

UNIVERSITI TEKNOLOGI MARA

**DIAGNOSTIC PERFORMANCE OF
DIFFERENT CRITERIA AND
STATUS OF PROTHROMBOTIC
BIOMARKERS IN SUBJECTS WITH
FAMILIAL
HYPERCHOLESTEROLAEMIA**

RADZI BIN RAHMAT

MSc

January 2018

AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This topic has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

Name of Student : Radzi bin Rahmat
Student I.D. No. : 2011204058
Programme : Master of Science (Medicine) - MD780
Faculty : Medicine
Thesis Tittle : Diagnostic Performance of Different Criteria and Status
Of Prothrombotic Biomarkers in Subjects with Familial
Hypercholesterolaemia

Signature of Student :

Date : January 2018

ABSTRACT

Familial Hypercholesterolaemia (FH) have several diagnostic criteria including the Dutch Lipid Clinic Criteria (DLCC). However, the comparative diagnostic reference and association between these criteria have yet to be established. Furthermore, the literatures on the prothrombotic status of FH and diagnosed using the DLCC compared to related unaffected (RUC) and normal controls (NC) is scarce. In this study, the diagnostic performance evaluations of Simon Bromme's (SB) criteria, USMEDPED and Japanese FH Criteria against DLCC were done and association between DLCC FH subgroups with the criteria were analyzed along with investigation of prothrombotic status in FH patients based on DLCC compared to RUC and NC. 415 modified DLCC positive FH subjects and 340 normal controls were tested with the three other criteria. In the biomarkers study, 120 FH, 68 RUC and 178 NC recruited and matched for age, gender, ethnicity, smoking status, and hypertension. Blood samples were collected and analysed for the biomarkers. Correlation between LDL-c and the biomarkers were tested by using biomarker assays. All tested criteria showed comparable high specificity (99.4-98.8%). SB criteria showed highest sensitivity (51.1%) but USMEDPED showed lowest (25.3%). The prothrombotic biomarkers were higher in overall FH and definite FH compared to NC. There were correlation between prothrombotic markers and LDL-c. In diagnosing FH, as alternative, SB criteria and JFHC preferred to be used as diagnostic criteria of FH. As the conclusion, along with FH, RUC group are at risk of developing thrombotic complication but less severe.

ACKNOWLEDGEMENT

Alhamdulillah. Firstly, I would like to thank Allah for giving me the opportunity to embark on my MSc and for completing this long and challenging journey successfully. My gratitude and thanks goes to my parents, Rahmat bin Md. Akib and Esah binti Mohd and my whole family. Without their support, vision and determination from both of them, it is impossible for me to get myself to complete my study. Not to forget gratitude and thanks to my supervisor Prof. Dr. Hapizah binti Mohd. Nawawi and co-supervisors Dr. Thuhairah Hasrah binti Abd Rahman and Dr. Nur Alicezah binti Kassim. Thanks you for the support, patience and ideas in assisting me with this project. I would like to express my gratitude and thanks to all my friends including Radzi Ikhsan Ahmad, Nurul Atikah binti Mokhsin, Hanis binti Saimin, Wan Nur Hanis binti Wan Ahmad, Mohd Sufian Hamid and many others. Thank you for all of your great effort in helping me in completing this journey.

Finally, this thesis is dedicated to all supporting staff members of CPDRL and CTC of UiTM. Thank you.

TABLE OF CONTENTS

	Page
CONFIRMATION BY PANEL OF EXAMINERS	ii
AUTHOR'S DECLARATION	iii
ABSTRACT	iv
ACKNOWLEDGEMENT	v
TABLE OF CONTENTS	vi
LIST OF TABLES	xi
LIST OF FIGURES	xiii
LIST OF SYMBOLS	xiv
LIST OF ABBREVIATIONS	xv
LIST OF NOMENCLATURES	xvi
CHAPTER ONE: INTRODUCTION	1
1.1 Study Background	8
1.2 Problem Statement	9
1.3 Research Objectives	9
1.4 Research Questions	9
1.5 Hypotheses	9
1.6 Significance of Study	10
1.7 Scope and Limitation of the Study	10
CHAPTER TWO: LITERATURE REVIEW	12
2.1 Coronary Artery Disease	12
2.1.1 Atherosclerosis	14
2.2 Hypercholesterolaemia	17
2.2.1 Familial Hypercholesterolaemia	18
2.2.2 Familial Hypercholesterolaemia Diagnostic Criteria	23
2.2.2.1 The Simon Broome's Criteria	23
2.2.2.2 Dutch Lipid Clinic Criteria	27