)	7(15.6)	1.80(0.50-6.47)	
O	24(53.3)	21(46.7)	1.51(0.57-4.02)	
AB	-(0)	2(4.4)	0.000	
History of transfusion	24(53.3)	20(44.4)	1.44(0.62-3.38)	
History of pregnancy	20(44.4)	9(20.0)	4.93(1.57-15.50)*	
Days of storage ;				
0-14	6(13.3)	43 (95.6)	Reference	
>14	39(86.7)	2(4.4)	65.29(4.64-918.05)*	65.29(4.64-918.05)
Blood groups ;				
A	11(24.4)	14(31.1)	Reference	
B	10(22.2)	6(13.3)	2.00(0.51-7.79)	
O	24(53.3)	23(51.1)	1.33(0.50-3.57)	
AB	-(0)	2(4.4)	0.000	

*significant with p<0.05

Discussion

i. Prevalence and Types of ATR

The prevalence of ATR during the study period was 0.34% or one in 294 units transfused, which is lower compared to the previous study by Sharma et al. (2015) which was 0.92% and Rabeya et al. (2011) which was 0.54% (9,11). Haslina et al. (2012) and Hussain et al. (2015) reported slightly lower prevalence of ATR, 0.23% (5, 10). Cases of allergic reaction were the highest frequency of acute transfusion reaction (52.5%), presented with urticaria and rashes, followed by febrile non-haemolytic transfusion reaction (FNHTR) (38.1%). These findings are similar to findings by Haslina et al. (2012), who reported that the most commonest ATRs were allergic reactions (50.2%), followed by febrile non-haemolytic transfusion reaction (38%) (5). A study Sharma et al. (2015) in India reported that allergic reactions and FNHTR were the most common among all types of acute transfusion reactions (9). However, a study by Hussain et al. (2015) in Pakistan observed FNHTR as the most frequent reaction (47%), followed by allergic reactions (45%) (10). The reported suspected TRALI cases were not further investigated to look for the presence of anti-HLA for TRALI diagnosis confirmation as the patients were discharged well.

ii. Association between Patients' Demographics and Characteristics of Blood Components with ATR

This current study found that adult patients showed a higher frequency of ATRs (83.9%) compared to the paediatrics age group. This could be because the higher demand for blood transfusion for adult patients in the study location. The results of this study also indicated that the frequency of ATRs was higher in females (65.3%) than in males (34.7%), with a significant difference. This finding is consistent with the finding by Sharma et al. (2015), who found that