STUDY OF RED CELL TRANSFUSION PRACTICE AMONG PAEDIATRIC ONCOLOGY PATIENTS AT HOSPITAL USM

By

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DISCLAIMER

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

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LIST OF ABBREVIATION

HUSM	Hospital Universiti Sains Malaysia
USM	Universiti Sains Malaysia
WHO	World Health Organization
JEPeM	Jawatankuasa Etika Penyelidikan (Manusia)
OMJ	Oman Medical Journal
SPSS	Statistical Package for the Social Sciences
RBC	Red blood cell
Hb	Haemoglobin
SD	Standard Deviation
ALL	Acute lymphoblastic leukaemia
AML	Acute myeloid leukaemia
NHL	Non-Hodgkin lymphoma
TRIPICU	Transfusion strategies for patients in paediatric intensive care units

LIST OF APPENDICES

ABSTRAK

PENGENALAN: Transfusi darah sejak dahulu menjadi salah satu daripada rawatan sokongan bagi kanak-kanak yang menghadapi penyakit onkologi. Kajian ini bertujuan untuk melihat amalan transfusi sel darah merah dan kesan sampingannya terhadap pesakit onkologi pediatrik di Hospital USM.

KAEDAH: Kajian kohort retrospektif ini dilakukan di Hospital USM. Seramai 192 pesakit kanak-kanak yang menghidapi penyakit hematologic onkologi dan ketumbuhan jenis kanser telah menyertai kajian ini. Data demografi, klinikal dan transfusi pesakit yang terlibat dikumpul dan dianalisa.

KEPUTUSAN: Kadar transfusi sel darah merah di kalangan pesakit onkologi pediatrik adalah 82.3%. Sebaliknya, peratusan pesakit onkologi pediatrik hanya menyumbang 7.2% daripada jumlah keseluruhan populasi pesakit pediatrik yang mendapat transfusi darah di Hospital USM. Sebelum mendapat transfusi darah, majoriti pesakit mempunyai tahap hemoglobin 6.8 g/dL dan mempunyai gejala anemia. Kejadian reaksi transfusi berlaku pada kadar 6.3%, sementara alloimunisasi sel merah berlaku pada kadar 1.9%. Tiada hubungan yang signifikan secara statistik antara kejadian reaksi transfusi terhadap usia; jantina; etnik; kategori penyakit; jumlah episod transfusi dan isipadu darah; antibiotik; kemoterapi, atau ubatan pra-transfusi.

KESIMPULAN: Meskipun transfusi sel darah merah biasa berlaku dalam kalangan pesakit onkologi pediatrik, mereka bukanlah pengguna sel darah merah paling banyak di HUSM. Secara umumnya keadaan imun pesakit yang terjejas telah menyebabkan kadar alloimmunisasi yang rendah. Walaupun kadar reaksi transfusi terhadap sel darah merah yang tinggi dalam kajian ini, faktor seperti kurangnya kes reaksi transfusi yang dilapor dari wad perlu diambil kira. Tiada kaitan yang dijumpai antara faktor yang disiasat dengan berlakunya reaksi transfusi. Protokol transfusi sel darah merah yang spesifik terhadap pesakit pediatrik onkologi mampu

membimbing para doktor membuat keputusan untuk transfusi. Amalan transfusi yang terbaik dapat mengurangkan risiko kesan sampaingan terhadap transfusi darah.

Kata kunci: Pediatrik, Onkologi, Transfusi sel darah merah, reaksi terhadap transfusi, Alloimmunisasi

ABSTRACT

INTRODUCTION: Blood transfusion has long been part of the supportive treatment for children with oncology. This study aims to look at the red blood cell (RBC) transfusion practice and its adverse effect on paediatric oncology patients at Hospital Universiti Sains Malaysia (HUSM).

METHODS: This retrospective cohort study was conducted at HUSM. A total of 192 paediatric patients with haematological and solid tumour malignancies were enrolled. Demographic, clinical and transfusion data were collected and analysed.

RESULTS: The prevalence of red blood cell transfusion among paediatric oncology patients is 82.3%. In contrast, the paediatric oncology group accounts for only 7.2% of the total transfused paediatric population at HUSM. Before the transfusion, the majority of patients had an average haemoglobin level of 6.8 g/dL and symptomatic anaemia. Transfusion reactions occurred at a rate of 6.3%, while red cell alloimmunisation occurred at a rate of 1.9%. There was no statistically significant association between transfusion reaction with patients' demographic characteristics; disease category; total transfusion episodes and volume; antibiotic; chemotherapy; and pre-transfusion medication.

CONCLUSION: Even though RBC transfusion is common in paediatric oncology, it was not the group with the highest recipient for RBC transfusion at HUSM. Due to the general patients' immunocompromised state, there is a low incidence of alloimmunisation. The possibility of underdiagnosis of transfusion reaction must be considered. The existence of established protocols is critical in assisting clinicians in justifying blood transfusion decisions. Vigilant transfusion practise lowers the risk of adverse events in blood transfusion.

Keyword: Paediatrics, Oncology, Red cell transfusion, Transfusion reactions, Alloimmunisation

CHAPTER 1
INTRODUCTION

1.1 Title

Study of Red Cell Transfusion Practice Among Paediatric Oncology Patients at Hospital Universiti Sains Malaysia (HUSM)

1.2 Overview

Unlike in adults, leukaemias and lymphomas account for a much higher proportion of all malignancies in children. Haematological malignancies account for more than 40% of new cancer diagnoses in children aged 2-14 years. Acute lymphoblastic leukaemia was the most common type in Japan, followed by acute myeloid leukaemia, non-Hodgkin lymphoma (NHL), and histiocytosis (Horibe et al., 2013). The most common solid tumours in children and adolescents are the brain and central nervous system tumours, while thyroid carcinoma and testicular germ cell tumours are more common in adolescents (Ward et al., 2014). The most common childhood tumours in Malaysia, according to the National Childhood Cancer Survey, were leukaemias, brain and spinal cord tumours, lymphoma, neuroblastoma, gonadal and germ cell tumours, kidney tumours, soft tissue sarcomas, and retinoblastoma (Lim et al., 2002).

Blood transfusion has always been a part of supportive care in children with malignancies, particularly in haematological malignancies, because the production of blood cells from bone marrow is directly affected by neoplastic diseases and can also be affected by the invasion of solid tumours and haematological malignancies' metastases. Furthermore, due to the underlying condition, bleeding from surgical procedures, and chemotherapy and radiotherapy treatments, paediatric oncology patients frequently develop anaemia. Currently,

there is a trend toward more intensive treatment protocols, which is increasing the incidence of anaemia and the need for transfusions (Ruggiero et al., 2002).

Adult red blood cell (RBC) transfusion practices are far more established than paediatric transfusion practices. The presentation of substantial literature encourages the development of systematic clinical practice guidelines for appropriate blood transfusion management in adults. Due to the lack of evidence, there has been a large gap in the management of transfusion in paediatrics. In particular, there are different age groups of paediatric patients with different disease management.

To date, only a few studies have quantified and compared the use of transfusion among paediatric patients with various cancer diagnoses (Lieberman et al., 2014). Although paediatric oncology is a major user of blood transfusion services, data on transfusion practices such as indication, the haemoglobin level before red blood cell transfusion that triggers the clinicians' decision to transfuse, and transfusion complications are still lacking. The research on transfusion practices among paediatric patients with various cancer diagnoses is limited, resulting in disparities in practices between centres and patient groups (Bercovitz et al., 2016). Clinical decisions in paediatric oncology are frequently based on guidelines for different paediatric cohorts, expert opinion, or adult patients due to the lack of a specific guideline or protocol for transfusion practices. Therefore, more study will help to fill a knowledge gap, which may aid in the advancement of research in a similar area.

1.3 Literature review

According to data collected by the International Agency for Research on Cancer (IARC), approximately 175,000 new cases of cancer among children and adolescents are diagnosed each year. Eighty-four per cent of new cases occurred in developing countries with lower life expectancy (Stefan et al., 2014). Paediatric cancer patients frequently require intensive treatment and management, such as chemotherapy, which can disrupt the production of normal functioning RBC and cause anaemia (Shah et al., 2015). Furthermore, malignant cell infiltration of bone marrow, the effects of radiotherapy, chronic inflammation, blood loss and nutritional deficiency due to nausea and vomiting symptoms can contribute to anaemia (Michon, 2002). Anaemia in paediatric oncology patients is generally characterised by normocytic normochromic anaemia associated with reduced serum iron and transferrin saturation but elevated or normal ferritin levels (Ruggiero et al., 2002).

There is a lack of research on transfusion practices in the paediatric oncology cohort. Lieberman et al., found that 65% of patients received RBC transfusions in the first epidemiological cohort study assessing the practice of blood transfusion in 647 paediatric patients with various types of solid tumour and haematological malignancies over nine years. Patients with acute lymphoblastic leukaemia (ALL) are more likely to require blood transfusions during their treatment (97%). Patients with acute myeloid leukaemia (AML) required the most RBC transfusions (25 units of RBCs transfused per patient). The median haemoglobin threshold was 7.2 g/dL, with a 2.3 g/L increase after an RBC transfusion. Transfusion reactions were reported in 4.5% of patients and transfused patients with acute leukaemia being the most common affected (46%). Approximately 0.5% of patients developed antibodies, resulting in a 0.04% alloimmunisation rate per RBC unit transfused.

Some studies look at the number of transfusions that patients received during their hospitalizations, whether they were single or multiple transfusions. For example, a study of the use of red blood cell transfusions in children and infants (New et al., 2014) on 1,302 paediatric and non-neonatal patients between September 1st and November 30th, 2009 found that a higher percentage of patients received a single RBC transfusion. More than half (53%) had an underlying haematological or oncological condition. The prescribed median volume was 15 mL/kg and the median pre-transfusion haemoglobin level was 7.9 g/dL. The mean Hb increase was 2.8 g/dL.

A restrictive transfusion strategy aims to keep patients' haemoglobin levels between 7.0 g/dL and 9.0 g/dL without jeopardising their health or interfering with their recovery, whereas a liberal transfusion strategy aims to keep patients' haemoglobin levels between 10 g/dL and 12 g/dL with a low transfusion trigger (Estcourt et al., 2017). With the current trend of comparing restrictive and liberal transfusion practices, a study of the transfusion thresholds for haemoglobin in paediatric patients at a large academic health centre involving 3,370 paediatric patients in various sub-specialties between 1st January 2009 and 31st December 2012 was conducted. The mean haemoglobin trigger value for oncology patients was found to be consistent with transfusion strategies for patients in paediatric intensive care units (TRIPICU) study's restrictive haemoglobin trigger (7 g/dL) (Klaus et al., 2015). There have been a fair number of studies comparing restrictive transfusion practice and liberal transfusion practice among general paediatric patients in intensive care units, but there was very little literature comparing the two practies, particularly among paediatric oncology patients (Akyyildiz et al., 2018).

Approximately 4.25 transfusion of blood products per patient were observed and transfusions were mostly used in oncology patients (46.5 %). Transfusion reactions occurred in 3.8% of patients, and 1.3% of total blood products were transfused. These blood products have been filtered and/or irradiated in 79.17% of the cases. There is a link between patients' age and the type of transfusion reaction (Pedrosa et al., 2013). Among paediatric patients, the most common types of transfusion reactions were allergic transfusion reactions and febrile non-haemolytic transfusion reactions (Oakley et al., 2015).

The frequency of red cell alloimmunisation was 1.5% in a study of transfusion-related alloimmunisation in children, which included 324 paediatric oncology patients receiving chemotherapy, 909 control patients (paediatric patients without cancer), and 40 patients with haemoglobinopathy. Antibodies to Rhesus (Rh) blood group antigens, such as anti-D and anti-E, were found in the study (Solh et al., 2016). A Japanese study found that the overall frequency of alloimmunization in paediatric recipients was 1.8%, with anti-E and anti-Jka antibodies found among patients who developed alloimmunization from RBC transfusion exposure (Ohto et al., 2018).

Immunosuppression is commonly seen in paediatric oncology patients due to complications from underlying diseases or aggressive treatments that compromise their immune system. In this group of patients, leukoreduced or irradiated blood products are recommended to reduce the risk of complications such as transfusion reactions and alloimmunization (Nellis et al., 2019).

1.4 Research questions

a) What is the prevalence of RBC transfusion in Paediatric oncology patients and relation to total paediatric patients in HUSM?
b) What are the standard haemoglobin levels before red blood cell transfusion and the red blood cell transfusion indication in paediatric oncology patients?
c) What are the complications post red cell transfusions in paediatric oncology patients?
d) What are the relationships between demographic characteristic, type of diagnosis, number of transfusions, the total volume of transfusion, medication and/or chemotherapy regime and pre-medication before transfusion with the occurrence of transfusion reaction?

1.5 Justification and benefit of the study

Even though children of different ages have different anatomy and physiology, the need for blood transfusion must be determined on an individual basis. Perhaps in paediatric transfusion, there are various types of diagnoses with corresponding transfusion management. Due to the differences in physiology and haematology systems between children and adults, different transfusion practices are usually required to optimise therapeutic interventions and their efficacy. Oncology patients are the top consumers of blood transfusions in the paediatric age group because their underlying diseases and management can lead to recurrent anaemia and bleeding tendencies, necessitating multiple blood transfusions. Clinical decisions for red blood cell transfusion in paediatric oncology patients are frequently based on recommendations for different paediatric cohorts, guidelines based on expert opinion, or the transfusion management of adult patients. As a result, more research into red blood cell transfusion management in paediatric oncology patients is beneficial, and it may help in developing specific guidelines for this paediatric group.

There is an increasing trend of restrictive transfusion practices among adult patients as opposed to liberal transfusion practices at the moment; however, this is debatable in paediatric transfusion practices, particularly because there is a scarcity of knowledge about paediatric oncology patients' transfusion practices. This study intends to collect data on transfusion practices such as haemoglobin levels before red blood cell transfusion, indications for transfusion, and the use of red cells transfusion among paediatric oncology patients at HUSM.

Furthermore, the purpose of this study was to investigate the effects of red blood cell transfusion on transfusion reaction and alloimmunisation development in paediatric oncology patients. There is a paucity of evidence describing the negative effects of paediatric transfusion, particularly in the paediatric oncology cohort. This study could provide useful data to clinicians in the transfusion management of paediatric oncology patients.

1.6 Problem statement

Red cell transfusion practices in the adult are far more established than paediatric red cell transfusion practices. The availability of substantial literature prompts the development of a systematic clinical practice guideline for appropriate blood transfusion management in adults. Due to a lack of evidence, there has been a large gap in knowledge in transfusion practices in paediatrics, particularly among different age groups of paediatric patients with different disease management.

Only a few studies have quantified and compared transfusion practice among paediatric patients with various types of cancer (Bercovitz et al., 2016). Although the paediatric oncology group is one of the most frequent users of blood transfusion services, data on transfusion practice, such as indication, transfusion trigger through haemoglobin level before transfusion, and transfusion complication is still lacking. The research on transfusion practises among

paediatric patients with various types of malignancies is limited, resulting in disparities in practice between different centres and patient groups (Lieberman et al., 2014).

Over 10 years, researchers conducted the first epidemiologic cohort study to assess transfusion practises in paediatric oncology patients. This study uncovered differences in transfusion practice between adult and paediatric patients. The findings of this epidemiologic study provide a foundation for developing hypotheses that will be tested in future studies (Lieberman et al., 2014). We believe there are yet no studies focusing on transfusion practice in paediatric oncology patients that are currently available in Malaysia. This study hopes to aid in filling the knowledge gaps, which may contribute to the advancement of research in a similar area.

CHAPTER 2

OBJECTIVES

2.1 General objective

To assess the red blood cell transfusion practices among paediatric oncology patients at Hospital USM

2.2 Specific objectives

i. To determine the prevalence of red blood cell transfusion in paediatric oncology patients and in relation to the total paediatric transfusion.

ii. To determine the haemoglobin level prior to transfusion and the indication for red blood cell transfusion.

iii. To determine the red blood cell alloimmunisation frequency and types of RBC alloantibody post red blood cell transfusion.

iv. To determine the transfusion reaction rate among paediatric oncology patients.

v. To determine the sociodemographic, clinical and transfusion characteristics association with transfusion reactions.

2.3 Research Hypotheses

i. Null hypothesis

The red blood cell transfusion practice among the paediatric oncology patients in HUSM follows a restrictive transfusion practice.

ii. Alternative hypothesis

The red blood cell transfusion practice among the paediatric oncology patients follows a liberal transfusion practice.

iii. Null hypothesis

There is no association between age, gender, race, the type of diagnosis, transfusion episode, total volume of transfusion, medication and chemotherapy regime with the occurrence of transfusion reaction.

iv. Alternative hypothesis

There is association between age, gender, race, the type of diagnosis, transfusion episode, total volume of transfusion, medication and chemotherapy regime with the occurrence of transfusion reaction.

CHAPTER 3

METHODOLOGY

3.1 Study Location

This study was conducted at the paediatric oncology wards, Hospital Universiti Sains Malaysia (HUSM). The hospital is located at Kubang Kerian, Kelantan. HUSM is a tertiary and referral center of paediatric oncology covering the East Cost of Peninsular Malaysia.

3.2 Study Design

A retrospective cohort study by medical record review of paediatric oncology patients at Hospital Universiti Sains Malaysia (HUSM) from 1st January 2012 to 31st December 2016.

3.3 Study Duration

Study was conducted within 12 months (1st June 2018-31st May 2019)

3.4 Subject Criteria

Patients that fulfilled the inclusion and exclusion criteria are eligible for the study. The subject details were collected as in research performa.

3.4.1 Inclusion Criteria

a) Paediatric patients with diagnoses of haematological and solid tumour malignancies.

b) Paediatric oncology patients admitted to Hospital Universiti Sains Malaysia (HUSM) from 1st January 2012-31st December 2016.

3.4.2 Exclusion Criteria

a) Paediatric patients with benign haematological disorder and benign solid tumour.

3.5 Calculation of Sample Size

The sample size in this study was calculated for the objectives 1, 4 and 5. The biggest sample size calculated will be used as the sample size required in this study.

Objective 1: To determine red cell utilisation rate in paediatric oncology and compare the utilisation rate with the total paediatric transfusion, a single proportion formula as the following was used:

Single proportion formula

$$n = \left(\frac{Z}{\Delta} \right)^2 p(1-p)$$

p = Proportion of

Δ = precision

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

Based on Lieberman et al. (2014), the proportion of patients received RBC transfusions is 65%. This study wished to estimate true proportion within 5% detectable difference with 95% confidence interval. The minimum sample size required with an additional 20% non-response rate is:

$$n = \left(\frac{1.96}{0.05} \right)^2 0.65(1 - 0.65)$$

$$= 1536 \times 0.2275$$

$$= 350 + 20\% \text{ non-response rate}$$

$$= 420$$

The calculated sample size with 20% non-response rate is 420.

Objective 4: A single proportion formula was used to determine the transfusion reaction rate among paediatric oncology patients who received red cell transfusion. According to Lieberman et al. (2014), the proportion of reported transfusion reaction cases is 4.5%. The goal of this study was to estimate the proportion within a 5% detectable difference with a 95% confidence interval. With an additional 20% non-response rate, the minimum sample size required is:

$$n = \left(\frac{1.96}{0.05} \right)^2 0.045(1 - 0.045)$$

$$= 1536 \times 0.043$$

$$= 66 + 20\% \text{ non-response rate}$$

$$= 79$$

The calculated sample size with 20% non-response rate is 79.

Objective 5: To determine the factors that associated with the occurrence of transfusion reaction. Using two-proportion formula in PS power and Sample Size Calculation software and information required:

$\alpha = 0.05$

power = 0.08

P_0 = proportion of exposure in controls (without irradiated/filtered product) = 38.6%

P_1 = proportion of exposure in cases (with irradiated/filtered product) = 61.3%

n = (80 + 20% non-response rate) x 2

= 192

Based on Pedrosa et al., approximately 38.6% of paediatric patients will not receive irradiated/filtered blood products and 61.3% will receive irradiated/filtered blood products. Using a significance level of α=0.05 (two-tailed) and a power of 80%, the minimum required sample is 80 per group. Here, the total required sample size with an additional 20% non-response rate is 192.

3.6 Sampling method

This study's sample size was determined by the first objective. The total sample size involved purportedly was 420 patients. However, because the registered data from the institution's patient record division only showed admission of 192 paediatric oncology patients, a convenience sampling method was used in this study. There were 192 paediatric oncology patients in Hospital USM with records that could be retrieved. All the 192 patients were included in this study.

3.7 Data collection

The data was collected at the Medical Record Division and blood bank of the Hospital Universiti Sains Malaysia (HUSM). The potential subjects' names were obtained from the HUSM patient record division. All paediatric oncology patients who met the inclusion and exclusion criteria were included in the study. The subjects had been given a code number. The names of subjects were not identified in the perfoma to ensure anonymity. The manual medical

records were retrieved from the recording unit. While the electronic data such as 'MyTransfusi' blood bank electronic database and HUSM App Result System were included in the study. Data from electronic databases, such as the HUSM App Result System and blood request forms, were used to retrieve information about the blood investigation, particularly the haemoglobin level before red blood cell transfusion.

3.8 Data Resources

Data was traced and collected from

a) Patient's medical record
b) Blood Transfusion Request Form
c) Blood Bank System
d) Hospital USM App Result System

3.9 Development of Research Performa

The research Performa (**Phase I**) was created based on a review of the literature and previous studies on paediatric transfusion. Several meetings and a group discussion with the expert were held before the development of the research Performa.

The research data will be divided into 4 mains components

i. ***Demographic data***

Demographic information such as age, gender, nationality, and race are recorded.

ii. ***Clinical diagnosis data***

Clinical diagnoses of relevant patients were documented, including types of diagnoses, date of the first diagnosis, age of the first diagnosis, other comorbidities, and a history of allergies to blood products, contrast, or medication.

iii. ***Transfusion history and laboratory investigations***

Transfusion history, including date and age of the first transfusion, total transfusion received pre-transfusion Hb, Hb increment post-transfusion, indications of transfusion, any irradiated/filtered blood product used in a transfusion, and any pre-medication (steroid, anti-pyrexia, anti-histamine) given before blood transfusion, was also documented.

iv. ***Red cell transfusion complication***

Data on red cell transfusion complications such as transfusion reaction and RBC alloimmunisation were recorded.

3.10 Statistical Analysis

For categorical variables, descriptive statistics were used to report the frequency and percentage, and for continuous variables, the mean and standard deviation. If the distribution is skewed, the normality of the continuous variables was checked, and the median and interquartile range will be reported. Univariable and multivariable logistic regressions were used to identify predictors of transfusion reaction occurrence. The level of significance was set at a *p*-value of 0.05 with a 95% confidence interval. Statistical analysis will be performed using SPSS version 24.0 for window-software (SPSS, Chicago Illinois, USA).

Parameters	Formula
Prevalence of red blood cell transfusion among paediatric oncology patients:	Number of transfused paediatric oncology patients/total number of paediatric oncology patients
Prevalence of red blood cell transfusion compare to total paediatric transfusion:	Number of transfused paediatric oncology patients/total transfused paediatric patients
Alloimmunisation frequency:	Number of cases with alloimmunisation/ number of transfused paediatric oncology patients
Transfusion reaction rate:	Number of cases with transfusion reaction/ number of transfused paediatric oncology patients

3.11 Ethical Issue

Ethical approval from Hospital Universiti Sains Malaysia was received on *20th August 2018*; **USM / JEPeM / 18050246** (Appendix 1)**.** The desired medical record data was recorded anonymously using an index number and therefore the respective patients could not be identified either directly or indirectly via linkage codes assigned to the data.

3.12 Conflict of Interest

The investigator has no conflict of interest during this study.

3.13 Community sensitivities and benefits

The study had no bearing on any community sensitivities. This research would help to fill a knowledge gap in paediatric transfusion and provide local data for future local Guideline Protocol for Paediatric Oncology Transfusion.

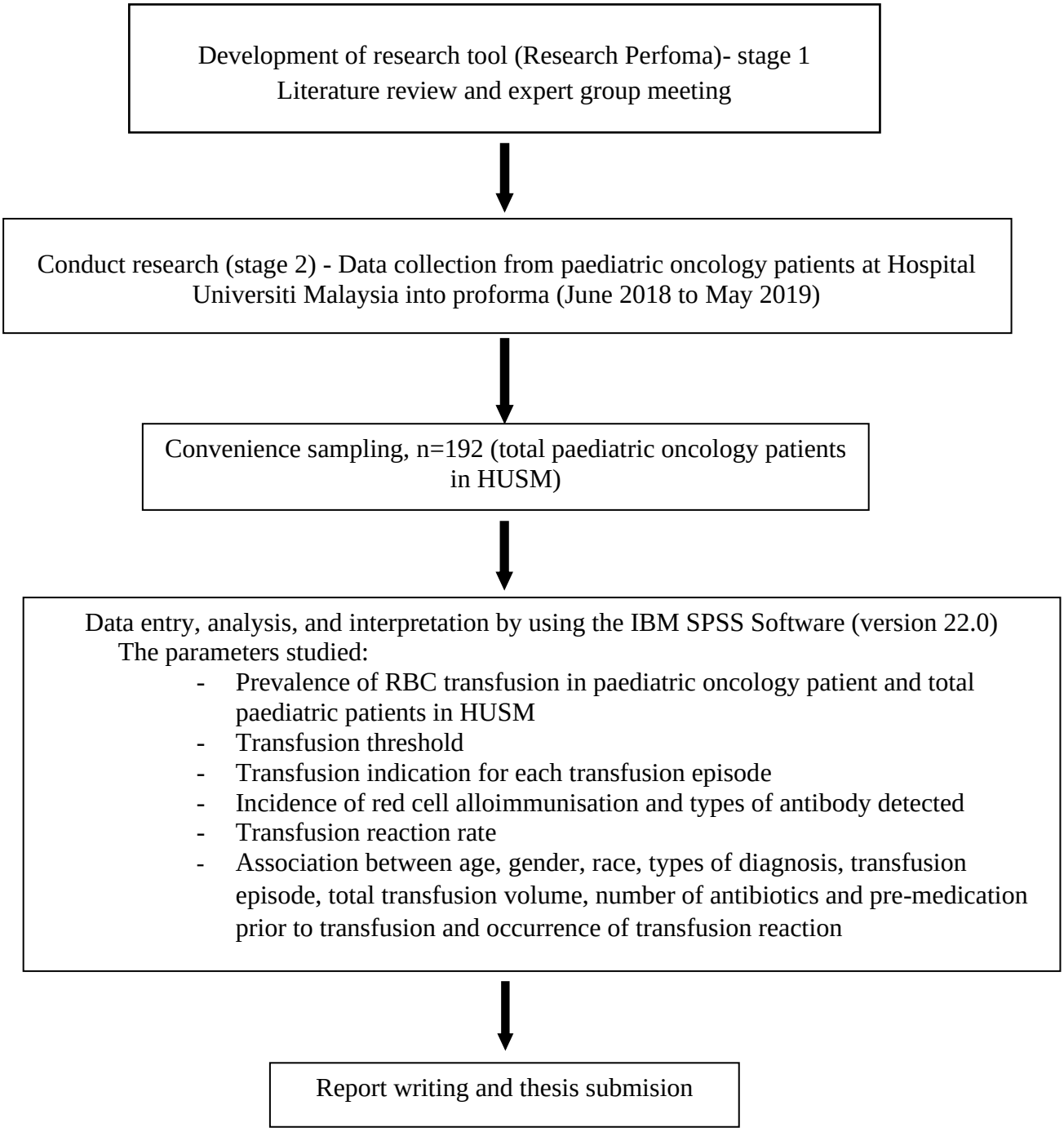
3.14 Operational Definition

Transfusion practice	: Define as the exercise of the profession of medicine in the process of transferring whole blood or blood components from donor to recipient.
Paediatric patient	: Defined as a child under the age of 18 years old or below than 18 years old who received care from the health personnel with children care subspecialty.
Oncology	: Defined as a branch of medicine that specialises in the diagnosis and cancer treatment.
Paediatric oncology	: Paediatric patients with diagnosis of either haematological malignancy or solid tumour malignancy.
Red cell transfusion	: Defined as the process of receiving whole blood or red cell concentrate into one circulation intravenously.
RBC alloantibody	: Defined as an antibody formed in response to the exposure of red blood cell transfusion

Transfusion reaction	: An undesirable response or effect in a patient temporally associated with the administration of blood or blood component
Haemoglobin level prior to transfusion	: Described as the haemoglobin values at which packed red cells are usually order for transfusion by clinician.
Medication before transfusion	: Is the option of giving certain medication prior to blood transfusion in order to prevent or reduce the risk of transfusion reaction for instances anti-pyrexia, antihistamine or steroids.

3.15 Research Flow Chart

The research was divided into two phases which is ***phase 1*** is for development of research performa and ***phase 2*** is for data collection up to report writing**.** A research performa was developed to collect data of paediatric oncology patients with transfusion history in HUSM. A total 192 subjects will be included in the study. The phase 2 will involve research data collection. The flow chart as shown below:



CHAPTER 4

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ABSTRACT

INTRODUCTION: Blood transfusion is an important supportive treatment for children with oncological diseases. This study aims to look at the red blood cell (RBC) transfusion practice and its adverse effects on paediatric oncology patients at Hospital Universiti Sains Malaysia (HUSM).

METHODS: This retrospective cohort study was conducted at HUSM. A total of 192 paediatric oncology patients were enrolled. Demographic, clinical and transfusion data were collected and analysed.

RESULTS: The prevalence of red blood cell transfusion among paediatric oncology patients was 82.3%. In contrast, the paediatric oncology group accounts for only 7.2% of the total transfused paediatric population at HUSM. Before transfusion, the majority of patients had an average haemoglobin level of 6.8 g/dL pre-transfusion and had symptomatic anaemia. Transfusion reactions occurred at a rate of 6.3%, while red cell alloimmunisation occurred at a rate of 1.9%. There was no statistically significant association between transfusion reaction with patients' demographic characteristics; disease category; total transfusion episodes and volume; antibiotic; chemotherapy; and pre-transfusion medication.

CONCLUSION: Even though RBC transfusion is common in paediatric oncology, it was not the group with the highest recipient for RBC transfusion at HUSM. Due to the general patients' immunocompromised state, there is a low incidence of alloimmunisation. The possibility of underdiagnosis of transfusion reaction must be considered. The existence of established protocols is critical in assisting clinicians in justifying blood transfusion decisions. Vigilant transfusion practice lowers the risk of adverse events in blood transfusion.

Keyword: Paediatrics, Oncology, Red cell transfusion, Transfusion reactions, Alloimmunisation

INTRODUCTION

Children have a much higher prevalence and incidence of haematological malignancies than adults.[1] The incidence rate of paediatric malignancies in Malaysia was 77.4 per million children under the age of 15 years old. In comparison to solid tumour malignancies, haematological malignancies were diagnosed in the majority of paediatric oncology patients.[2]

The causes of anaemia in paediatric oncology patients are typically affected by multifactorial pathophysiology, such as decreased red blood cell (RBC) production, increased degradation, and decreased RBC survival due to autoantibodies or acute blood loss. Furthermore, there are direct malignancy-specific effects, such as leukaemic infiltration of bone marrow.[3] Anaemia can occur as a result of erythropoietin suppression with underlying chronic inflammation or as a result of renal dysfunction. Chemotherapy and radiation will also have a direct impact on myelosuppression.

Oncology patients are immune-compromised as a result of their underlying oncological disorder and the treatment they require, putting them at risk of multiple infections, which further complicates the escalation of anaemia.[4] Furthermore, if patients experience intraoperative bleeding in some solid tumour malignancies, it may necessitate surgery involving blood transfusion. Besides, shift toward more intensive chemotherapy treatment protocols will also result in a higher incidence of anaemia and transfusion requirements in paediatric oncology patients.[5]

The existence of significant evidence-based medicine literature has led to the establishment of standardised clinical practice guidelines for the proper management of blood transfusion in adults; however, in paediatric patients, there is a wide knowledge gap in transfusion management caused by a lack of data, particularly due to the various age ranges of paediatric patients with a different disease.[6, 7] Furthermore, the benefit of restrictive transfusion

strategies in paediatric transfusions, particularly in oncology patients, is still being debated. Restrictive transfusion strategies in previous studies demonstrated that the 7 g/dL haemoglobin threshold could reduce transfusion requirements without increasing adverse outcomes.[3, 15]

Although transfusion can save a person's life, there is also risk of adverse reactions. General paediatric patients may have 1.9 to 2.6 times the number of reactions as adults.[8] An allergic reaction to RBC transfusion is the most common transfusion reaction in paediatric patients. Aside from transfusion reactions, 2-6% of paediatric patients who receive RBC transfusions are at risk of developing alloantibodies.[9]

While paediatric oncology is a major user of blood transfusion services, evidence on transfusion practice such as indication, haemoglobin level before transfusion, and transfusion complications are still lacking. Clinical decisions in paediatric oncology are frequently based on recommendations from specific paediatric cohorts, expert opinion guidelines, or adult patients due to the lack of a clear guideline or protocol for transfusion practice. Even in Malaysia, knowledge of blood transfusion practice, particularly in paediatric oncology, is limited.

The purpose of this study was to determine the prevalence of RBC transfusion among paediatric oncology patients. In addition, we also look at the RBC transfusion practice, adverse reactions towards RBC transfusion and association factors in transfusion reaction in paediatric oncology patients in Hospital Universiti Sains Malaysia (HUSM). This study also aimed to assess the transfusion practice and adverse transfusion reactions among the paediatric oncology patients.