VALIDATION OF THE AIMS65 SCORE IN PREDICTING OUTCOMES IN UGIB PATIENTS IN PAHANG POPULATION

BY

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A dissertation submitted in fulfillment of the requirement for the degree of Master of Surgery (General Surgery)

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ABSTRACT

Upper gastrointestinal bleeding (UGIB) is a gastrointestinal emergency that can result in significant mortality, morbidity, and use of health care resources. International consensus and American guidelines recommend early risk stratification for acute UGIB to identify patients at higher risk for mortality and morbidity. The currently available scores are complicated, and the usage in local settings is low. The newly proposed AIMS65 score is easy and accurate in predicting outcomes in UGIB. The objective of this study aims to validate the AIMS65 score as a predictor of mortality in patients with acute UGIB in the Pahang population. This was a retrospective study of emergency endoscopies performed in IIUM Hospital, Kuantan, and Sultan Haji Ahmad Shah Hospital, Temerloh from 1st January 2017 to 31st December 2019 for upper gastrointestinal bleeding (UGIB). AIMS65 scores were calculated in 150 patients involved in the study. Patients were monitored throughout their hospitalization. The outcomes measured were in-patient mortality, rebleeding, and the clinical intervention required in UGIB patients. The study included 150 patients with UGIB. There is a male predominance with 72.7%. The median age of patients in our analysis was 63 years old. Forty-three patients (28.7%) had rebleeding. Endoscopic therapy was performed in 40(26.7%), radiological intervention in 3 (2%), and surgery required in 7 (4.7%) among patients who had rebleeding. The predictive accuracy of AIMS65 scores more than 2 was high for inpatient mortality (AUROC 0.89), rebleeding (AUROC 0.867), and endoscopy therapy (AUROC 0.881). The overall mortality was 11.3% (n=17) and was 6%, 36%, 60% and 100% for AIMS65 score of 2,3,4 and 5 respectively. However, AIMS65 scores were not statistically significant to predict radiological intervention and surgery for UGIB patients. As a conclusion, the AIMS65 score is a simple, accurate, and valid risk score that can be applied to patients with acute UGIB.

APPROVAL PAGE

I certify that I have supervised and read this study and that, in my opinion, it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Master of Surgery (General Surgery)

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DECLARATION

I hereby declare that this dissertation is the result of my investigations, except where otherwise stated. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at IIUM or other institutions.

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This dissertation is dedicated to my beloved parents, whose support has always been unwavering

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LIST OF ABBREVIATION

RS	Rockall score
GBS	Glasgow-Blatchford score
AIMS65	Age, INR, Mental state, Systolic blood pressure, Age more than 65
ROC	Receiver Operating Curve
AUROC	area under the receiver operating characteristic
UGIB	Upper gastrointestinal bleeding
IIUM	International Islamic University Malaysia
HOSHAS	Hospital Sultan Haji Ahmad Shah
GCS	Glasgow Coma Scale
OGDS	Oesophagealgastroduodenoscopy
ICU	Intensive care unit
dL	Decilitre
Hg	Mercury
Vs	Versus
SD	Standard Deviation
PPI	Proton pump inhibitor

CHAPTER ONE

INTRODUCTION

1.1 STUDY BACKGROUND

Acute upper gastrointestinal bleeding (UGIB) is a common cause of hospital admission worldwide, with an overall incidence of 100 per 100,000 adults each year in the United Kingdom. The overall mortality from acute UGIB varies from 10 -15%. A local multi-center study done in Malaysia reported incidence of UGIB of 72 per 100,000 population and peaked around 4^{th} to 6^{th} decade. The incidence of UGIB is higher in men compared to women, with a ratio of 3:2. The mortality rate from UGIB in Malaysia was 10.2 % and increased substantially with age

International guidelines recommend early risk stratification for patients presented with upper GI bleeding to help in management with an appropriate level of care. Several prognostic scores have been designed to predict outcomes in UGIB. There are scoring tools that rely on endoscopic results and, therefore, not ideal for early evaluation. Another scoring only requires clinical and laboratory values to be incorporated into the calculation. Examples are the AIMS65 score, pre-endoscopy Rockall score, and Glasgow – Blatchford risk score (GBS)

The newly proposed scoring system, AIMS65, was an easy, uncomplicated, and accurate risk score to predict mortality in patients with UGIB. The score comprises five variables; Albumin level, International normalized ratio (INR), Altered mental status, Systolic blood pressure, and age older than 65. When they are more than one component involved, the mortality rate is considered high. Saltzman et al. concluded in his study that for those with no risk factors, the mortality rate was 0.3% compared to 31.8% in patients with all 5 ($p<0.05$)

Marwan et al. in 2015, based on the 298 patients, showed that AIMS65 was superior in predicting mortality and length of hospital stay. In another recent study

conducted in China, Lei Gu et al. reported AIMS65 scores as a powerful predictor in predicting inpatient mortality.

Currently, available scores have not been widely used in local clinical practice. Risk stratification is essential to predict the prognosis of the disease. There are limited studies regarding the usage of the AIMS65 score in Malaysia. This study can be useful for using the more comfortable, practical, and fast tool in patients presented with acute UGIB. The primary purpose of the study is to validate the AIMS65 as a scoring tool to predict outcomes in patients with acute UGIB in the Pahang population.

1.2 RESEARCH QUESTIONS

1. Is AIMS65 a valid prognostic scoring to predict outcomes in patients with UGIB in the local setting
2. Can the AIMS65 score predict the mortality rate, re-bleeding rate, and clinical intervention to stop the rebleeding in patients with acute UGIB
3. What are the demographic characteristics of patients with acute UGIB in the Pahang population?

1.3 OBJECTIVE

1.3.1 GENERAL OBJECTIVE

- To validate AIMS65 score as a scoring tool to predict outcomes in patients with UGIB in Pahang population

1.3.2 SPECIFIC OBJECTIVES

I. To validate the accuracy of the AIMS65 score in predicting mortality in patients with UGIB

II. To validate the accuracy of the AIMS65 score in predicting rate of re bleeding in UGIB patients

III. To validate the accuracy of the AIMS65 score in predicting the need for clinical intervention in UGIB patients

IV. To describe the demographic characteristics of patients with UGIB in Pahang population

CHAPTER TWO

LITERATURE REVIEW

2.1 DEFINITIONS, AND EPIDEMIOLOGY

Upper gastrointestinal bleed (UGIB) is defined as bleeding in the upper gastrointestinal tract proximal to the ligaments of Treitz.[1]Acute UGIB needs to be suspected in patients presented with haematemesis, coffee ground vomiting, melaena, or an unexplained drop in hemoglobin. The severities of upper gastrointestinal bleeding are varied, ranging from insignificant bleeds to fatal outcomes resulting in death.

Acute UGIB is a common cause of hospital admission worldwide with overall incidence of 100 per 100,000 adults each year in United Kingdom[1] The overall mortality from acute UGIB varies from 10-15%, with higher rates in elderly patients with multiple comorbidities. A local multi-centre study done in Malaysia reported incidence of UGIB of 72 per 100,000 population and peaked around 4th to 6th decade[2]. Incidence of UGIB is higher in men compared to women with ratio of 3:2. The mortality rate from UGIB in Malaysia was 10.2% and increased substantially with age[2]

Aetiology can be widely divided into variceal and non-variceal bleeding. Peptic ulcer disease is the most common cause of UGIB [3], accounting for more than 60% of the cases.

2.2 SCORING IN UGIB

Upper gastrointestinal bleeding (UGIB) is a common gastrointestinal emergency that requires hospital admission, with a reported mortality of 10-15%. Prediction of the outcome and severity of the UGIB has a significant impact in determining the need for urgent endoscopy. International guidelines recommend risk stratification early in managing patients with UGIB. This can be achieved with usage of a prognostic scoring. The international consensus in 2012 recommend patients with upper gastrointestinal

bleeding should be classified as low and high risk based on its risk of mortality and re-bleeding [4]

Unfortunately, the existing risk stratification score for UGIB are not commonly used in a clinical setting for a variety of reasons, including that there are many scores available, the differences between these existing scores are poorly understood, they can be challenging to calculate, and some require endoscopic information not readily available at the time of presentation[5]

Several scoring systems have been developed for patients with UGIB, including those that incorporate endoscopic findings such as Rockall score and those that can be calculated early at admission or pre-endoscopy. Each of this score was designed to predict various outcomes, such as the risk of mortality and rebleeding. Pre-endoscopy scores have greater practical use because of the ability to predict risk soon after the presentation to help in the direction of management. Studies have suggested that these scores identify high-risk patients who might require urgent endoscopy and low-risk patients who could be managed as outpatients[6].

The most well established and widely used pre endoscopic scores are the Glasgow-Blatchford score (GBS) and the AIMS5 score for patients with UGIB. Malaysian CPG for non-variceal bleed recommended using Rockall score as a risk assessment tool in the management of acute UGIB. However, this was prior to the introduction of the new prognostic scoring, AIMS65 in the medical practise in the acute UGIB patients.

2.3 ROCKALL SCORE (RS)

Rockall et al created Rockall score (RS) in 1997. The Ro scoring system was designed to identify patients at risk of adverse outcomes following acute upper gastrointestinal bleeding. The Rockall score is a valid predictor of mortality and re-bleeding. The score combines information such as the patients' age, the occurrence of shock assessed from systolic blood pressure and pulse rate, presence and severity of comorbidities, and stigmata of hemorrhage. Based on the original study by Rockall, there was an increasing trend of re-bleeding with increasing Rockall scores[7,8]

There have been conflicting results for Rockall score as a scoring system to accurately stratify patients at high risk of rebleeding. A study conducted in Amsterdam population in 1999 found negative results and was not good in predicting the risk of re-bleeding [7] . In another study conducted in Malaysia concluded that Rockall score has a low discriminative ability and poorly calibrated for mortality, re-bleeding, and the need for surgery in UGIB [2]

2.4 GLASGOW-BLATCHFORD SCORE (GBS)

The Glasgow-Blatchford score was developed by Blatchford et al at the University of Glasgow, Scotland, UK to determine outcomes in patients presented with UGIB. It was published in The Lancet in the year 2000 and has been widely used as a simple tool. It did not require any endoscopy elements to be include into the score. The parameters used to calculate the score are based on the laboratory values, hemodynamic parameters, presence of melaena or syncope and the underlying medical condition [9,10].

The GBS scores ranges from 0-23 points with the higher score means higher likelihood of a need for endoscopic intervention. GBS was useful to predict the need for blood transfusion, intervention either thru surgery or endoscopy, and mortality among patients with UGIB[11]

A prospective study conducted in Spain concluded GBS is a valid scoring tool to predict rebleeding and the blood transfusion requirement[12].

2.5 AIMS65 SCORE

A newly proposed scoring system, AIMS65 score was found to be easy, accurate and has high predictive value to predict mortality, length of hospital stay and health care costs in patients with acute UGIB [13]

The AIMS65 score was a study conducted on patients in the United States. The score comprised of 5 variables: serum albumin lower than 3 mg/dL, international normalised ratio (INR) higher than 1.5, altered mental status, systolic blood pressure lower than 90 mmHg and age more than 65. When there are more than 2 components

involved, the mortality rate is considered high. In his study, Saltzman concluded that for those with no risk factors, the mortality rate was 0.3% compared with 31.8% in patients with all five risk factors. The model had a high predictive accuracy. A study conducted in Japan in 2013 found that the AIMS65 score is useful for predicting the prognosis of patients with acute gastrointestinal bleeding[14]

In another study conducted in Korea to validate the AIMS65 score for predicting mortality, Park concluded that the AIMS65 score is useful in predicting mortality in patients with non-variceal upper gastrointestinal bleeding. Urgent endoscopic performed in patients with high AIMS65 scores may be linked to reduced length of hospital stay [15]. Chandra et al reported that the AIMS65 score has high accuracy in predicting 30- and 90-day mortality in patients with UGIB[16].

2.6 COMPARISONS BETWEEN RS, GBS, AND AIMS65 SCORE

Various studies have been performed to compare the performance of Rockall score (RS), Glasgow-Blatchford score (GBS) and AIMS65 in predicting outcomes in patients with upper gastrointestinal bleeding (UGIB). A large retrospective study conducted in China involving 799 patients of both non-variceal bleeding and variceal bleeding published in 2018. The author concluded that AIMS65, GBS, and RS scoring approaches were all acceptable for predicting in-hospital death among UGIB patients regardless of subtype of UGIB. The AIMS65 might be the most powerful predictor [11].

A large multicentre prospective study conducted in six hospitals in Europe, North America, Asia, and Oceania in patients with UGIB, found that GBS was superior at predicting the need for hospital-based intervention or death compared to RS and AIMS65 [17]

A recent study was conducted to compare the performance of AIMS65 score, GBS and RS for predicting clinical outcomes in patients with etiology of both non variceal and variceal UGIB. The authors concluded that AIMS65 is far more superior to GBS and RS in predicting mortality and has high accuracy in predicting the need for blood transfusion in UGIB patients[3]

In another study, the AIMS65 score is best in predicting the mortality in patients with UGIB, but GBS is better in predicting the need for intervention[18]

Hyett Bh et al compared the AIMS65 score to GBS and found that GBS is better in estimating the need for blood transfusion. Abougergi et al. also compared the AIMS65 score and GBS and concluded the AIMS65 is more accurate in predicting in-hospital mortality and hospital length of stay; however, both AIMS65 and GBS are similar in predicting 30-day mortality and rebleeding in UGIB[19]

In a study conducted in Australia, Robertson compared the AIMS65 score to the GBS and RS and showed that AIMS65 has superior accuracy to GBS and RS in predicting mortality and the need for ICU admission[20]. A prospective study was designed to compare the performance of AIMS65 with GBS and RS concerning mortality and multiple secondary outcomes such as rebleeding, transfusion requirement, six-month mortality, and length of hospitalization. The Authors concluded that GBS is far more superior in predicting the rebleeding rate and the blood transfusion in UGIB patients; however, AIMS65 performed better in predicting a delayed 60 days mortality[21]

CHAPTER THREE

MATERIALS AND METHODS

3.1 STUDY DESIGN

3.1.1 Study Type

This was a multi-centre, retrospective cohort study conducted in patients with acute presentation of UGIB. The AIMS65 score were calculated upon admission for each patient. All patients diagnosed with acute UGIB in hospitals between 1st January 2017 until 31st December 2019 will be recruited in the study.

3.1.2 Study Area

This study was conducted in Sultan Ahmad Shah Medical Centre @IIUM, Kuantan, Pahang and Hospital Sultan Haji Ahmad Shah, Temerloh, Pahang.

3.1.3 Study Period

The study period was from 15th May 2020 until 31st December 2020

3.2 SELECTION CRITERIA

3.2.1 Target population

Patients with acute UGIB in Pahang

3.2.2 Study Population

All patients with acute UGIB who were admitted between 1st January 2017 until 31st December 2019 in these hospitals.

I. Sultan Ahmad Shah Medical Centre @ IIUM Medical Centre, Kuantan
II. Hospital Sultan Haji Ahmad Shah (HOSHAS), Temerloh, Pahang

3.2.3 Sampling

Convenience sampling was employed. All subjects with diagnosis of acute UGIB fulfilling the inclusion criteria from 1st January 2017 until 31st December 2019 was recruited in this study.

3.2.4 Inclusion Criteria

I. All patients with UGIB age 18 years old and above
II. Patients diagnosed with UGIB of both variceal and non-variceal origin confirmed with endoscopy
III. Patients with signs and symptoms of UGIB either at the time of presentation to the emergency department or if they developed UGIB as inpatient

3.2.5 Exclusion Criteria

I. Incomplete data required for calculation of AIMS65 score
II. Age below 18 years old
III. Normal endoscopy results
IV. Confirmed oesophageal, gastric or duodenal malignancies

3.2.6 Sample Size

I. The Receiver Operating Characteristic Curves (ROC) are used to assess the relationship between each score with the primary and secondary outcomes
II. The Area Under ROC (AUROCs) are then calculated using binomial confidence intervals
III. Based on the ROC curve analysis (version 3.1)
IV. Based on a power 80% and Type 1 error 0.05
V. Expected patients 130
VI. Accounting 10% drop out rate, a final sample size of 143 patients

3.3 DATA COLLECTION

At each center, data on patients presenting to the hospital with UGIB were collected over a period between 1st January 2017 until 31st December 2019. A designated doctor collected data at each site. For every participant, the following data were collected from the medical records: diagnosis, age, sex, race, race, comorbidities, the level of serum albumin, INR level, hemoglobin, systolic blood pressure, altered mental status and either melaena, haematemesis or coffee ground vomiting on presentation. The data collected included patient characteristics and haemodynamic and laboratory variables at presentation necessary to calculate AIMS65 score. Besides, endoscopic findings and timing of the endoscopy, blood transfusion requirement, and patient outcomes: mortality, rebleeding, and the need for clinical intervention through radiology, endoscopy, or surgical procedures. The main primary outcome required was the inpatient mortality, which defined death from any cause trough out hospitalization. The other outcomes were in hospital re-bleeding, and the need for clinical intervention (endoscopic, radiologic, or surgical treatment).

3.4 FLOW CHART

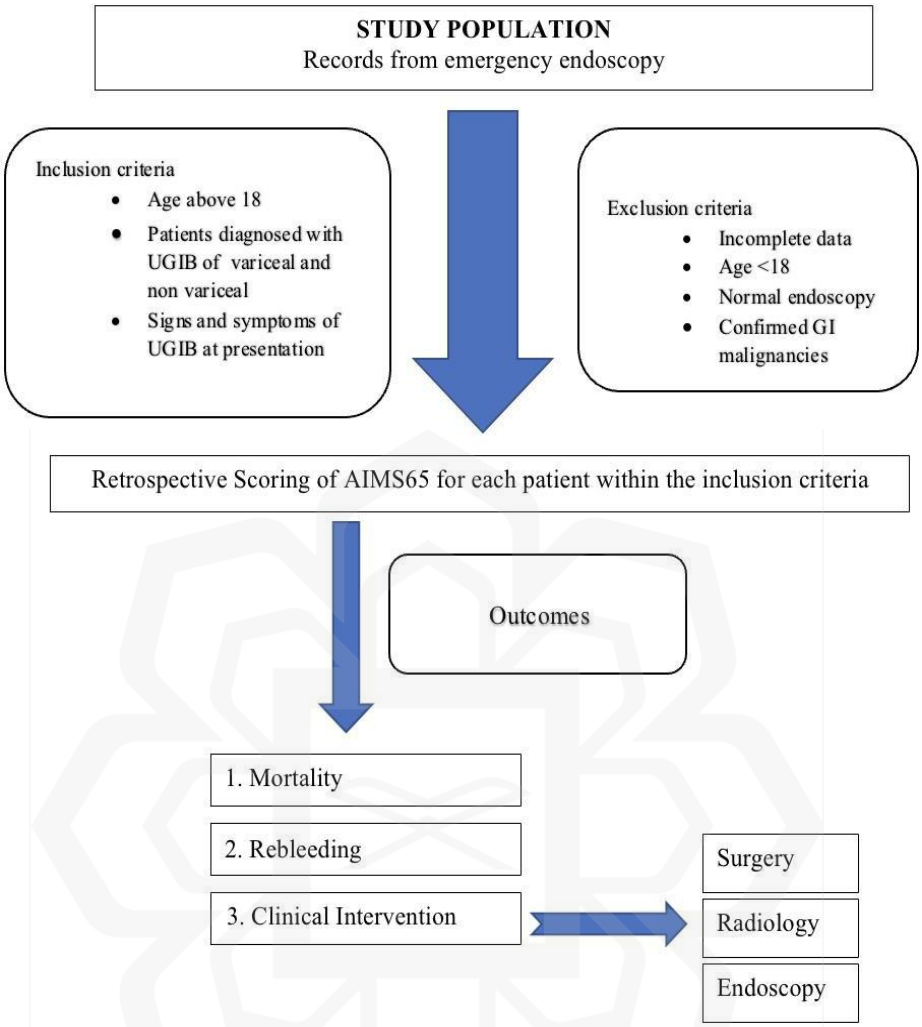

Figure 3.1 Study Flowchart

3.5 OUTCOMES VARIABLE DEFINITIONS

3.5.1 Acute UGIB

Acute UGIB is defined based on the presence of at least one of the following features:

I. Hematemesis
II. Melenic stool
III. Coffee ground emesis