IMPACT OF BLOOD TRANSFUSION ON CLINICAL OUTCOME OF AUTOLOGOUS HAEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) PATIENTS IN HOSPITAL USM

BY

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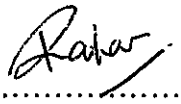
DISCLAIMER

I hereby declare that this research has been sent to Universiti Sains Malaysia for the degree of Master of Medicine in Transfusion Medicine. It is not to be sent to any other universities. With that, this research might be used for consultation and can be photocopied as reference.



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Nurulraihan Mohamed Zawawi, May 2019

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BHT	Bed Head Ticket
SPSS	Statistical Package for the Social Sciences
JEPeM	Jawatankuasa Etika Penyelidikan Manusia
ESA	Erythropoietic Stimulating Agents
TRICC	Transfusion Requirement in Critical Care Patients
JPAC	Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee
AABB	American Association of Blood Banks
BSH	British Society for Haematology
Epo	Erythropoietin
COPD	Chronic Obstructive Lung Disease
TAS	Transfusion Associated Sepsis
CMV	Cytomegalovirus
G-CSF	Granulocyte-Colony Stimulating Factor
TRA	Thrombopoietin Receptor Agonist
ASCO	The American Society of Clinical Oncology
PBM	Patient Blood Management

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ABSTRACT

Background / Objective: Autologous haematopoietic stem cell transplantation (HSCT) is one of the treatment modalities to treat various haematological malignancies and require a high number of blood transfusion. However, the impact of blood transfusion on the clinical outcome always associated with various morbidity and mortality. In this study, the impact of blood transfusion on clinical outcome of autologous HSCT patients in Hospital USM were determined. The association of pre-transplantation haemoglobin (Hb) and episodes of blood transfusions requirement were also compared.

Methods: A total of 72 haematological patients who underwent autologous HSCT in Hospital USM between 2007 until 2018 had been included in this study. Data were retrieved from Haematology-Oncology Unit and analysed. Demographic data, blood transfusion parameters and clinical data of patients were captured.

Results: There were 43 (59.7%) autologous HSCT patients who required RBC transfusion post-transplant and from those patients, 40 (93.0%) of them had their pre-transplantation Hb of more than 9g/dL. There were significant associations between blood transfusion with mortality and infection. There was also significant association between RBC transfusion with the length of hospitalisation.

Conclusion: This study has shown that episodes of blood transfusion had an impact on morbidity and mortality. There was no correlation between pre-transplantation haemoglobin and the RBC requirement.

Keywords: HSCT, RBC transfusion, Hb, mortality, impact

CHAPTER 1: INTRODUCTION

1.1 Overview of The Autologous Haematopoietic Stem Cell Transplantation Unit in Hospital Universiti Sains Malaysia (HUSM)

Haematopoietic stem cells (HSC) can be characterised as multipotent, capable to self-renew and differentiate into mature cell lineages. Hence, it is used as one of the treatments for a variety of diseases especially related to haematological diseases. HSC for the use of transplantation can be collected or harvested either direct from bone marrow or from peripheral blood (bloodstream). Autologous haematopoietic stem cell transplantation (HSCT) is one of the modalities of treatments nowadays. It is performed by using the patients' own stem cells which are collected before transplantation and re-infused to the same patient after myeloablation therapy. Indications for autologous HSCT for haematological diseases include lymphoma, acute myeloid leukaemia and multiple myeloma.

HUSM is a teaching hospital which is located in Kubang Kerian, Kelantan. It is also a referral centre for most hospitals in East Coast of Peninsular Malaysia including haematological diseases. As a teaching hospital, HUSM provides resources and advanced facilities for the research purposes.

Haematology-Oncology Department is one of the division under Medical Department (HUSM) that provides autologous HSCT. In HUSM, autologous HSCT was performed since 2007 for haematological disease patients such as multiple myeloma and lymphoma (Hodgkin & Non-Hodgkin lymphoma). Till now, there were 73 patients who had undergone autologous HSCT in HUSM in which multiple myeloma accounts for the highest number.

demonstrated a correlation between RBC transfusion and increase in morbidity rates including susceptibility of infections, multi-organ failure and also mortality.

However, insight regarding transfusion requirements in HSCT patients is still inadequate. In this group of patients, we still do not understand well regarding the clinical impact of transfusion specifically to the outcomes after transplant (length of stay, infections, and mortality) (Tay, Tinmouth *et al.* 2011).

The vital function of RBC transfusion in HSCT patients remains poorly appreciated and with regards to that, there is a need of more prospective randomised study of transfusion to be done in the future to gain more insight and also information on optimal transfusion practices that can be used in this type of patients (Tay, Tinmouth *et al.* 2011).

1.3 The Practice of Blood Transfusion in Autologous Haematopoetic Stem Cell Transplantation (HSCT) in HUSM

In HUSM, three main underlying diseases are being selected for autologous transplantation which are multiple myeloma, Hodgkin lymphoma and Non-Hodgkin lymphoma. There are 4 processes involved in the Autologous HSCT which includes treating underlying diseases, stem cell collection and storage, conditioning chemotherapy and stem cell infusion.

Stem cell collection is done either by bone marrow harvest or peripheral blood stem cell (PBSC) collection. Nowadays, PBSC is the choice of stem cell collection due to more practical and convenient compared to bone marrow harvest. PBSC mobilisation is done by S/C Granulocyte-Colony Stimulating Factor (G-CSF) and collection is done when peripheral $CD34^+$ cell reaches >20/micL. Target for stem cell dose is at least $CD34^+$ cells 3.0 x 10^9/kg for one stem cell transplantation. For conditioning chemotherapy, BEAM (Carmustine, Etoposide, Cytarabine and Melphalan) with or without monoclonal

antibody is used for lymphoma case while for multiple myeloma, melphalan 200mg/m^2 is used.

In HUSM, patients' blood counts are optimised first before undergoing autologous HSCT with the aim to target the Haemoglobin (Hb) of 10g/dL and platelets of 50 x 10^9/L. Possible complications are being monitored during and after the HSCT to minimise the requirement of blood transfusions such as central venous catheter insertion, volume redistribution, hypocalcemia, hypothermia, and anxiety. Usually stem cell re-infusion is done 1-2 days after completion of conditioning. The stored stem cell is thawed and post thawing $CD34^+$ enumeration and viability study is then performed.

Daily Full Blood Count (FBC) is monitored to assess neutrophil and platelet engraftment. Neutrophil engraftment is normally defined as absolute neutrophil count (ANC) of more than 0.5 x 10^9/L for 3 consecutive days while platelet engraftment is noted to happen when the platelet count is more than 20 x 10^9/L without blood transfusion (Claudia *et al.*, 2014).

1.4 Autologous Haematopoietic Stem Cell Transplantation in Malaysia

The earliest HSCT in Malaysia was performed in 1987 at University Malaya Medical Centre (UMMC) in Kuala Lumpur, Malaysia which was done on paediatric patients while the first adult transplantation was done back in 1993 also at the same hospital. Since then, more centres in our countries had developed and set up HSCT services. To date, currently, there are more than eight transplant centres. Few centres are owned by the government, few centres are private and the other 3 are university-based (UMMC, UKMMC and HUSM).

The first autologous HSCT was performed in 1989 and by the end of 2016, a total of 1858 patients being transplanted. Most of the autologous HSCT cases were performed in Hospital Ampang, Hospital Pulau Pinang, Hospital Universiti Kebangsaan Malaysia (HUKM), Subang Jaya Medical Centre (SJMC), UMMC and Hospital USM. According to GG Gan et al, the total number of transplantations performed yearly ranges from 100 to 150 and also showed an increment when calculated per million populations in Malaysia. It might be due to the opening of more transplant centres. Hospital Ampang still continued to be one of the busiest hospital which contribute about 55% of all transplants performed. For patients' characteristics, Malays account for the highest number (58%) with Chinese and Indians making 28% and 7% respectively for year 2016.

A National Transplant Registry has been set up by the Malaysian Society of Transplantation and the Ministry of Health Malaysia. It gathers information about all patients who had undergone tissue or organ transplantation. This information provides the progress of transplant activity in our country. From the data that we gather from the registry, it shows increment in the numbers of bone marrow transplantation from 1987 until now. Besides that, the new transplant rate per million populations also showed a tremendous increase since 1987 until now.

Autologous HSCT noted to exceed allogeneic HSCT since 2011. From the 13th report of the National Transplant Registry 2016, autologous HSCT comprises about 58% of the total in year 2016. Peripheral blood stem cells (PBSC) became the most common stem cell source which constitute 89% of stem cells used followed by bone marrow and cord blood. It reveals that the haematopoietic stem cell transplantation services have been well practiced in our country. ("13th Report of National Transplant Registry," 2016)

1.5 Problem Statement

In the Department of Haematology-Oncology HUSM, the Senior Medical Officer, Registrar in charge or consultant in charge will decide on the blood transfusion requirement during the ward round or by consultation. The current practice is by evaluating patients clinically before the exact decision of transfusion is made. So far, the practice is by using the therapeutic transfusion (transfusion given when patient is bleeding or with appropriate thresholds) and not by the prophylactic management (transfusion given to prevent bleeding). However, lack of standardisation for transfusion in autologous HSCT patients could be one of the challenges nowadays as different practice is made among different clinician. It also depends on local practices.

Prolonged transfusion dependence can still occur together with all the complications although we already have advanced technologies facilities and knowledge on transfusion. Direct or indirect impact of blood transfusion also have not been explored or studied well yet in Malaysia. So, it becomes one of the challenges faced currently as the impacts are still unknown. The number of transfusion requirement can be reduced with early detection and treatment of complications. Besides that, knowledge in blood transfusion can help us in deciding only necessary transfusion for the patients.

To minimise the requirement of blood transfusion, we can lower the haemoglobin trigger by using Hb level of 7 or 8 g/dL as the transfusion threshold. A lot of literature reviews have shown that the patient's clinical outcome will be as effective as by using the higher haemoglobin trigger. For platelet transfusion, it can also be minimised by using platelet level of 10×10^9/L as a platelet transfusion threshold in non-bleeding patients.

1.6 Justification

HSCT is among one of the procedures which require a high number of blood transfusion. In HUSM, autologous HSCT procedure is increasingly in trend nowadays to treat haematological malignancies such as lymphoma (Hodgkin and Non-Hodgkin) and multiple myeloma. Blood transfusion can save HSCT patients' life if used judiciously and carefully but inappropriate transfusion will have a bad impact on the patients' outcome after transplantation.

To date, knowledge of the information on evidence-based transfusion practices in HSCT is still inadequate. Furthermore, the impact on patients' outcomes after underwent HSCT due to blood transfusion are not really understood (Tay, Tinmouth *et al.* 2011*)*. There was also not enough data to study on the impact of other blood products or components (ie platelet, fresh frozen plasma, cryoprecipitate) transfusion on the patients' outcome. Therefore, a study on the impact of blood transfusion on patient's outcome in autologous stem cell transplantation is needed to help us improve our transfusion services to that area. In Malaysia also, there is still no sufficient data to demonstrate the effectiveness of blood transfusion as well as the impact on the patient's outcome in autologous HSCT patients. Review by Gan, Teh et al regarding Malaysian experience in stem cell transplantation including bone marrow is a mixture review of autologous and allogeneic transplant (Gan, Teh *et al.* 2008). To date, there is no specific study that focuses on the effectiveness of transfusion in autologous HSCT patients per se.

This study was aimed to determine the impact of blood transfusion on patient's outcome (transplant-related mortality, infection and length of hospitalisation) in autologous (HSCT) patient in Hospital Universiti Sains Malaysia (HUSM) from 2008 until 2016 and to study the demographic data of patient who received red cell transfusion with those who

did not. This study also examined the correlation between pre-transplant haemoglobin and transfusion requirement.

1.7 Research Objectives

1.7.1 General Objective:

To determine the impact of blood transfusion on clinical outcome of autologous haematopoietic stem cell transplantation (HSCT) patients in Hospital Universiti Sains Malaysia (HUSM)

1.7.2 Specific Objectives:

I) To describe the demographic characteristics of autologous haematopoietic stem cell transplant (HSCT) patients in HUSM.

II) To determine the association between pre-transplant haemoglobin and transfusion requirement.

III) To determine the association between episodes of blood transfusion with the mortality and infection

IV) To determine the association between episodes of blood transfusion with the length of hospitalisation

1.8 Hypothesis

1.8.1 Reduced haemoglobin level pre-transplantation associated with increased red blood cell (RBC) transfusion requirements after autologous transplantation.

1.8.2 There is a association between blood transfusion with the transplant-related mortality and infection

1.8.3 There is a association between blood transfusion with increased length of hospitalisation

CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

Haematopoietic stem cell transplantation (HSCT) is a form of a management for various haematological diseases. According to study by Claudia et al, patients who receive HSCT normally require prolonged transfusion support until they achieve red blood cell and platelet engraftment. The platelet lineage is considered engrafted when the platelet level achieves 20 x 10^9/L after 3 consecutive days without the support of platelet transfusion. Most of the clinicians having difficulty to evaluate engraftment of RBC as it is hard to be assessed. It could be described as the circulation of 1% reticulocytes in the bloodstream. Another definition is the last day of RBC transfusion, with no blood transfused for the next 30 days (Claudia *et al.*, 2014).

For the neutrophil engraftment, it is achieved when the absolute neutrophil count (ANC) reaches more than 500/μL for 3 consecutive days. Engraftment is noted to be affected by many factors, such as the source of the stem cell given, type of transplantation (allogeneic or autologous transplantation) and can be influenced also by the dose of CD34+ cells in the transplantation (Claudia et al, 2014).

To date, knowledge of evidence-based transfusion practices in HSCT is still inadequate. The impact of blood transfusion (RBC and non-RBC) on HSCT patients' outcome (mortality, infection, and length of hospitalisation) are not well understood too (Tay, Tinmouth *et al.* 2011). Therefore, a study on the impact of blood transfusion on patient's outcome in autologous stem cell transplantation is needed to help us improve our transfusion services to that area.

transfusion. TRIST study by Tay Tinmouth et al supported the use of restrictive transfusion strategy as compared to a liberal transfusion strategy in HSCT patients as the Health Related Quality of Life (HRQOL) are similar for both arms and there were no differences in term of clinical outcomes of those patients (Tay Tinmouth *et al.*, 2011).

When compared to liberal strategies, restrictive transfusion strategies were known to have a lesser unit of RBC transfused as well as the total number of patients received a transfusion, but there was no significant difference on mortality, overall morbidity, and heart complication such as myocardial infarction noted. In most clinical setting, restrictive transfusion strategies are considered safe while liberal transfusion strategies have not been proved to give any benefit to patients (Holst, Petersen *et al.* 2015).

With regards to the rate of infection, it is reduced among patients managed by a restrictive transfusion strategy as compared to liberal transfusion strategies. The recent Transfusion Requirements in Septic Shock (TRISS) trial, which randomized 1005 patients suffered from septic shock in the intensive care unit (ICU) had concluded that there was no exact difference in mortality or morbidity noted with the use of leukoreduced RBC at a transfusion trigger of 7 versus 9 g/dL (Holst, Petersen *et al.*, 2015).

2.3 Correlation between pre-transplant haemoglobin with transfusion requirement in HSCT patients

A study by Kasbia, Al-Gahtani et al had shown that a lower level of haemoglobin (Hb) before transplantation (< 10g/dL) was associated with increased RBC transfusion requirements after transplant.

The study also showed that pre-transplant anaemia in autologous HSCT patients may influence marrow recovery which then would affect the engraftment of all the cell lines (Kasbia, Al-Gahtani *et al.*2008).

A study by Xenocostas, Yee et al on the other hand showed that there was a correlation between reduced Hb level before allogeneic HSCT with an increased incidence of mortality and other complications (Xenocostas, Yee *et al*,. 2003).

2.4 Impact of blood transfusion on clinical outcome

Tay, Tinmouth et al concluded that RBC transfusion provides patients with advantages and benefits in term of increment in Hb and improvement in health, however, there are a number of patients who developed complications after being transfused (Tay, Tinmouth *et al*., 2011). Unfortunately, the role of RBC transfusion on the HSCT patients remains poorly understood, therefore further research on blood transfusion is needed to acquire insight and also knowledge on the optimal transfusion practices in this types of patients.

A study by Aderinto et al had shown that there was a correlation between allogeneic blood transfusion and increased rate of mortality as well as adverse transfusion reactions from mild reactions to severe haemolytic transfusion reaction (HTR). Apart from that, an allogeneic blood transfusion can also predispose patients to the risk of transfusion-transmitted illness (TTI) including hepatitis B, C, HIV, and syphilis (Aderinto *et al*., 2004).

Another study by Tom-Harald et al showed that RBC transfusion was associated with the risk of infectious morbidity in injured patients (Tom-Harald *et al*., 1992). Blood transfusion in those trauma patients may further destroy the patient's immune status, thus the possible immune-mediated complications can be reduced by avoiding or reducing unnecessary blood transfusion. Cytokines and other substances in the stored blood might cause immunosuppression in patients who received blood transfusion (Tom-Harald *et al*., 1992).

The results of a study by Christou, Kekre et al concluded that platelet transfusion was correlated with adverse clinical outcomes after HSCT (Christou, Kekre *et al.*, 2015). The possibility of platelet transfusion influences patients on the clinical outcomes after HSCT cannot be ascertained but in this study, few strategies to reduce platelet transfusion in post-transplant patients had been developed in order to improve patients' outcome.

Several studies had shown that bleeding intraoperatively and RBC transfusion requirements to those patients had a bad impact on the outcome after orthotropic liver transplant. The risk of allogeneic blood transfusion was not only focusing on viral transmission alone but also includes other adverse reactions either immune or non-immune such as alloimmunisation, allergic reactions, anaphylactic reactions, transfusion-associated sepsis, transfusion-related acute lung injury (TRALI), transfusion associated circulatory overload (TACO), renal failure, and haemolytic transfusion reactions. On the other hand, patient survival after orthotropic liver transplant was noted to be dependence on the total number of blood transfusion required by the patients before, during and after the surgery (de Boer, Christensen *et al.* 2008).

A study by Feltracco Paolo et al, concluded that blood transfusion was the reasons that lead to bad impact to the clinical outcome of the transplant patients besides other factors that contribute to the post-transplant outcome such as underlying co-morbidities, engraftment of cells and any infections (Feltracco Paolo *et al.*, 2013).

There were other adverse events too such as increment in graft failure rates and mortality post-transplant that have been observed in older studies. On the other aspect, more than 6 units of RBC transfusion had been associated with an increment in duration of hospital stay and also reduced in survival rates (Feltracco Paolo *et al.*, 2013).

Orthotropic liver transplant patients who received platelet transfusion were shown to have a higher rate of mortality which was due to acute lung injury. These might be the reason for diminished survival in those patients. (Pereboom, de Boer *et al.* 2009).

2.5 Conceptual Framework

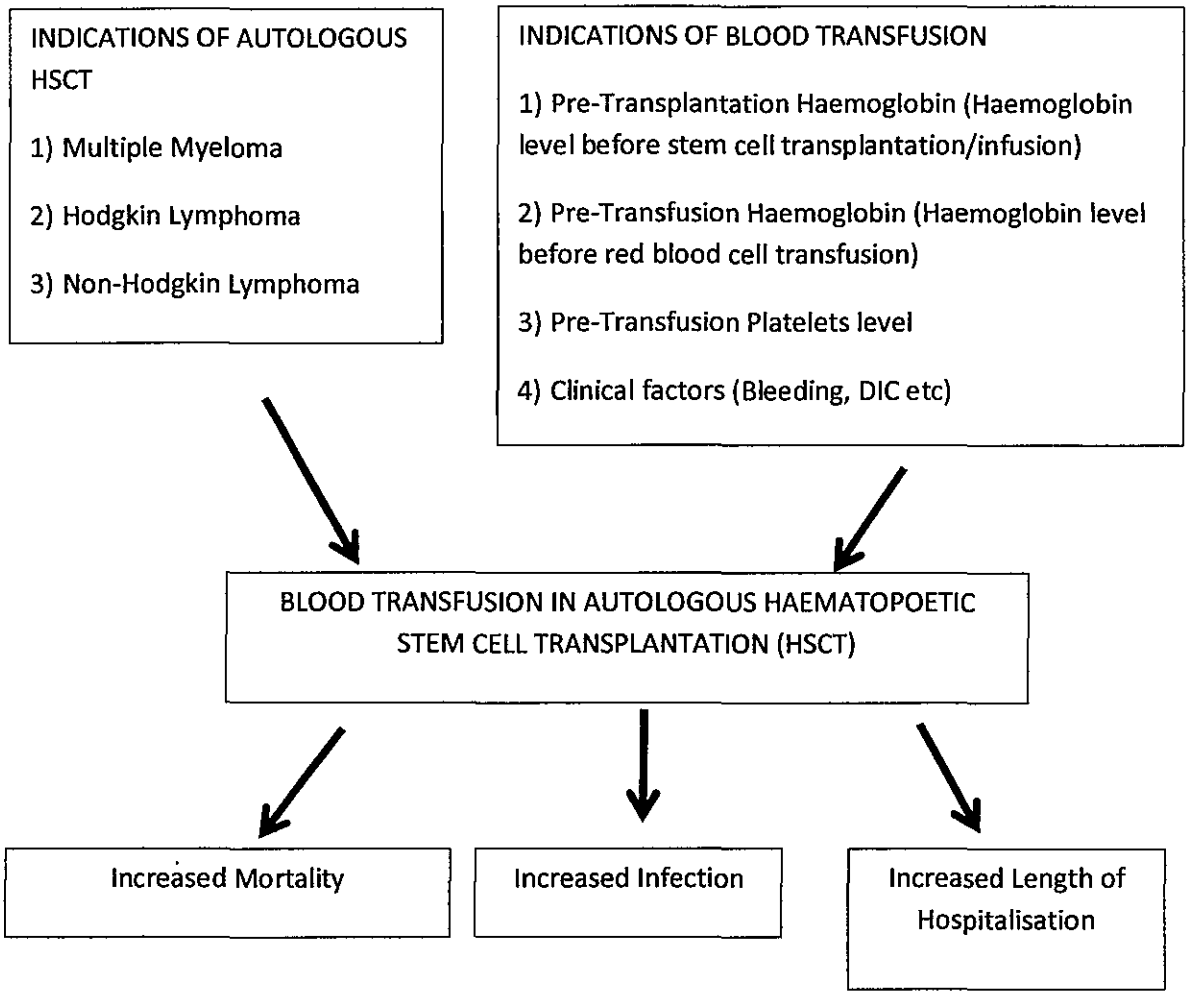

Figure 2.5: Conceptual Framework

CHAPTER 3: METHODOLOGY

3.1 Study Background

3.1.1 Study Design

This was a retrospective cohort study. The study population included all autologous HSCT patients in HUSM. Patients' data were retrieved from the record system which included number of transfusion given, presence of infection, data on transplant-related mortality and length of hospitalisation. Demographic data such as age and gender were also retrieved.

3.1.2 Study Location

This study was conducted in Haematology-Oncology Department in Hospital Universiti Sains Malaysia (HUSM). A total of 73 patients who underwent autologous HSCT in HUSM from 2007 until 2018 were available for this study.

3.1.3 Study Duration

Study duration period was from 1st January 2017 until 31st December 2018 (24months).

3.2 Sample Size

3.2.1 Objective 1: To describe the demographic data of Autologous Haematopoietic Stem Cell Transplant (HSCT) Patients in HUSM.

As these objectives were solely for descriptive statistic only, therefore no sample size estimation needs to be done.

3.2.3 Objective 3: To determine the association between episodes of blood transfusion with mortality and infection

For objective No 3, to determine the association between episodes of blood transfusion with mortality and infection, we calculated based on (Kasbia, Al-Gahtani et al. 2008), (Kneyber, Hersi et al. 2007) Sample was calculated by using the 2 proportions formula. By using p1 as the proportion of the mortality among autologous HSCT patient and p2 as the proportion of the mortality among normal transfusion and an alpha of 0.05, the necessary sample size to reach a power of 80% plus 10% drop out rate is 58.8.

- $n= p_1 (1-p_1) + p_2 (1-p_2)/$

  $(p_1-p_2)^2 \quad x \quad (z_\alpha + z_\beta)^2$

- n= sample size

- p_1 =proportion of the mortality among autologous HSCT patient

- p_2 =proportion of the mortality among normal transfusion

- z_α =1.96 for α=0.05 (two tailed) or 2.58 for α=0.01 (two tailed)

- z_β =0.84 for 80% power or 1.28 for 90% power

- $n= 0.43 (1-0.43) + 0.11(1-0.11) / (0.43-0.11)^2 \quad x \quad (1.96 + 0.84)^2$

- $0.43 (0.57) + 0.11 (0.89) / (0.32)^2 \quad x \quad (2.8)^2$

- 0.2451+ 0.098

- (0.343 / 0.10) x 7.84

- 3.43 x 7.84

- 26.89 x 2= 53.8 + 10% drop out =

n= 58.8

Final sample size after 10% dropout rate taken into consideration was 58.8

3.2.4 Objective 4: To determine the association between episodes of blood transfusion with length of hospitalisation

For objective No 4, to determine the association between episodes of blood transfusion with length of hospitalisation, we calculated based on (Corwin, Gettinger et al. 2004) Sample was calculated by using the 2 mean formula. By using standard deviation of 0.89 and an alpha of 0.05, the necessary sample size to reach a power of 80% plus 10% drop out rate is 68.6.

- $\frac{2\sigma^2 \ (z\alpha + z\beta)^2}{\Delta^2}$

- σ= standard deviation

- Δ=precision

- $Z\alpha$= 1.96 for α=0.05 (two tailed) or 2.58 for α=0.01 (two tailed)

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

- $n = \frac{2(0.89)^2 \ (1.96 + 0.84)^2}{0.40}$

n=4 (7.84)

n= 31.3 x 2 = 62.6 + 10% drop out=68.6

n= 68.6

Final sample size after 10% dropout rate taken into consideration was 69.

The largest sample size is from objective 4. The total sample size required for this study is 69. Estimated sample size calculation using sample size formula α=0.05 and power=0.8 which using double mean formula and the value is taken from (L. Corwin *et al*, 2004).

3.3 Inclusion and Exclusion Criteria

3.3.1 Inclusion Criteria

I. All patients who underwent autologous haematopoietic stem cell transplantation (HSCT) in HUSM

3.3.2 Exclusion Criteria

I. Patients underwent allogeneic stem cell transplantation

II. Patients who develop clinically important infections before stem cell transplantation which include serious infection such as nosocomial pneumonia, deep tissue infections (peritonitis, mediastinitis) and bacteremia from organisms not considered normal skin flora

(We want to study the association of blood transfusion with infection post-transplantation)

III. Missing data or record

3.4 Data Collection Method

The sampling method was universal sampling. All the patients who received autologous HSCT at HUSM from 1st January 2007 until 31st May 2018 would be documented. List of patients who received autologous HSCT was traced and recorded from Haematology-Oncology Unit in which the book that documented the details of patients who received autologous HSCT was available in that unit. A total of 73 patients who received autologous HSCT in HUSM for that period was available for this study.

Patient's Bed Head Tickets (BHT) were traced from Record Unit HUSM. The appropriate informations were transcripted into Proforma form. Other than BHT, other informations were traced from the computer system also.

The data that had been collected included demographic data (age, gender and race of the patient), underlying disease which was the indication of HSCT, date of admission, date of discharge, date of HSCT, pre-transplantation haemoglobin, red blood cell and other blood component transfused, date of platelet and neutrophil engrafted, presence of infection and any transplant-related mortality.

Other data such as transfusion reaction, co-morbidities, and number of stem cell mobilization were also collected. All the data were then recorded in the Proforma.

3.5 Statistical Analysis

Data were analysed using Statistical Package for the Social Sciences (SPSS) version 24

There are multiple dependent and independent variables that were evaluated.

OBJECTIVES	ANALYSIS
To describe the demographic data of Autologous Haematopoietic Stem Cell Transplant (HSCT) Patients in HUSM.	Descriptives Analysis
To determine the association between pre-transplant haemoglobin and transfusion requirement.	Chi-Square Test
To determine the association between numbers of blood transfusion with mortality and infection	Chi-Square Test
To determine the association between blood transfusion with the length of hospitalisation	Chi-Square Test

3.6 Operational Definition

3.6.1 Length of the day of hospitalisation

The number of days admitted to hospital after infusion of haematopoetic stem cell, excluded days for administering the preparative chemotherapy or radiation.

3.6.2 Infection

Any clinically important infection that occurs post autologous haematopoeitic stem cell transplant such as nosocomial pneumonia, deep tissue infections (peritonitis, mediastinitis) and bacteremia from organisms not considered normal skin flora.

3.6.3 Transplant-related mortality

The incidence of death from any cause within 100 days post Hematopoietic Stem Cell Transplantation

(Tay, Tinmouth *et al.*,2011)

3.6.4 Autologous Haematopoietic Stem Cell Transplantation (HSCT)

Transplantation in which stem cells (undifferentiated cells from which other cell types develop) are removed from a person, stored, and later given back to that same person.

3.6.5 Blood transfusion

All blood products received by the recipient including red blood cells, platelets, fresh frozen plasma, cryoprecipitate, and granulocytes

3.6.6 Transfusion requirements

Number of transfusions times / episodes received by the recipient between the 1st day of stem cell reinfusion (Day 0) and Day 100 post Hematopoietic Stem Cell Transplantation

(Tay, Tinmouth *et al.*,2011)

3.6.7 Impact

Strong effect on the patient's outcome.

3.6.8 Patient's outcome

Post HSCT infection, increased the length of the day of hospitalisation, and transplant-related mortality.

3.6.9 Demographic data

Gender, age, primary disease (multiple myeloma, Hodgkin lymphoma, and Non-Hodgkin lymphoma), race, pre-transplant haemoglobin

3.6.10 Neutrophil engraftment

ANC $\geq 0.5 \times 10^9$/L for 3 consecutive days

(Claudia *et al*, 2014)

3.6.11 Platelet engraftment

Platelet count > 20×10^9/L

(Claudia *et al*, 2014)

3.6.12 No of stem cell infusion

Total number of stem cell transplantation within period of study

3.7 Ethical Issues

This study had been approved by The Human Research Ethics Committee of USM (JEPeM USM) (Code: USM/JEPeM/16120582)