DAY AND NIGHT TIME PACKED RED BLOOD CELLS TRANSFUSION PRACTICE AMONG ADULT PATIENTS IN NON-EMERGENCY WARDS AT HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM) KELANTAN

By

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DISCLAIMER

I hereby declare that this manuscript including the writing-up is my work. I have acknowledged all references used either quoted directly or paraphrased have been indicated by in-text citations. I declare that I have no financial interest in the instruments or materials used in this study.

Date: 17th May 2021

Dr. Mohd Redzuan Bin Abdullah

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LIST OF SYMBOLS ABBREVIATIONS OR NOMENCLATURE

CS	Caesarean section
FFP	Fresh frozen plasma
HA	Health attendance
Hb	haemoglobin
HREC	Human Research Ethics Committee
HUSM	Hospital Universiti Sains Malaysia
MLT	Medical Lab Technologist
NBC	National Blood Centre
NS	Nurse sister
O&G	Obstetrics and gynaecology
OFMS	Oral maxillofacial surgery
PRBC	Packed red blood cells
SHOT	Serious Hazard of Transfusion
SN	Staff nurse
SPSS	Statistical Package for the Social Science
IBM	International Business Machines Corporation
TMU	transfusion medicine unit
UKMMC	Universiti Kebangsaan Malaysia Medical Centre
USM	Universiti Sains Malaysia

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ABSTRAK

PENGENALAN: Polisi perkhidmatan transfusi adalah tidak mengalakkan transfusi darah pada waktu malam kecuali untuk kes-kes kecemasan. Walaubagaimanapun, transfusi darah pada waktu malam masih lagi berleluasa di kebanyakan hospital terutamanya di wad-wad bukan kecemasan. Kajian ini bertujuan untuk mengaudit amalan semasa transfusi darah merah dan melihat pematuhannya terhadap garis panduan transfusi darah kebangsaan.

KAEDAH: Kajian rentas melibatkan pengumpulan data retrospektif telah dijalankan bagi 385 pesakit dalam dewasa yang menerima transfusi darah merah di Hospital Universiti Sains Malaysia (HUSM) bermula pada 1 Januari 2017 sehingga 31 Disember 2018. Pesakit-pesakit yang terpilih dibahagikan kepada kumpulan transfusi pada waktu siang dan malam. Definisi transfusi darah pada waktu malam adalah mereka yang menerima transfusi di antara jam 8 malam dan 8 pagi. Data berkenaan demografi, ciri-ciri klinikal, dan tiga selang masa proses transfusi telah dikumpulkan daripada borang permintaan transfusi darah, sistem dalam talian MyTransfusi, dan fail klinikal pesakit. Faktor-faktor berkaitan pemindahan darah pada waktu malam di analisa menggunakan "multiple logistic regression" analisis.

KEPUTUSAN: Jumlah transfusi darah merah adalah sebanyak 13,090 unit. Kadar peratusan transfusi darah merah pada waktu malam adalah 19.3% (2,523 unit). Secara amnya, pesakit yang menerima transfusi pada waktu malam adalah wanita (56.2%),

berbangsa Melayu (93.8%), kumpulan darah jenis O (35.7%), dan daripada disiplin perubatan (28.6%). Hanya seramai 44 (39.3%) pesakit yang menerima transfusi darah pada waktu malam diklasifikasikan ke dalam kumpulan indikasi transfusi klinikal akut. Kebanyakan transfusi darah merah pada waktu malam berlaku selepas 30 minit unit darah merah dikeluarkan dari tabung darah iaitu sebanyak 70 pesakit (62.5%). Selain itu, 29 pesakit (25.9%) pada waktu malam juga menerima transfusi melebihi 4 jam. Transfusi cryoprecipitate adalah 2.7 kali ganda lebih kerap pada waktu malam (adjusted OR= 2.70; 95% CI= 1.04,7.01; P= 0.041). Tambahan pula, kesan sampingan transfusi 7.1 kali ganda lebih berisiko berlaku pada waktu malam (adjusted OR= 7.07; 95% CI= 1.26,39.71; P= 0.026).

KESIMPULAN: Walaupun amalan transfusi darah merah pada waktu malam adalah rendah, terdapat kenaikan risiko kesan sampingan transfusi pada waktu ini lalu meningkatkan risiko morbiditi dan kematian pesakit.

Kata kunci: pemindahan darah, waktu, sel darah merah, bukan kecemasan

ABSTRACT

Day And Night Time Packed Red Blood Cells Transfusion Practice Among Adult Patients In Non-Emergency Wards At Hospital Universiti Sains Malaysia (HUSM), Kelantan

Background: Most of the transfusion services have a policy of strongly discouraging blood administration at night unless for emergency cases. However, blood transfusion at night is still a common practice in most hospitals even in the non-emergency wards. Thus, this study aimed to audit the practice of PRBC transfusion and its compliance towards national transfusion guideline.

Methods: This is a cross-sectional study involving a retrospective data collection of 385 adult inpatients who received PRBC transfusion in Hospital Universiti Sains Malaysia (HUSM) from 1st January 2017 to 31st December 2018. The selected patients were grouped into day and night time transfusion. Night time blood transfusion is defined as those who received PRBC between 8.00 pm to 8.00 am. Data for demographics, clinical characteristics, and three time intervals of transfusion process were collected from blood transfusion request form, MyTransfusi online system, and patient case note. Factors associated with night time blood transfusion were analysed using multiple logistic regression.

Results: Total PRBC transfusion was 13,090 units. The prevalence of night time PRBC transfusion was 19.3% (2,523 units). Generally, female (56.2%), Malay (93.8%), blood

group O (35.7%), and from the medical discipline (28.6%) were the highest group of patients transfused at night. There were only 44 (39.3%) patients who received night time transfusion classified into acute clinical need group of transfusion indication. Most of the night time PRBC were transfused after 30 minutes issued by the blood transfusion service which were 70 patients (62.5%). Besides, 29 patients (25.9%) for night time group of patients received transfusion beyond four hours limit. Cryoprecipitate was 2.7 times more likely to be transfused at night (adjusted OR= 2.70; 95% CI= 1.04,7.01; P= 0.041). Adverse transfusion reaction was 7.1 times higher risk to develop at night (adjusted OR= 7.07; 95% CI= 1.26,39.71; P= 0.026).

Conclusion: Even though the practice of the night time PRBC transfusion was low, there was an increased in adverse transfusion reactions during this time and thus potentially increased morbidity and mortality of patients.

Key words: transfusion, time, red blood cells, non-emergency

CHAPTER ONE

INTRODUCTION

1.1 Overview

This chapter covers the outline of the day and night time packed red blood cells transfusion practice among adult patients in non-emergency wards. This chapter also highlights the research justifications and research questions.

1.2 Background of the study

Red cell concentrate or packed red blood cells (PRBC) is defined as a component obtained by removing most of the plasma from whole blood (NBC, 2016). Indications of PRBC are replacement of red cells in anaemic patients and in acute blood loss (WHO, 2005).

Most of the transfusion services in Malaysia have a policy of strongly discouraging blood administration at night unless in an emergency. Data regarding the appropriateness of blood transfusion at night in our hospital is lacking. A normal working hour in Malaysia including HUSM is from 8.00 am to 5.00 pm. In most hospital settings, the staff is at a minimal number outside normal working hours. Thus, limited staff available for blood preparation, administration, and monitoring during a blood transfusion. An inadequate number or shortage of staff will obscure early clinical detection of adverse transfusion reactions. The Transfusion Medicine Unit (TMU) has fewer resources to respond in the event of adverse transfusion reaction and transfusion error. Additionally, non-urgent night transfusion

interrupts the sleep of the patient and others in their cubicle throughout the procedure (Rachel D et al., 2016, Xu T et al., 2016).

Australian and New Zealand Society for Blood Transfusion (ANZSBT), British Committee for Standards in Haematology (BCSH), and Serious Hazard of Transfusion (SHOT) United Kingdom recommended avoiding blood transfusions outside of core hours unless indicated clinically (Rachel D et al., 2004, Stainsby D et al., 2005, BCSH, 2009). Available data and audits indicate blood transfusion activities outside normal working hours are less safe. The blood component should not be transfused at night unless indicated by thorough clinical judgement.

1.3 Literature review

1.3.1 Time of blood transfusion

A normal working hours in most workplaces including in Malaysia is between 8.00 am and 5.00 pm. However, night blood transfusion is defined as those who received blood products between 8.00 pm and 8.00 am (Stainsby D et al., 2005, Rachel D et al., 2016, Aubron C et al., 2018). In another study, it is defined as blood transfusion between 8.00 pm and 6.00 am (Ambler E, 2006). These are the period in which medical and nursing staffs are at their minimum. The difference in definition is due to different hospital settings and working shift.

1.3.2 Night time transfusion and transfusion error

Annual report SHOT United Kingdom in 2003 (Stainsby D et al., 2003) reported 232 errors in collection and administration of 187 transfusion cases. Of the 176 transfusion cases, 65

cases (37%) occurred between 8.00 pm to 8.00 am. It is of note that of the 33/176 (19%) transfusions started between 12.00 am to 8.00 am, 48% (16 cases) transfusions were considered as 'routine'. Frietsch et al analysed blood product administration errors submitted to The German Interdisciplinary Task Force for Clinical Hemotherapy (IAKH) registry from 2009 to 2013 (N:138 cases) (Frietsch T et al., 2017). Transfusion steps with errors were administration to the patient (27.2%), indication and blood order (17.1%), patient identification (17.1%), and blood sample withdrawal and tube labeling (18.0%) (Frietsch T et al., 2017). Circumstances and contributing factors were routine (66%), night/weekend service (39%), communication error (36%), emergency (26%), and leasing or personnel in education (19%) (Frietsch T et al., 2017).

1.3.3 Factors associated with night time blood transfusion

National Health Service Blood and Transplant (NHSBT) conducted an audit regarding overnight blood transfusion in NHS Trusts and independent hospitals across England, Wales, Northern Ireland, and Scotland in 2008. The transfusion indications were grouped as acute clinical need (group 1) which was for patients with active bleeding/hemolysis at the time of transfusion, or patients with low haemoglobin (Hb) and symptomatic, less acute clinical need (group 2) which was for patients transfused while in theatre or to raise their Hb before surgery/procedure the following days, and group 3 was for patients who received transfusion so that they could be discharged same/next day, oncology/hematology patients with limited line time, and patients transfused outside normal working hours to complete transfusion episode. Group 4 was patients that were transfused for reasons that did not fall into the above categories are classified. This audit found that out of 2138 patients transfused, those that received after hours transfusion were 1237 (57.9%) from group 1,

29 (1.4%) patients from group 2, 196 (9.2%) patients from group 3, and 676 (31.6%) patients from group 4 (Tanya H et al., 2008).

Rachel D et al assessed 535 red cell units that were transfused between 8.00 pm and 8.00 am in eight of New Zealand's largest public hospitals over four weeks in 2010. They found that the indication for most overnight transfusion was symptomatic anaemia (43%) and active bleeding/hemolysis (23%). However, a significant proportion of patients (16%) had asymptomatic anaemia. Of concern, the latter group had a higher mean pre-transfusion Hb of 82 g/dl compare to symptomatic anaemia which was 72 g/dl (t-test, $P<0.0001$) (Rachel D et al., 2016).

Another study by Aubron C et al 2018 conducted a research to compare the characteristic of patients and transfusion during the day (8.00 am-8.00 pm) and night (8.00 pm-8.00 am) in critically ill patients (N: 874). They found that no difference in clinical severity (based on APACHE score III), and mortality between patients receiving blood products day time and night time. Major bleeding was the indication for transfusion in 33 (12%) of patients transfused in day time only and 78 (30%) of patients transfused at night ($P<0.001$). Improvement of oxygen delivery is the commonest indication among patients transfused day time, overnight, and both day and night with 51%, 32%, and 53% of patients respectively ($P<0.01$). Night time transfusion was independently associated with increased odds of major bleeding (odds ratio 3.16, 95% confidence interval, 2.00–5.01). Pre-transfusion Hb at night (median 76 g/dL) was lower compared to 78 g/dL during day time (P-value<0.01) (Aubron C et al., 2018).

1.3.4 Decision of blood transfusion

PRBC transfusion decision depends on several factors such as overall clinical condition, patient preferences, alternatives therapies, and pre-transfusion Hb. The overall clinical condition includes cardiopulmonary reserve, volume of blood loss, oxygen consumption, and atherosclerotic disease. Furthermore, there is also a recommendation for PRBC transfusion based on pre-transfusion Hb level such as the guideline by National Health and Medical Research Council (NHMRC):

Table 1.1: NHMRC guidelines for PRBC transfusion based on Hb level (NHMRC, 2001)

Haemoglobin threshold	Description
Hb < 70 g/L	- Transfusion of red cells is usually indicated. A lower threshold may be acceptable in patients without symptoms and/or where specific therapy is available, e.g.vitamin B12 administration in patients with pernicious anaemia to correct the anaemia.
Hb: 70–100 g/L	- Transfusion is likely to be appropriate during surgery associated with major blood loss or if there are signs of symptoms of impaired oxygen transport.
Hb: <80 g/L	- Transfusion may be appropriate to control anaemia-related symptoms in a patient on a chronic transfusion regime or during bone marrow suppression therapy.
Hb: >100 g/L	- Transfusion of red cells is not likely to be appropriate unless there are specific indications.

In another study, a Hb level of 70 g/L is recommended as a transfusion threshold for the haemodynamically stable adult patient including in a critically ill patient. This study also recommended that Hb level of 80 g/L as a transfusion threshold for the patient that

undergoing orthopaedics or cardiac surgery and those with pre-existing cardiovascular disease. However, these recommendations do not apply to a certain condition such as acute coronary syndrome, severe thrombocytopenia (haematological or oncological disorders that are at risk of bleeding), and chronic transfusion-dependent anaemia (Carson JL et al., 2016).

1.3.5 Risk of blood transfusion

Although lifesaving, PRBC transfusion is not without risk as it can lead to adverse transfusion reactions such as acute transfusion reactions which occur less than 24 hours post-transfusion (examples such as acute haemolytic transfusion reaction, febrile non-haemolytic transfusion reaction, allergic reaction, anaphylaxis, transfusion-related acute lung injury, transfusion-associated circulatory overload, septic transfusion reaction), or delayed transfusion reaction (examples such as delayed haemolytic transfusion reaction, transfusion-associated graft-versus-host disease, post-transfusion purpura, and transfusion-transmitted infection) (Sahu S et al., 2014, Kohorst MA et al., 2020). In addition to morbidity and mortality following transfusion reaction, it has also added to an extra cost to the healthcare facility with the estimation of RM 596,771 for non-serious and RM 2,985,151 for serious transfusion reactions (Janssen MP et al., 2018).

1.4 Research justification

The decision of PRBC transfusion treatment is decided upon a balance between benefits and harms to the patients. Thorough clinical examination and judgement before transfusion are essential. Every transfusion has a risk of adverse reaction either acute or delayed. The risk is increased especially at night due to reduced staffing and resources, reduced lighting,

and the patient likely to be asleep. In HUSM, transfusion at night is still a common practice as shown in Table 1.2.

Table 1.2: Dispense time of all blood components in Transfusion Medicine Unit, HUSM from January to May 2018 (Salamah AS, 2018)

Months	Office Hour (8 am-5 pm) N (%)	Outside office hour(5 pm-8 am) N (%)	Weekend N (%)	Total N (%)
Jan	954 (51.1%)	576 (30.9%)	336 (18.0%)	1866 (100%)
Feb	950 (50.5%)	531 (28.2%)	399 (21.2%)	1880 (100%)
Mar	983 (49.1%)	595 (29.7%)	426 (21.3%)	2004 (100%)
Apr	1367 (52.6%)	748 (28.8%)	483 (18.6%)	2598 (100%)
May	1074 (45.8%)	778 (33.2%)	494 (21.1%)	2346 (100%)
Total	5328 (49.8%)	3228 (30.2%)	2138 (20.0%)	10694 (100%)

Preferably, transfusion therapy shall be carried out during normal working hours (8.00 am-5.00 pm). The decision for transfusion shall be made after a thorough clinical examination and discussion between the treating physician and transfusion medicine specialist.

Transfusion therapy activity involves multiple medical personnel such as a clinician, staff nurse, transfusion medicine specialist, transfusion medical technologist, and others. However, there is a shortage of staff both in the ward and laboratory during the after normal working hours as shown in Table 1.3 and Table 1.4. Subsequently, this will lead to adversity in the whole transfusion process such as in terms of blood product preparation, testing, administration, and monitoring of the patient during the transfusion.

Table 1.3: Number of in-house staff in Transfusion Medicine Unit (TMU) according to work shift

Time	8am-5pm (office hour)	5pm-10pm (evening shift)	10pm-8am (night shift)
Number of staff (weekdays)	14 MLT	2 MLT	2MLT
Number of staff (weekend and public holiday)	2 MLT	2 MLT	2 MLT

MLT: Medical Lab Technologist

Table 1.4: Staff nurse working shift in HUSM (1 Timur Depan Ward)

Time	7am-2pm (am shift)	2pm-10pm (pm shift)	10pm-7am (night shift)
Number of staff (weekday, weekend, and public holiday)	* 4 NS (office hour 8 am-5 pm) 5 SN	* 4 NS (office hour 8 am-5 pm) 4 SN	3 SN

NS: Nurse Sister
SN: Staff Nurse

Therefore, the main purpose of this study is to have an audit study on the practice of PRBC transfusion. Transfusions that are not appropriate and not clinically indicated to occur at night and thus can be performed during normal working hours shall be identified. Additionally, even though previous studies had shown that the majority of night time transfusion was due to acute clinical need but the sample selection for those studies had included transfusion that was performed in the Emergency Department or Operation Theater (Tanya H et al., 2008, Tang YL et al., 2019). Therefore, this study focused on non-emergency wards for assessment of PRBC transfusion.

By reducing the inappropriate night time transfusion practice, it will also reduce the risks associated with blood transfusions such as transfusion reaction, near-miss, and error. Furthermore, human resources for blood transfusion services in HUSM can be utilised efficiently and economically after normal working hours. Besides that, the national guideline recommended that PRBC should be transfused within 30 minutes after taken from transfusion service and the transfusion of each PRBC shall not exceed 4 hours (NBC, 2016). The data regarding compliances towards the recommendation is lacking.

The blood component involved in this study data collection and analysis was PRBC only. The reasons are due to PRBC is the commonest blood component being used, it is associated with severe adverse transfusion reaction if an error occurs, and crossmatching is required prior to transfusion (Fung MK et al., 2014). The current study involved adult patients only. In the future, it will be extended to a patient in the pediatric age group, and other blood components such as platelet, fresh frozen plasma (FFP), and cryoprecipitate.

1.5 Research questions

(i) What is the prevalence of PRBC transfusion at day and night time among adult inpatients?

(ii) What are the patient's demographics, clinical characteristics, and time interval of PRBC transfusion of day and night time PRBC transfusion?

(iii) What are the factors associated with PRBC transfusion practice at night among adult patients admitted to HUSM?

CHAPTER TWO

OBJECTIVES

2.1 General objective

To study the day time and night time packed red blood cells (PRBC) transfusion among adult patients admitted to non-emergency wards in Hospital Universiti Sains Malaysia (HUSM), Kelantan.

2.2 Specific objectives

(i) To determine the prevalence of day and night time PRBC transfusion among adult patients.

(ii) To determine the patient's demographics, clinical characteristics, and time interval of PRBC transfusion of day and night time PRBC transfusion.

(iii) To determine factors associated with PRBC transfusion practice (demographics, clinical characteristics, and time interval of transfusion process) at night among adult patients admitted to HUSM.

2.3 Null Hypotheses

(i) H_{01}: There is no association between patient's demographics (age, gender, race, and blood group) with night time PRBC transfusion.

(ii) H_{02}: There is no association between clinical characteristics (clinical discipline, transfusion indications, pre-transfusion Hb, transfusion of other blood components, length of hospital stay, adverse transfusion reaction, and mortality) with night time PRBC transfusion.

(iii) H_{03}: There is no association between time interval of the transfusion process (interval between GXM completion until first PRBC taken by clinician, interval between PRBC issued by blood bank until start of transfusion, and interval between start of PRBC transfusion until time of completion) with night time PRBC transfusion.

2.4 Alternative hypotheses

(i) H_{a1}: There is an association between patient's demographics (age, gender, race, and blood group) with night time PRBC transfusion.

(ii) H_{a2}: There is an association between clinical characteristics (clinical discipline, transfusion indications, pre-transfusion Hb, transfusion of other blood components, length of hospital stay, adverse transfusion reaction, and mortality) with night time PRBC transfusion.

(iii) H_{a3}: There is an association between time interval of the transfusion process (interval between GXM completion until first PRBC taken by clinician, interval between PRBC issued by blood bank until start of transfusion, and interval between start of PRBC transfusion until time of completion) with night time PRBC transfusion.

CHAPTER THREE

METHODOLOGY

3.1 Study background

HUSM is established in the year 1983 and is located in Kubang Kerian, Kelantan. Kelantan is located on the East Coast of Peninsular Malaysia with a size of 14,922 square kilometres (4.4% of the total area of Peninsular Malaysia) and facing the South China Sea. It is a centre of referral that provides both medical and dentistry services to the community as well as a teaching hospital. It has 733 beds with 20 clinical disciplines. HUSM has managed to be both a service and a clinical research centre of excellence.

3.2 Study design

This was a cross-sectional study that involved retrospective data collection of adult inpatient, who received PRBC transfusion in Hospital Universiti Sains Malaysia (HUSM) from 1st January 2017 to 31st December 2018.

3.3 Study area

The study was conducted in Transfusion Medicine Unit (TMU) and Medical Record Unit of Hospital Universiti Sains Malaysia (HUSM), Kelantan.

3.4 Study population

(i) Reference population: Adult patients who lived in Kelantan and neighbouring states.

(ii) Source population: Adult patients who registered and received treatment in HUSM.

(iii) Target population: Adult patients who received a blood transfusion in HUSM.

(iv) Sampling frame: Adult inpatient who received packed red blood cells (PRBC) transfusion.

3.5 Subject criteria

3.5.1 Inclusion criteria

- Adult patients aged at least 18 years old.

- Adult patients that received PRBC transfusion during hospital admission.

3.5.2 Exclusion criteria

- Adult patients that received blood transfusion in the emergency department, intensive care unit (ICU), operation theatre, labour room, or daycare.

- Patients that received second onward PRBC transfusion from similar blood transfusion request form.

- Incomplete blood transfusion data.

3.6 Sample size

Objective 1: To determine the prevalence of day and night time PRBC transfusion among adult patients.

Single proportion: $n = (z/\Delta)^2 p (1-p)$

n = sample size

z= z statistic for a level of confidence = 1.96 (95% confidence interval)

p=expected prevalence or proportion (in proportion of one; if 100%, p=1)

Δ = precision (in proportion of one; if 5%, $\Delta = 0.05$)

Where,

n=calculated sample size

z= 1.96 for 95% confidence interval

p=expected prevalence of PRBC transfusion at night = 0.285 (Tinegate HN et al., 2007)

Δ=0.05

$n=(1.96/0.05)^2 \times 0.285 (1-0.285)$

n= 313 + 10% drop out

n= 344

Objective 2: To determine the patient's demographics, clinical characteristics, and time interval of PRBC transfusion of day and night time.

Single proportion: $n = (z/\Delta)^2 p (1-p)$

n = sample size

z= z statistic for a level of confidence = 1.96 (95% confidence interval)

p=expected prevalence or proportion (in proportion of one; if 100%, p=1)

Δ = precision (in proportion of one; if 5%, $\Delta = 0.05$)

Where,

n=calculated sample size

z= 1.96 for 95% confidence interval

p= male patient received PRBC transfusion at night = 0.65 (Aubron C et al., 2018)

Δ=0.05

$n=(1.96/0.05)^2 \times 0.65 (1-0.65)$

n= 350 + 10% drop out

n= 385

Objective 3: To determine factors associated with PRBC transfusion practice (demographics, clinical characteristics, and time interval of transfusion process) at night among adult patients admitted to HUSM.

Two proportions:

$$N = \frac{[p1(1-p1) + p2(1-p2)]}{(p1-p2)^2} \times (z\alpha + z\beta)^2$$

n=sample size

p1=proportion of the associated factor in high risk group

p2=proportion of the associated factor in low risk group

$z\alpha = 1.96$ for $\alpha = 0.05$ (two tailed) or 2.58 for $\alpha = 0.01$ (two tailed)

$z\beta = 0.84$ for 80% power or 1.28 for 90% power

Where,

n=calculated sample size

p1=proportion of major bleeding as indication of PRBC transfusion at night = 0.39 (Aubron C et al., 2018)

p2= proportion of major bleeding as indication of PRBC transfusion at daytime = 0.23 (Aubron C et al., 2018)

$z\alpha = 1.96$ for $\alpha = 0.05$ (two tailed)

$z\beta = 0.84$ for 80% power

$n = [\,[0.39(1-0.39) + 0.23\,(1-0.23)]/\,(0.39-0.23)^2\,] \times (1.96 + 0.84)^2$

n=127 + 10% drop out

n=140, 140 x 2 = **280**

The largest sample size of 385 participants was selected.

3.7 Sampling method and subject recruitment

3.7.1 Sampling method

Systematic random sampling was used as a sampling method for this study. It is a probability sampling in which the chances of each subject being selected as a study sample are equal. Our target population is large (18,580 subjects), readily available, and spread over the targeted period without hidden periodicities. Besides that, this type of sampling is simple and convenient to adopt in our limited time as a clinician to conduct the study. Inability to identify the actual time (day or night) of transfusion upfront before trace the patient's case note makes another probability sampling such as stratified random sampling, not an ideal choice.

3.7.2 Subject recruitment

A total sample of 385 patients was selected from a list of 18,580 adult patients that received PRBC transfusion in the list. Based on the systematic random sampling, the selection was started from a starting point of 37^{th} which was selected randomly using Microsoft Excel. Every 48^{th} patient on the list was chosen as a participant of our study (fixed periodic interval = 18,580/385). The first sample was selected at number 37^{th} of the list, subsequently, samples at number 85, 133, 181, and so on were selected. All the selected samples were checked against the inclusion and exclusion criteria. The count looped to the beginning of the sample list to select additional samples. Finally, the total samples selected were 436 with 51 samples were excluded. The selected patients were determined their night time and day time transfusion based on the time start of the first PRBC unit transfusion as stated in the patient's case note.

3.8 Research tool

Research tools that were used include blood transfusion request form (HUSM/MHT/L21), MyTransfusi system, and transfusion record in the patient's case note. The blood transfusion request form is a standardised request form provided by the National Blood Centre that is used throughout all hospitals in Malaysia. The form was filled up by the clinician and sent to Transfusion Medicine Unit for PRBC request. MyTransfusi system is an online system to record the transfusion activity of a patient in HUSM. A hospital case note is a legal record to document patient well-being and treatment given during the hospitalisation.

3.9 Data collection method

The request for blood transfusion was identified from the blood transfusion request form (HUSM/MHT/L21) and MyTransfusi online system. The list of patients that had received PRBC transfusion during the study period was extracted from MyTransfusi online system. The starting and completing time of PRBC transfusion was obtained from the patient's case note. Data regarding patient's demographics (age, gender, race, and blood group), clinical characteristics (discipline, indication, pre-transfusion Hb, other blood components transfusion, length of hospital stay, adverse transfusion reaction, and mortality), and time interval of transfusion process were collected from blood transfusion request form HUSM/MHT/L21, MyTransfusi online system, and transfusion record in patient's case note. Blood transfusion request form (HUSM/MHT/L21) and MyTransfusi online system were available in Transfusion Medicine Unit. The patient case note had to be obtained from

Hospital Record Unit. All the data collected was kept properly to maintain the confidentiality of the subject.

3.10 Statistical analysis

All the data were tabulated and analysed using International Business Machines Corporation (IBM) Statistical Package for the Social Science (SPSS) Statistics Version 26 IBM, New York, USA. Descriptive statistic was used to determine the prevalence of total PRBC transfusion and night time PRBC transfusion among adult inpatients. Simple and multiple logistic regression was used to analyse the association between patient's demographics, clinical characteristics, and time interval of transfusion process with time of PRBC transfusion. A two-tailed test was used and the level of significance was set at $P<0.05$.

3.11 List of variables

3.11.1 Dependent variables

(a) Day time transfusion (0)

(b) Night time transfusion (1)

3.11.2 Independent variables

(a) Age

(b) Gender

(c) Race

(d) Blood group

(e) Discipline

(f) Indication

(g) Pre-transfusion Hb

(h) Length of hospital stay

(i) Platelet

(j) Fresh frozen plasma

(k) Cryoprecipitate

(l) Adverse transfusion reaction

(m) Mortality

(n) Interval between GXM completion until 1st PRBC taken by the clinician

(o) Interval between PRBC issued by blood bank until the start of transfusion

(p) Interval between the start of PRBC transfusion until time of completion

3.12 Variables definition

(a) Adult is defined as a person at least age of 18 years old (Revision, 2006).

(b) Red cell concentrates/packed red cells is defined as a component obtained by removing most of the plasma from whole blood (NBC, 2016).

(c) Night time blood transfusion is defined as those who received blood products between 8.00 pm and 8.00 am (Stainsby D et al., 2005, Aubron C et al., 2018).

(d) Day time blood transfusion is defined as those who received blood products between 8.00 am and 8.00 pm (Stainsby D et al., 2005, Aubron C et al., 2018).

(e) Time of PRBC transfusion is defined as time start of blood transfusion as stated in the patient's case note.

(f) Age is defined as the period of time someone has been alive or something has existed (Cambridge, 2021). In this study, the actual age of the patients was recorded.

(g) Gender is defined as the physical and/or social condition of being male or female (Cambridge, 2021).

(h) Race is defined as any social group into which humans can be divided according to perceived similarities in their physical characteristics (Cambridge, 2021).

(i) Discipline is defined as clinical department or expertise available in HUSM such as medical, surgery, orthopaedic, obstetric, and gynaecology, etc.

(j) Indication for transfusion was categorised as the table below based on adaptation from previous studies (Tanya H et al., 2008, Angela W et al., 2011, Rachel D et al., 2016, Tang YL et al., 2019):

Table 3.1: Classification of transfusion indication

Group	Indication
1: Acute clinical need	- Patient with active bleeding /haemolysis at the time of transfusion regardless of haemoglobin (Hb) level. - Patient with low Hb (<10g/dL), and had symptoms/signs of anaemia such as chest pain, shortness of breath, palpitation, tachycardia, conjunctiva pallor, etc.
2: Less acute clinical need	- Patient whom received transfusion to raise their Hb before surgery/procedure. - Patient whom received transfusion during haemodialysis.
3: Pragmatic need	- Patient whom received transfusion so that they can be discharged on the same/next day. - Oncology/haematology patients with limited line time (PRBC transfusion had to be fitted in alongside many intravenous infusion).
4: Other	- Patient with low Hb (<10g/dL) but had no symptom/sign of anaemia. - Patients transfused for reasons that do not fall into the above categories.

(k) Pre-transfusion Hb is defined as Hb level prior to PRBC transfusion.

(l) Length of hospital stay is defined as the interval between admission and discharge from the hospital.

(m) Platelet is defined as a component derived from whole blood containing a majority of the original platelet content, suspended in plasma (NBC, 2016).

(n) Fresh frozen plasma (FFP) is defined as a component that contains labile clotting factors and other constituents, for transfusion or fractionation (NBC, 2016).

(o) Adverse transfusion reaction is an undesirable response or effect in a patient temporarily associated with the administration of blood or blood component (NBC, 2016).

(p) Mortality is defined as the death of the patient that happened during hospitalisation period.

(q) Interval between GXM completion until first PRBC taken by clinician is defined as time period when GXM procedure completed until first unit of PRBC taken from TMU for transfusion in the respective ward (Tang YL et al., 2019).

(r) Interval between PRBC issued by blood bank until start of transfusion is defined as time period when first unit of PRBC taken from TMU until transfusion to the patient was started. National guidelines recommended that PRBC should be transfused within 30 minutes of removal from the dedicated and validated refrigerator in transfusion service (NBC, 2016).

(s) Interval between start of PRBC transfusion until time of completion is defined as time period when PRBC transfusion was started until its completion. National guidelines recommended that transfusion duration of each PRBC unit shall not exceed 4 hours (NBC, 2016).

(t) Non-emergency ward is defined as an area in the hospital that is not dealing with patients who need acute treatment.

3.13 Methods to minimise study error

The accuracy of the acquired data was confirmed by comparing the patient's information between 3 sources which are blood transfusion request form (HUSM/MHT/L21),

MyTransfusi online system, and patient case note. The data collection was performed in stages to avoid overloading of information. Data entry mistakes were minimised by double-checking the work at 2 different times.

3.14 Ethical issue

Ethical approval for this study was granted by the Human Research Ethics Committee (HREC) Universiti Sains Malaysia (USM) with research number USM/JEPeM/18110755. This study was initiated after obtaining ethical approval which is valid until 14th April 2021. Each subject was assigned with designated codes to protect the subject's data confidentiality. The subject data can be retrieved by the researcher and team members only. Data were presented as a group and not as an individual. The use of disclosure of protected health information involves no more than minimal risk to the privacy of individuals.

(i) Subject vulnerability

No direct contact, communication, or change in the subject's clinical management. All the information was purely gathered from historical data in Transfusion Medicine Unit (TMU) and Hospital Record Unit, HUSM.

(ii) Conflict of interest

The research was not a remuneration-driven study. There was no advantage/reward in any form of any researchers in the team from the study result. There was no conflict of interest in any circumstances by other secondary bodies that may create influence on the researcher's professional judgments or actions on the conduct, procedure, and interpretation of the result.