

UNIVERSITI TEKNOLOGI MARA

**A COMPARISON
OF THE
INCIDENCE AND
HAZARD RATIO
OF TYPE II DIABETES MELLITUS
AMONG STATIN
USER GROUPS IN A
MALAYSIAN
HEALTHCARE
SETTING**

ADIBAH BINTI MD SHARIFF

MSc

August 2020

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 thesis 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 : Adibah bt Md Shariff

Student I.D. No. : 2015884346

Programme : Master of Science (Clinical Pharmacy) – PH770

Faculty : Pharmacy

Thesis Title : A Comparison of the Incidence and Hazard Ratio of Type II diabetes mellitus among Statin User Groups in a Malaysian Healthcare Setting

Signature of Student :

Date : August 2020

ABSTRACT

Background. As the usage of certain conventional medications are becoming increasingly common among the current generation, their previously unexplored side effects and long-term effects have started to become a subject of scrutiny, and the link between these medications and long-term effects is starting to be explored. Recently, there has been a massive discovery in terms of the possible contribution of statins in the development of Type II diabetes mellitus (T2DM). This discovery has led to many subsequent debates or uncertainties over the safety and necessity of statins. As the discovery of the relationship between statins and diabetes is still relatively new, there has yet to be extensive research exploring on the more specific details of the association. The individual risk of statin types has been explored but not extensively, among the Malaysian population.

Objectives. To investigate the incidence of new-onset Type II diabetes mellitus and to compare the risk of development of new-onset Type II diabetes mellitus among different statin user cohorts in a Malaysian healthcare setting

Research Design. This was a retrospective cohort study

Methods. 507 patients without Type II diabetes mellitus who were given statin treatment in Hospital Sungai Buloh were retrospectively enrolled and subsequently divided into four cohorts according to the types of statin given.

Results. The mean duration of this study was 32.5 months (± 18.1) while the median duration was almost the same at 31.0 months (± 26.3). The minimum duration of study was 2.9 months, while the maximum duration was 87.9 months. Between the three main cohorts, the incidence of T2DM was found to be highest in the simvastatin user group (20 of 114: 17.5%), followed by the mixed statin user group (35 of 213: 16.4%), and lastly the lovastatin group (28 of 172: 16.3%), $p=0.956$. As the p value was >0.05 , it was found that there was no significant difference in the incidence of T2DM among the three statin user cohorts. Meanwhile, the risk of T2DM was found to be significantly higher in the lovastatin and simvastatin user groups compared to the mixed statin user group, with a hazard ratio of 1.88 ($p=0.017$) for lovastatin compared to the mixed statin user cohort, and a hazard ratio of 1.87 ($p=0.029$) for simvastatin compared to the mixed statin user cohort.

Conclusions. The risk of new-onset T2DM from lovastatin alone or simvastatin alone was significantly greater than that of mixed statin users, in which the statin type was switched at least once throughout the study. The risk of new-onset T2DM posed by lovastatin and simvastatin was almost the same. There was no significant difference in the incidence of T2DM among the three statin user cohorts.

ACKNOWLEDGEMENT

My appreciation goes to everyone who has helped me throughout the journey of completing this thesis. It was a long and arduous journey, but one that has made me grow and learn in so many ways, and one which I will treasure and cherish. This work is dedicated to my late parents, Md Shariff Abdullah and Maimunah Mohamed Tamby, who had always had unwavering faith in me and took pride in everything I did.

I also dedicate this work to my wonderful husband, Amirul Mohd. Mahfuz, who had provided continuous encouragement and support, and who had assisted me without fail, through every plight I faced and through every adventure in our life. I also dedicate this to my four lovely kids: Adam Hafiz, Amelia Sophia, Ariq Yusuf, and Anna Sarah Dahlia.

I would also like to thank my siblings, Azni, Azlina, Aliza, and Anita, and my whole family, including my parents in-law, brothers and sisters in-law, nieces, and nephews.

Special thanks to my supervisors Dr Mahmathi Karuppanan, Dr Shubashini Gnanasan, and Prof Noorizan Abd Aziz, without whom the thesis would not have been completed.

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	xii
LIST OF FIGURES	xv
LIST OF ABBREVIATIONS	xvi
CHAPTER ONE INTRODUCTION	1
1.1 Introduction to the Study	1
1.2 Background of the Study	1
1.2.1 Studies That Found an Increase in the Risk of Diabetes among Statin Users	4
1.2.2 Studies That Found an Association between the Dose Intensity of Statin Treatment and the Risk of Diabetes	7
1.2.3 Studies That Found an Association between the Dose Intensity and Duration of Statin Treatment to the Risk of Diabetes	7
1.2.4 Studies That Found an Insignificant Risk of Diabetes among Statin Users	7
1.2.5 Studies on the Association between Individual Statin Types and the Risk of Diabetes	8
1.3 Problem Statement	9
1.4 Aim of Study	11
1.5 Research Question	11
1.6 Objectives of the study	12
1.6.1 Primary Objectives of the Study	12
1.6.2 Secondary Objectives of the Study	12
1.7 Significance of the Study	12