

UNIVERSITI TEKNOLOGI MARA

**DEVELOPMENT AND VALIDATION
OF PROGNOSTIC MORTALITY
SCORING TOOL AMONG
HOSPITALISED COVID-19
PATIENTS WITH
THROMBOEMBOLIC
COMPLICATIONS
(PROG-M COVID-19 SCORE)**

HANIES YUHANA BINTI OTHMAN

Thesis submitted in fulfilment
of the requirements for the degree of
**Master of Science
(Clinical Pharmacy)**

Faculty of Pharmacy

July 2025

ABSTRACT

Hospitalised COVID-19 patients frequently experience thromboembolic (TE) complications resulting in life-threatening outcomes like multiorgan failure and death. A prognostic mortality scoring tool is a novel clinical instrument that integrates relevant demographic, clinical and laboratory parameters to predict the risk of mortality in the subgroup of COVID-19 patients with TE complications. This study aimed to 1) determine the prevalence of mortality associated with TE complications in hospitalised COVID-19 patients, 2) develop a prognostic scoring tool for mortality among hospitalised COVID-19 patients with TE complication and 3) perform internal validation of the prognostic mortality scoring tool. This retrospective study was conducted in multicentre hospitals: Hospital Sungai Buloh, Hospital Melaka, Hospital Queen Elizabeth and Hospital Wanita dan Kanak-Kanak Sabah. Data was collected based on the hospital admission from March 2020 to August 2022. A Prog-M COVID-19 scoring tool was developed based on a development cohort study of 247 COVID-19 patients with TE complications. The prevalence of all-cause mortality among hospitalised COVID-19 patients reported with TE complications was 26.2% (95% CI: 21.9–30.4) (n=107/409). Univariate risk prediction algorithm was performed and examined variables significantly associated with mortality in the development cohort ($p \leq 0.25$). These variables were age ≥ 58 years old ($p < 0.001$), hypertension ($p < 0.001$), type II diabetes ($p = 0.018$), kidney disease ($p < 0.001$), ischemic heart disease ($p = 0.005$), heart failure ($p = 0.075$), abnormal APTT ($p = 0.025$), abnormal D-dimer result during admission ($p = 0.200$), antihypertensive medication ($p = 0.24$), enoxaparin prophylaxis ($p = 0.133$), and enoxaparin treatment ($p < 0.001$). We developed a final model of the Prog-M COVID-19 scoring tool, which included four variables: age ≥ 58 years old ($p = 0.003$), kidney disease ($p = 0.004$), abnormal APTT result ($p = 0.091$), and enoxaparin treatment during hospitalisation ($p = 0.036$) and it is able to stratify patients at low (score < 0), intermediate (score: 1-10), and high risk (score > 10) of mortality associated with TE complications with an AUROC: 0.726, 95% CI: 0.656-0.797). The Prog-M model was internally validated (n=162) with an AUROC of 0.646 (95% CI: 0.513-0.779) and the nonsignificant Hosmer–Lemeshow goodness of fit test ($p = 0.773$) was achieved by the internal validation cohort. In summary, this scoring tool may help to improve management of TE complications in COVID-19 population by stratifying patients' risks hence indirectly influencing their treatment strategies. Furthermore, this study provides evidence-based data that has potential to assist policymakers in optimising healthcare delivery and protecting public health.

ACKNOWLEDGEMENT

First and foremost, Alhamdulillah, all praise is due to Allah, the Most Gracious and Most Merciful and uncountable salutation upon our beloved prophet Muhammad. I would like to thank Allah S.W.T for granting me ease throughout completing my research journey.

I would like to express my deepest gratitude to my supervisors Dr Hanis Hanum bin Zulkifly, Dr Mohamad Rodi bin Isa and Miss Izzati binti Abdul Halim for their invaluable guidance, encouragement, and expertise throughout the process of completing this thesis. Their insights and feedback made it possible for me to finish this thesis.

I would like to thank Universiti Teknologi Mara under grant Malaysia Research Assessment 225 (MYRA-PHD 2022/1, RD/85/012/2022), Ministry of Higher Education, Malaysia for the financial and management support in this study.

My appreciation goes to the Clinical Research Centre (CRC) Hospital Sungai Buloh, Hospital Melaka, Hospital Wanita dan Kanak-Kanak Sabah and Hospital Queen Elizabeth who provided the facilities and assistance during crucial data collection stage.

Finally, this thesis is dedicated to my parents, Haji Othman bin Ishak and Hajjah and my husband Azirul bin Afneh for their prayers, never-ending love, support, patience, and encouragement throughout my life. I will forever be grateful for their love and inspiration. Finally, special thanks to my siblings and best friends for continuously supporting me to achieve my dream.

Thank you all for making this achievement possible.

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	x
LIST OF FIGURES	xii
LIST OF ABBREVIATIONS	xiii
CHAPTER 1 INTRODUCTION	1
1.1 Introduction	1
1.1.1 Research Background	1
1.1.2 Thromboembolic (TE) complications in COVID-19 Patients	2
1.1.3 Scoring Tool During COVID-19 Pandemic	3
1.2 Analysis of Problem Statement	4
1.3 Rationale of Study	5
1.4 Justification of Study	5
1.5 Research Hypothesis	5
1.6 Research Objectives	6
1.7 Significance of Study	6
1.8 Thesis Layout	6
CHAPTER 2 LITERATURE REVIEW	8
2.1 Introduction	8
2.2 Emergence of COVID-19 Outbreak	8
2.3 Transmission and Pathophysiology of COVID-19 Induced TE Complications	9
2.4 Epidemiology of COVID-19 with TE Complications and Mortality Associated with TE Complications	11

CHAPTER 1

INTRODUCTION

1.1 Introduction

This chapter introduced the research background for the study and provided overview of the research problem, rationale of study, justification of study, research hypothesis, research objectives and significance of the study.

1.1.1 Research Background

The COVID-19 outbreak was first identified in Wuhan, China and was initially thought to be caused by a novel virus, referred as the coronavirus named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and later became widely known as coronavirus disease (COVID-19). On 30th January 2020, the World Health Organisation (WHO) declared a Public Health Emergency of International Concern (PHEIC) as the virus spread rapidly worldwide with accumulated cases of approximately 15,000 cases (Jee, 2020). COVID-19 cases had surged to more than 900,000 cases in three months duration which forced the WHO to declare pandemic on 11th March 2020 (Khan et al., 2020). Until Feb 2024, there were over 704 million reported cases, along with more than 6.8 million mortality cases recorded worldwide (Worldometers.info, 2022).

During the early phase of the outbreak, the clinical manifestation was mainly focused on the effect of the respiratory system whereby those with severe disease experienced alveolar damage causing respiratory failure, leading to death (Adhikari et al., 2020). A significant clinical presentation has been widely observed in hospitalised COVID-19 patients involved thromboembolic (TE) complications, including both arterial and venous thrombosis (Ribes et al., 2020). Arterial thrombosis is commonly manifested as myocardial infarction (MI), stroke or peripheral artery embolism, while venous thrombosis includes deep vein thrombosis (DVT) and pulmonary embolism (PE) (Avila et al., 2021; Thomas et al., 2020).