UNIVERSITI TEKNOLOGI MARA

MOLECULAR BASIS OF RHD VARIANTS AMONG RHD NEGATIVE BLOOD DONORS IN MALAYSIA: A CROSS-SECTIONAL STUDY

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ABSTRACT

Rhesus blood group system consists of a few variants such as partial D, Weak D and DEL phenotype. Rhesus genotyping on those phenotypes has been intensively studied and found vary in different populations. To date, there is a paucity of data for DEL and weak D phenotype in Malaysian population, thus the purpose of this study was to determine the molecular basis and the prevalence of DEL and weak D phenotype in Malaysia. A total of 322 RhD negative blood samples were collected from the blood donors at National Blood Centre, Kuala Lumpur Malaysia. Serological and molecular analyses was performed, and positive samples from the *RHD* gene amplification were further tested for the the presence of *RHD 12227A* allele by using SSP-PCR to detect DEL phenotype. Meanwhile, a specific kit was used to determine the the subtype of weak D. Among the 322 blood samples, 21 samples (6.5%) were confirmed as DEL phenotype by the presence of *RHD1227A* allele and two samples positive for weak D type 15 (0.6%). Majority of DEL samples came from Malays donors (n=10), followed by Chinese (n=6) and Indians (n=5), whereas all weak D samples came from Chinese ethnic. In conclusion, the prevalence of DEL and weak D phenotype is lower in Malaysia compared to other Asian countries. This study added to the understanding of molecular basis underlying DEL and weak D phenotypes in our population and provided useful information for adopting suitable genotyping strategies in future.

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CHAPTER ONE
INTRODUCTION

1.1 Background of Study

Rhesus (Rh) blood group system was first discovered in 1940 by Landsteiner and Wiener, a world's most eminent figures in transfusion medicine (Westhoff C., 2007). Generally, Rh has subscribed to the theory that it is second most clinically important and immunogenic blood group in transfusion medicine after ABO blood group system. Rh was traditionally categorized into Rh positive or Rh negative groups based on the foundation of the presence or correspondence of D antigen either its presence or not correspondingly. Genetically, Rhesus proteins were encode by two genes which are *RHD* and *RHCE* gene, that located in a tail to tail direction toward the end of the short arm of chromosome 1 (p34–36) (Huang, 2009). RhD encodes D antigen while RHCE encodes CE antigens in various arrangements such as ce, CE, Ce or cE. Van Kim, Colin, & Cartron, (2006) postulated that RHD and RHCE are closely related and differs in 36 out of 417 amino acids. Central to the entire theory of RhD negative diversity, the frequency of RhD negative has been reported to vary among different ethnic groups.

In a multi-ethnic society country such as Malaysia, it is of outmost important to understand D-negative phenotype distribution to estimate compatible blood unit availability and to evaluate risk of Hemolytic Transfusion Reaction (HTR) and Hemolytic Disease of Newborn (HDN). A documented report from University Malaya stated that ccee phenotype is the most prevalent phenotype among D-negative donors in Malaysia, (Kyaw, Maniam, Nadarajan, & Shanmugam, 2012). Another recent study conducted by Musa, Muhamad, Hassan, Ayob, & Yusoff, (2015) revealed that the most prevalent RhD negative phenotypes among Malaysian's blood donor was ccee phenotypes. In contrast, a study in Australia revealed that the most common RhD negative phenotypes among RhD negative blood donors are ccEe and Ccee (Scott, et al., 2014), while another finding in Taiwan denoted that Ccee and CCee are predominant phenotypes in their population (Chen et al., 2004).