VASOVAGAL REACTION AMONG BLOOD DONORS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

DR NUR NASUHA BINTI IBRAHIM

DISSERTATION SUBMITTED IN PARTIAL

FULLFILLMENT OF THE REQUIREMENTS FOR

THE DEGREE OF MASTER OF PATHOLOGY

(HAEMATOLOGY)

UNIVERSITI SAINS MALAYSIA

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In the name of ALLAH, the Most Gracious, the Most Merciful,

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LIST OF ABBREVIATIONS AND SYMBOLS

VVR	Vasovagal Reactions
AE	Adverse Event
TMU	Transfusion Medicine Unit
ISTH	International Society of Blood Transfusion
ADR	Adverse Donor Reaction
HUSM	Hospital Universiti Sains Malaysia
IHN	International Haemovigilance Network
LOC	Loss of Consciousness
NBC	National Blood Center
BTS	Blood Transfusion Service
WHO	World Health Organization
USM	Universiti Sains Malaysia

ABSTRAK

REAKSI VASOVAGAL DALAM KALANGAN PENDERMA DARAH DI HOSPITAL UNIVERSITI SAINS MALAYSIA

Pengenalan: Kadar pulangan penderma darah sangat dipengaruhi oleh kesan sampingan yang terjadi semasa proses menderma darah terutamanya kesan reaksi vasovagal. Reaksi vasovagal berlaku apabila sistem saraf parasympathetic diberi rangsangan oleh pelbagai faktor semasa atau selepas proses pendermaan darah berlaku.

Objektif kajian: Objektif utama kajian ini adalah untuk mengetahui kadar kejadian reaksi vasovagal dalam kalangan penderma darah dan juga mengkaji faktor biologi dan sosial penderma darah yang telah mengalami reaksi vasovagal di Hospital Universiti Sains Malaysia.

Bahan dan kaedah: Untuk objektif pertama, kajian keratan rentas dilaksanakan yang melibatkan semua penderma darah yang datang ke Unit Perubatan Transfusi Hospital Universiti Sains Malaysia dari tempoh bulan Jun 2018 hingga Jun 2021. Maklumat diperoleh daripada Sistem Maklumat Perubatan Transfusi (My Transfusi). Semua penderma darah yang mengalami reaksi vasovagal telah dikenal pasti oleh staf dan butiran lengkap penderma darah akan diisi di dalam Borang Laporan Kesan Sampingan penderma darah.

Untuk objektif kedua, kajian kawalan kes dilaksanakan untuk menganalisis hubung kait antara penderma darah yang mengalami reaksi vasovagal (kes) manakala untuk kontrol pula, penderma darah yang tidak mengalami sebarang kesan sampingan telah dipilih secara rawak. Segala maklumat termasuk maklumat peribadi dan maklumat pendermaan darah dianalisis dan dihubung kait menggunakan ujian analisis statistik.

Keputusan: Seramai 35 134 penderma telah menderma darah di Unit Perubatan Transfusi Hospital USM dalam tempoh masa kajian. Seramai 159 orang penderma telah mengalami reaksi vasovagal (kes), menjadikan kadar penderma darah yang mengalami reaksi vasovagal adalah 0.45%. Dalam kalangan ini, majoriti adalah perempuan (72.3%), berumur bawah 30 tahun (93%), populasi Melayu, mempunyai berat badan bawah 55kg (77.4%) dan merupakan penderma darah kali pertama. (53.5%). Melalui ujian analisis statistik, kajian menunjukkan hubung kait yang signifikan antara jantina, berat badan, jumlah darah yang diderma, dan penderma pertama kali dengan reaksi vasovagal.

Kesimpulan: Kadar kes reaksi vasovagal dalam kalangan penderma darah di Hospital USM adalah rendah. Walau bagaimanapun, sekiranya perkara ini tidak dibendung dari awal, kemungkinan ia boleh mengakibatkan kesan yang lebih serius terutamanya kepada kebajikan penderma dan yang lebih penting adalah kadar kepulangan penderma darah. Dengan mengenal pasti penderma darah yang mempunyai risiko, langkah- langkah pencegahan perlu diambil terlebih dahulu. Kaedah seperti menggalakkan minum air secukupnya sebelum proses pendermaan darah, mempraktiskan regangan otot dan sebagainya mampu mengurangkan kadar reaksi vasovagal.

ABSTRACT

VASOVAGAL REACTION AMONG BLOOD DONORS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

Introduction: The blood donor return rate is mostly affected by adverse events (AE), particularly vasovagal reactions (VVR). VVR are caused by the parasympathetic nervous system being stimulated during blood donation process.

Objectives: This study aims to determine the prevalence of VVR among blood donors and to study its associated biological factors at Hospital Universiti Sains Malaysia (USM).

Methodology: The first part of this study is a cross-sectional study that included all blood donors who attended the Transfusion Medicine Unit (TMU) of Hospital USM from June 2018 until June 2021. The donors who developed VVR within this time frame were identified. The information was obtained from the transfusion medicine information system (My Transfusi) and the donor's adverse reaction form. The second part is a case-control study that analyses the association of sociodemographic and donation details among blood donors using logistic regression. The case group includes a blood donor who developed a vasovagal reaction. The control group was chosen from blood donors who did not develop vasovagal reactions in a 1:2 ratio randomly. The biological data and details regarding the donation factors of all donors were analyzed, including age, gender, race, weight, the volume of blood collected, frequency of donation, and donation details such as place of donation, vital signs, and pre-donation hemoglobin level.

Results: Among 35,134 total blood donors who donated within the study period, 159 cases of VVR occurred, with a prevalence of 0.45%. The occurrence rate of VVR was 4.5 cases for every 1000 blood donors. Among the vasovagal blood donors, the majority were from the female gender (72.3%), young age group (93%), Malay population (95%), a body weight of less than 55 kg (77.4%), and first-time blood donors (53.5%). The result showed a significant association between gender, body weight, the volume of blood collected, and first-time blood donors with vasovagal reactions.

Conclusion: The prevalence of vasovagal reactions among the blood donors was relatively low. Even though it was low, if these events continue, they may have serious consequences for donors' welfare especially donor retention, and donor return rate. So, by identifying the potential donor who is at risk, few initial preventions can be practiced prior to the procedures, such as encouraging water intake, distraction techniques, and applying muscle tension in order to prevent VVR.

CHAPTER 1

INTRODUCTION

INTRODUCTION

The Transfusion Medicine Unit (TMU) has a major role in the blood management system in each hospital or institution. To supply adequate and safe blood to patients, TMU needs to have a good strategy. One of the most important aspects to meet the demand is donor recruitment. The main strategies are to recruit new donors as well as to retain the recruited donors. This is very challenging, especially in developing countries and over the years some strategies have been evolved (1,2).

It is known worldwide that whole blood donation is generally considered a safe procedure. For most regular donors, the procedure of blood donation is simple and without complications. Positive experiences during donation acted as motivational factors to donate blood again (3). However, some of the blood donors may experience an adverse event (AE) during or after the completion of the donation.

1.1 Definition of Donor Adverse Events

Donor AE has been defined as a symptom or sign of donor discomfort that is severe enough to either warrant the donor's calling for the attention of the blood bank staff or be noticed by the surrounding staff (3,4).

The International Society of Blood Transfusion Working Party on Hemovigilance (ISBT) concluded that AE related to the donation process is mainly divided into local and systemic symptoms. The local symptoms such as hematoma, pain or swelling at the donation site, and either nerve or arterial injury. Importantly, the common systemic reactions are vasovagal reactions (VVR).

1.2 Definition and Classification of VVR

A VVR is defined as the general feeling of discomfort experienced by blood donors described as light-headedness, dizziness, nausea, or vomiting with or without an accompanying loss of consciousness. VVR is classified as an immediate or delayed reaction in accordance with the Malaysia National Blood Centre (NBC) adoption of the Standard for Surveillance of Complications related to Blood Donation. An immediate VVR is when the symptoms first appeared before the donor has left the donation site and a delayed VVR occurs within 24 hours after the donor has left the donation location (10).

1.3 Prevalence of VVR in Malaysia and Worldwide

The incidence of adverse reactions among blood donors varies from one population to another. This might be associated with a few factors including sociodemographic characteristics of the donors, the place of donation, as well as the behavior of collection staff (5,8).

Based on the National Blood Centre Hemovigilance Report 2019, the incidence of donor AE in Malaysia was 0.33%, with the highest incidence of VVR (6). A study of donor VVR in North Malaysia reported that the occurrence of VVR was 1.5% (9).

Based on a previous study, the overall prevalence of VVRs in whole blood donors is estimated to be between 1- 4% worldwide (10-13). However, a few studies also reported that the incidence of VVRs is less than 1% with about 0.87% occurrence in the Greeks (11). While other studies showed a higher prevalence of VVRs about 8.2% to 11.6% in Karachi (7) (28).

1.4 Sign and Symptoms of VVR

Symptoms of VVR are different among all blood donors. The classification of VVR based on the National Hemovigilance Centre is divided into mild, moderate, and severe. Mild VVRs such as nausea, dizziness, anxiety, pallor, and sweating. Moderate reactions include hypotension, vomiting, and transient loss of consciousness; and severe when loss of consciousness is associated with other signs and symptoms such as recurrent vomiting, incontinence, prolonged pulse, and/or BP recovery times (14).

One of the serious immediate morbidities of medical significance during blood donation is syncope (15). A VVR case reported in 2019 showed most cases are mild reactions while the severe VVR was presented with fitting episodes (6).

1.5 Pathogenesis of VVR

VVR is a complex reaction. It results from a neurophysiological reflex which can also be seen in most healthy people. It is a benign condition characterized by a self-limited episode of systemic hypotension. The pathogenesis of VVR has been mainly due to the stimulation of the parasympathetic nervous system, which can be further augmented by psychological factors, and the volume of blood removed (7).

In the process of blood collection, donors are typically in the recumbent or semi-recumbent position. Many reactions occur after blood donation when donors are ambulating in an upright posture. The reactions are mediated due to the pooling of blood in calf muscles (16, 17). The activation of the parasympathetic autonomic nervous system causes reduced peripheral vascular resistance and heart rate, leading to a reduction in systemic blood

pressure and cardiac output, thus oxygen and nutrient supply to cerebral and peripheral tissues also were reduced. This will be manifested by signs and symptoms of VVR such as dizziness and pallor (15).

The synergistic psychological factors also might be contributed to these reactions. The known triggering factors such as pre-donation anxiety, fear of needles, the experience of pain at the donation site, seeing his or her own blood or other donors' blood and state of tension of undergoing the donation (Crocco and D'Elia, 2007, Agnihotri et al., 2012). Studies had observed an emotional factor such as feeling fear was associated with the female gender and among high school student (Newman, 2002, Fu and Levine, 2016, France et al., 2014). Indeed it is the strongest predictor of syncopal reaction during blood collection (Fu and Levine, 2016). Post donation events occurs when donors stand up after losing about 500ml of blood and these lead to drop in arterial blood pressure and cerebral perfusion, which reduces blood flow to the brain (Jardine et al., 2018).

1.6 Factors associated with VVR.

VVR related to blood donation are multifactorial. The factors can be classified as modifiable or non-modifiable. Modifiable factors or donor-related such as fear of needles, anxiety, sleep duration, and other social stressors such as waiting time and phlebotomist experience. While, non-modifiable include age, gender, ethnicity, and first-time donation (15, 22). The association between VVR and the characteristic of the donor is highly significant. Previous studies reported the association of multiple factors such as age,

gender, weight, and volume of blood collected with the development of VVR (8, 12, 19, 23-26).

1.7 Complication of VVR

VVR in blood donors have significant implications for donor retention and will compromise donor safety (27,28). Negative experiences such as VVR during blood donation are found to be the main reason for self-deferral and decreases the likelihood of return donations in the future (3). First-time donors who experienced VVR lead to lower return rates about 20% and 33% among repeats blood donors (26).

1.8 Interventions to VVR

The decision to donate blood again in the future may be affected by a donor's VVR experience. Study shows positive experience donations expressing stronger intentions to donate again (29). Donors who are at increased risk of VVR should be counselled and advised for pre-donation hydration (30). Donors who are pre-counselled will be able to tolerate the reaction better as they are already aware of the possibility of developing such symptoms (20) Exposure to a brief educational brochure can enhance prospective donor confidence and ability to avoid vasovagal reactions (31). However, some studies provide evidence that no interventions can prevent or reduce VVR (32).

1.9 Justification of study

The determination of such factors can greatly assist in reducing the incidence of the reaction in accordance with hemovigilance initiatives. This can ultimately result in better retention of blood donors to maintain a constant and reliable supply of blood for future usage.

As there is fewer local data available and in view of the significance of VVR to Blood Transfusion Services (BTS), it is essential for this study to be done to explore the rate of VVR and to identify the risk factors that can contribute to its occurrence in our multiracial local populations. Another justification of this study includes being able to identify a potential blood donor who is at risk of developing VVR. This may aid in the management of blood donors. An additional objective was to determine the association of various demographic and clinical characteristics of blood donors with VVR.

Thus, this study was conducted to estimate the prevalence of VVR among whole blood donors in Hospital USM and to determine the association of various demographic and clinical characteristics with the type and severity of VVR.

The first part of this study is a cross-sectional study that required the number of all blood donors who attended the Transfusion Medicine Unit of Hospital USM from June 2018 until June 2021 and to identify the donors who developed VVR within this time frame. The information was obtained from the transfusion medicine information system (My Transfusi) and from Donor Adverse Reaction Form. Second part is a case-control study which compare and analyse the association of sociodemographic and donation details of

between case and control donors using logistic regression. Case group include blood donor who developed VVR, and control group consisted of blood donor who do not develop VVR that was choosen randomly. All samples' biological data and donation factors, including age, gender, race, weight, volume of blood collected, frequency of donation, and donation details such as site of donation, vital signs, and the pre-donation haemoglobin level, were analysed using the Statistical Package for Social Software (SPSS) version 26.

This dissertation was arranged according to Format B (Manuscript Ready Format) according to the guidelines by the Postgraduate Office, School of Medical Sciences (2016). The following chapter contains the introduction and objectives of the study.

Chapter 2 contains the study protocol that has been submitted and obtained ethical approval from Jawatankuasa Etika Penyelidikan Manusia (JEPeM), Universiti Sains Malaysia (JEPEM Code: 21040288).

Chapter 3 is the manuscript entitled "Prevalence and factors associated with vasovagal reactions among blood donors in Hospital USM' that already published by the Journal Transfusion Clinique et Biologigue (TRACLI)

Chapter 4 includes the appendices contain an additional literature review and evidence of publication and poster submission. The raw data is included in the attached CD.

OBJECTIVES

General Objective

To determine the prevalence and factors associated with vasovagal reactions among whole blood donors in Hospital USM.

Specific Objectives:

1. To determine the prevalence of vasovagal reaction among whole blood donors in Hospital USM.

2. To determine the associated factors among whole blood donors who develop vasovagal reactions and who do not develop vasovagal reactions (control group in Hospital USM.

3. To determine the severity of vasovagal reactions that occur among whole blood donors in Hospital USM

CHAPTER 2

STUDY PROTOCOL

CHAPTER 2: STUDY PROTOCOL

2.1 FULL STUDY PROTOCOL

INTRODUCTION

The transfusion Medicine Unit have two major responsibilities in managing blood specially to meet the blood supply for the patient as well as to ensure maximum safety of the blood. Blood transfusion is known as a key component in every healthcare system which saves a million lives around the world. Although the blood donation process is considered as safe, small percentage of donors experienced an adverse reaction during or after completion of donation. The International Society of Blood Transfusion Working Party on Hemovigilance has classified the occurrence of adverse reactions mainly into local symptoms and generalized symptoms and to other complication related to apheresis, allergic reactions, and others.

Donor adverse reaction has been defined as symptom or sign of donor discomfort that is severe enough to either warrant the donor calling for attention of the blood bank staff or was noticed by the staff. The main concern is the systemic reaction, most common being the vasovagal reactions especially those associated with syncope which could endanger donor return.

Vasovagal reactions (VVR) in blood donors have significant implications for donor retention as well as in management of donor sessions. Based on previous study, a non-syncopal vasovagal reaction decreases the blood donor return rate by 30 to 56 percent after a 1-year follow-up and syncope decrease the donor return rate to 53 to 76 percent.

According to the Standard for Surveillance of Complications related to Blood Donation adapted by National Blood Centre, VVR are classified as an immediate and delayed whereby if the symptoms developed before the donor has left the donation site are termed as immediate VVR and if the symptoms appearing after the donor has left the donation site but within 24 h are classified as delayed VVR.

The vasovagal reactions, mainly with pre-syncope, are the most common ones and include a lot of symptoms such as pallor, weakness, sweating, nausea, dizziness, loss of consciousness, convulsions and involuntary passage of urine or faeces. Although the prevalence of VVR occurrence is low, but the implications to donor return rate is significant.

Study rationale / Justification of the study

Although the prevalence of vasovagal reaction among blood donor are vary worldwide, the available data on prevalence of vasovagal reaction among Malaysian population are still limited. Thus, from this study, we can determine the prevalence of vasovagal reactions among Malaysian population especially among Kelantanese blood donor.

From this study also, we can determine what are they most frequent type and severity of vasovagal reactions that commonly occur.

The important point in this study, determination of the donor factors that contribute to the risk of develop vasovagal reactions. Determination of this factors can ultimately result in better retention of blood donors to maintain a constant and reliable supply of blood in the future.

The purpose of this study is to find the prevalence of vasovagal reactions in blood donors during or immediately after blood donation in a blood bank of Hospital Universiti Sains Malaysia and to evaluate the contributory role of donors' biological factors in adverse reactions in blood donors. These factors include frequency of blood donation (first-time or repeat donors), age, sex, body weight, pre donation blood pressure and haemoglobin (Hb) level.

This study is different from another study that have been done in terms of our study population that involve the majority of them are Malay about 90%, from Kelantanese population that come from different ethnics group. Most of our donor also are from college and Form 6 student.

Research question

1. What is the prevalence of vasovagal reactions among blood donor in Transfusion Medicine Unit of Hospital USM?
2. What are the factors associated with Vasovagal reactions?
3. What is the severity of vasovagal reactions that commonly occur among blood donors?

OBJECTIVES

General: To determine the prevalence and factors associated with vasovagal reactions among whole blood donors in Transfusion Medicine Unit (TMU) of Hospital USM.

Specific:

1. To determine the prevalence of vasovagal reaction among whole blood donor in Transfusion Medicine Unit of Hospital USM.

2. To determine the associated factors among blood donor who developed vasovagal reactions in Transfusion Medicine Unit of Hospital USM.

3. To determine the severity of reactions that occur among vasovagal blood donor in Transfusion Medicine Unit of Hospital USM

LITERATURE REVIEW

According to systematic review and meta-analysis done by Amrein et al, the overall prevalence of VVRs in whole blood donors is estimated to be between 1- 4% and 7% (moderate reactions) and between 0·1 and 0·5% (severe reactions), (Amrein et al., 2012). VVRs have significant implications especially for the welfare of donors, staff time and training, the management of donor sessions and most crucially on the retention of donors and security of the blood supply (France et al., 2004; France et al., 2005; Newman et al., 2006a; van Dongen et al., 2013)**.** Syncope is the major cause of immediate morbidity of medical significance during blood donation and is the most severe of a spectrum of vasovagal reactions (VVRs) which range from mild pre-syncopal symptoms (e.g. nausea and light-headedness) to severe reactions involving syncope.

An increased risk of VVRs has been associated with multiple factors including pre-donation anxiety (Labus et al., 2000; Ditto & France, 2006a; Viar et al., 2010), first-time donation (Newman, 2003; Rios et al., 2010; Bravo et al., 2011; Wiersum-Osselton et al., 2014), young age (Tondon et al., 2008; Rios et al., 2010; Bravo et al., 2011), weight (Newman, 2003), low estimated blood volume (EBV) (Rios et al., 2010; Bravo et al., 2011) and female gender (Tondon et al., 2008).

While according to one year study done in Malaysia by Hasan et al,his statistical-epidemiological study showed that the occurrence of VVR rate in Hospital Pulau Pinang was 1.5%, and the association between vasovagal reactions and characteristics of the donor is highly significant. There was a significant association between occurrence of VVRs with

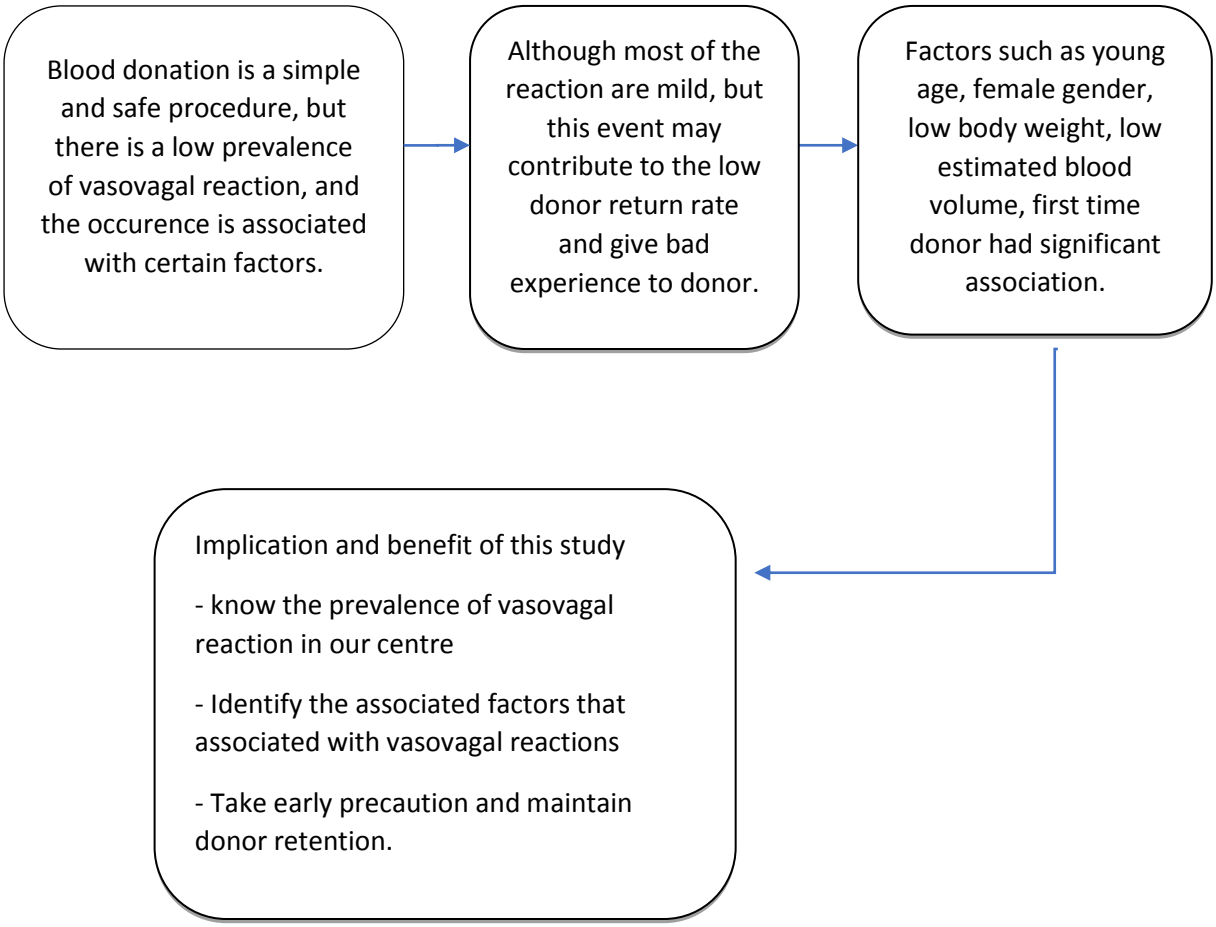
the young age group donor, female gender, race, frequency of donation and location of donation and pre-donation blood pressure. The most common vasovagal symptoms are lightheadedness, nausea, muscle twitching, vomiting and loss of consciousness (~1 %) (Hassan et al 2020).

The incidence of adverse reactions among blood donors varies from one population to another, and this might be related to the sociodemographic and characteristics of the donors. Among 3.8% developed adverse events and from that 41.9% blood donor developed vasovagal reactions, majority were female with young age group (<30 years old). Among those who developed vasovagal reactions, 23% felt nauseated or vomited, 14% hyperventilated, 6.9% syncope with delayed syncope, 6.1% felt dizziness and others are localized symptoms as well as developed miscellaneous reactions. Donors having education below Higher Secondary experienced more reactions and first-time donors have higher frequency 79.43% of adverse reactions than repeat donors (Newman et al.2002)

Based on study done by Tondon et al, donor reaction rate of 1.6% was observed, of which 7% donors experienced reaction of moderate and severe grade. Majority of the reactors had donated for the first time and age had a significant effect on the rate of reaction. There are higher predisposition of young age towards donor reaction. At the same time, age was found to be a significant factor in predicting the grade of reaction. Lower the age of donor, more are the chances of higher grade of reaction. His study proved that weight did not have an effect on the vasovagal reaction as the blood is drawn considering the weight and gender of the donor. Female gender was found to be a significant predictor of reaction when compared with male gender of similar weight group and blood volume drawn. There could be known, or unknown emotional or psychological factors associated with female gender

A retrospective single-centre study regarding various factors that influence vasovagal donors was conducted from March 2000 to November 2010, they found that the prevalence of occurrence 1.23% and there is significant association between gender (female vs male) with young age <45 year old, weight of less than 45 kg, estimated blood volume of 4.5L and in first time donors, although there is no association with volume of blood loss (Philip et al., 2014).

Figure 1: Conceptual framework



METHODOLOGY

Study design

For Objective 1, it is conducted by a cross sectional study and

For Objective 2 & 3, it is conducted by a case control study.

This is a case-controlled study that compare groups retrospectively. This study design is useful for studying a cause and effect in a low prevalence disease.

All the donor who developed vasovagal reactions are listed as a case group. The control group will be chosen randomly from all the list of donors who came to our blood bank in a ratio of 1 case to 3 control donors, and the data for both groups will be compared.

Control group is required to know the details and groups of donors who did not developed vasovagal reaction.

Study area

Transfusion Medicine Unit of Hospital Universiti Sains Malaysia.

Study period

From October 2020 until October 2022

STUDY POPULATION

I. Reference population

All blood donor attending Transfusion Medicine Unit of Hospital USM, Kelantan

II. Source population

All vasovagal blood donor attending Transfusion Medicine Unit Of Hospital USM from 1st June 2018 until 30th June 2021.

III. Sampling frame

Case: All blood donor attending Transfusion Medicine Unit of Hospital USM, from 1st June 2018 until 30th June 2021, who developed vasovagal reaction will be selected.

Control: All blood donor attending Transfusion Medicine Unit of Hospital USM from1st June 2018 until 30th June 2021 who did not developed vasovagal reaction.

STUDY CRITERIA

i. Inclusion criteria

Case: All whole blood donor who developed vasovagal reactions.

Control: All whole blood donor who do not developed vasovagal reactions

ii. Exclusion criteria

Apheresis donor

Autologous donor

SAMPLE SIZE ESTIMATION

Objective 1: To determine the prevalence of vasovagal reaction among blood donors in Transfusion Medicine Unit of Hospital USM.

Single proportion formula: $n = \left(\frac{Z\alpha/2}{d}\right)^2 [p(1-p)]$

n=sample size

Z=standard normal coefficient, typically 1.96 for 95% CI

P=prevalence of proportion

d=precision

Reference	P	d	Sample size	+ 10% drop out
Philip et al, 2014	0.0123(proportion of vasovagal reaction (1.23%).	0.25	76	85

n = 85

This is sample size estimation chosen for objective 1 as it produces big sample size.

Objective 2:

To determine the associated factors of vasovagal reactions among case and control group of blood donors in Hospital USM.

Calculated by PS software using two proportion formula

$\alpha = 0.05$ (the probability that will falsely reject the null hypothesis)

Power = the probability of correctly rejecting the null hypothesis

Po = the probability of the outcome for a control patient.

P1 = the probability of the outcome in an experimental subject

Variables	P_o	P_1	Power	m	Sample size	Sample size x (depend on m)	+10% drop out
Age ≥ 30 < 30	0.02 (Donor age less than 30 years old who developed vasovagal reactions, 1.08%) Tondon et al, 2008)	0.47 (Donor age more than 30 years old who did not developed vasovagal reactions.	0.8	2	68	204	**224**
Gender	0.021 (Female developed vasovagal reactions, 2.1%) Hasan I et al,2020	0.99 (Male did not develop vasovagal reactions, 98.8%)	0.8	1	101	202	222
Frequency of donation	0.02 (First time donor who develop vasovagal reactions, 2%) Hassan et al, 2020	0.99 (Regular blood donor who did not develop vasovagal reactions, 98.8%)	0.8	2	68	204	224

Objective 2: **n =224**

Objective 3:

To determine type and severity of reactions that occur among vasovagal blood donors in Hospital USM.

Single proportion formula:

$$n = \left(\frac{Z\alpha/2}{d}\right)^2 [p(1-p)]$$

n=sample size

Z=standard normal coefficient, typically 1.96 for 95% CI

P=prevalence of proportion

d=precision

$$n = \left(\frac{1.96}{0.05}\right)^2 [0.135(1-0.135)]$$

= 179.4 ~ 179

Objective 3: **n=179**

Based on all calculation, we choose n= 224 as final sample size.

Sampling method and subject recruitment

a. Blood donor who registered from 1st June 2018 until 30th June 2021 will be recruited.

b. All blood donors who developed vasovagal reactions (CASE), which fulfilled inclusion and exclusion criteria will be included as a case sample and no sampling method applied in view of small data.

c. For (CONTROL) sample which is blood donor who did not developed vasovagal reactions were sampled by simple random method in a ratio of 1 case to 3 control using online randomized sampling method.

RESEARCH TOOL

1.Data Collection Sheet

This form is available in Transfusion Medicine Unit of Hospital USM since 2015, this form is adapted and follow the definition of National Blood Centre. All staff of blood bank are aware about the definition for each category and grading. My study is focusing on generalised symptoms of adverse donor reactions (Vasovagal Reactions)

DATA COLLECTION SHEET

INCIDENT FORM FOR ADVERSE DONOR REACTION

DONOR DETAILS

Name:	I/C:
Gender:	Telephone no:
Weight:	Barcode:
Date of donation:	Number of previous donations:
Place of donation:	

DONATION DETAILS

Type of donation: Whole Blood	
Time starts:	Time end:
Time of reaction:	Time of recovery:
Volume collected:	Donation terminated: Yes No
Previous history of reactions: Yes No If yes, describe:	

TYPE OF REACTIONS (Tick where applicable)

Type of reaction				Grading of severity		
				mild	mod	severe
Local symptoms	Blood outside vessels	Hematoma				
		Arterial puncture				
		Delayed bleeding				
	Pain	Specified as	Nerve irritation			
			Nerve injury			
			Tendon injury			
		Or not	Painful arm			