

## ORIGINAL ARTICLE

# Haematochezia and Higher Glasgow-Blatchford Score are Predictive Factors for Higher Red Blood Cells Transfusion Units in a Hospital-based Retrospective Study

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## ABSTRACT

**Introduction:** The association between clinical characteristics and endoscopic profile of acute non-variceal upper gastrointestinal bleeding (NVUGIB) patients with red blood cell (RBC) transfusion has not been well explored in Malaysia. Therefore, a retrospective study was performed using a five-years database to analyse the factors clinically and endoscopically for RBC transfusion. **Methods:** All adult NVUGIB patients who received RBC transfusion within the study period of 2012-2017 in Putrajaya Hospital were enrolled. There were 180 patients selected by systematic random sampling. Our composed clinical data include demography, risk factor, aetiology, presenting symptoms, Glasgow-Blatchford Score (GBS), endoscopic findings according to Forrest Classification and number unit of RBC transfusion. These data were analysed using Mann-Whitney U-Test, Pearson Correlation and Multiple Linear Regression (MLR). **Results:** Total 180 patients, the mean age was 63.9 (SD 11.6). Their presenting symptoms were melaena (62.8%), haematemesis (38.3%), and haematochezia (10.6%), with the cause of bleeding was gastric erosion (65.6%), duodenitis/duodenal ulcer (26.1%), and oesophagitis (7.8%). The mean GBS score was 10.7, and the number of RBC transfusion unit was 2.8. The Forrest Classification showed Forrest III (36.1%), Forrest IIc (22.8%), Forrest IIb and Ib (14.4%) respectively. Pearson's Correlation showed a strong correlation between GBS and unit of RBC transfusion ( $r = 0.922$ ,  $p$ -value  $< 0.001$ ). MLR analysis revealed haematochezia ( $p = 0.022$ ) and higher GBS ( $p < 0.001$ ) were independent factors associated with a higher number of RBC transfusion unit. **Conclusion:** Haematochezia and higher GBS score were two predictive factors for a higher RBC transfusion unit in NVUGIB patients.

**Keywords:** NVUGIB, RBC transfusion, Forrest Classification, GBS score, Haematochezia

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## INTRODUCTION

Acute Non-Variceal Upper Gastrointestinal Bleeding (NVUGIB) remains a common gastroenterology emergency associated with high mortality in hospitalised patients, particularly those with severe co-morbidity (1, 2). The diagnosis of NVUGIB is confirmed by endoscopy when the clinical presentation of upper gastrointestinal bleeding (UGIB) appears, for example, haematemesis, melaena, haematochezia or laboratory evidence of blood loss from the gastrointestinal tract (2). It has an association with various aetiologies, risk factors and different risk assessment group with GBS score. GBS

will give an apprehension likelihood for urgent medical intervention include transfusion, endoscopic or surgical intervention (3). Esophagogastroduodenoscopy (OGDS) has a vital role in diagnosing NVUGIB for endoscopic features referring to Forrest Classification and offers therapeutic interventions (4).

RBC transfusion is an essential component of transfusion in UGIB management, accounting for about 11–14% of all RBC transfusions (5). Restrictive versus liberal transfusion practice in UGIB has been discussed thoroughly, whereby restrictive transfusion strategy significantly improved patients' outcomes (6). It has appeared to be as good as, or putatively better than a liberal approach concerning individual patient's condition based on clinical judgement (6-9).

In Malaysia, there are few studies published on

epidemiology, aetiologies, and risk factor about UGIB (10-12). However, there is no available report on the association between clinical characteristic and endoscopic profile of NVUGIB with RBC transfusion. Therefore, this study was done to evaluate the association statistically.

**MATERIALS AND METHODS**

**Subjects**

This retrospective cohort study was conducted at Putrajaya Hospital, the federal territory of Putrajaya, Malaysia involving patients with NVUGIB diagnosis from 2012 to 2017. The data was retrieved from the Total Hospital Information System (THIS) of Putrajaya Hospital. There were 180 patients have been selected by systematic random sampling. The study was carried out for two years, from 1st January 2017 through 31st December 2018, to collect data from selected patients who fulfil the inclusion criteria, including adult patient aged 18 years old and more, underwent OGDS, diagnosed as NVUGIB and received at least one unit of RBC transfusion. Those who had OGDS as a day-care case, concurrent with lower gastrointestinal bleeding (LGIB) and present episode of rebleeding on similar admission were excluded. The data collected on demographic information, presenting symptoms, risk factor, aetiology, GBS Score, endoscopic findings based on Forrest Classification and number of RBC unit transfusion. This study was conducted with the approval of Human Research Ethics Committee Universiti Sains Malaysia (USM) with the reference number of USM/JEPeM/17020127 and Ministry of Health through Medical Research & Ethics Committee number NMRR-17-139-34033.

**Statistical Analysis**

Statistical analysis of the data was performed using the IBM Statistics Package of Social Sciences System (SPSS) version 24.0. Frequency and percentage were used to present the categorical data while mean and standard deviation for continuous data for the descriptive statistics of variables. The Mann-Whitney U-Test was used to compare the two independent groups, whereas Pearson’s Correlation Coefficient was used to measure the statistical association between GBS and RBC transfusion unit. Meanwhile, Multiple Linear Regression participated in determining the association between presenting symptoms, aetiology, and GBS score with a unit of RBC transfusion. A probability value of P < 0.05 was taken as statistically significant.

**RESULTS**

A total of 180 subjects were included in the study, 118 (65.6%) were male, and 62 (34.4%) were female. The mean age was 63.9 (SD 11.6) years. The patients’ ethnicity distribution consisted of 76.1% Malays, 13.9% Chinese, 6.1% Indians and 3.9% others. General

clinical characteristics of study subjects are shown in Table I. The most predominant risk factor among NVUGIB patients was anticoagulant therapy (41.1%). The presenting symptoms of our patient cohort were melaena (62.8%), followed by haematemesis (38.3%), haematochezia (10.6%) and anaemic symptoms (8.9%) as the cause of bleeding was gastric erosion (65.6 %), duodenitis/duodenal ulcer (26.1%), malignancy (7.8%), Mallory-Weiss Tear (1.7%) angiodysplasia (0.6%) and others (2.2%). The Forrest Classification for NVUGIB patients were also analysed in this study, with 4.4% were found to have Forrest I ulcer, 14.4% with Forrest Ib and IIb ulcer, 12.2% with Forrest IIa ulcer, 22.8% with Forrest IIb ulcer. The majority was found to have Forrest III ulcer, which accounts for 36.1% of the patients (Table I).

The total RBC transfused in 180 subjects were 500

**Table I: Clinical characteristics of study patients (n=180)**

Clinical Characteristics	Frequency (%)	Mean (SD)
<b>Age (years)</b>		63.9 (11.6)
<b>Gender</b>		
Male	118 (65.6)	
Female	62 (34.4)	
<b>Ethnicity</b>		
Malay	137 (76.1)	
Chinese	25 (13.9)	
Indian	11 (6.1)	
Others	7 (3.9)	
<b>Risk Factor</b>		
Anticoagulant therapy	74 (41.1)	
Smoking	63 (35.0)	
NSAIDS Use	49 (27.3)	
Alcohol Consumption	23 (12.2)	
Traditional Drug Use	18 (10.0)	
Steroids Use	14 (7.8)	
<b>Aetiology</b>		
Gastric erosion	118 (65.6)	
Duodenitis/duodenal ulcer	47 (26.1)	
Oesophagitis/Oesophageal Ulcer	14 (7.8)	
Malignancy	9 (5.0)	
Mallory-Weiss Tear	3 (1.7)	
Angiodysplasia	1 (0.6)	
Others	4 (2.2)	
<b>Presenting Symptoms</b>		
Melaena	113 (62.8)	
Haematemesis	69 (38.3)	
Haematochezia	19 (10.6)	
Anaemic Symptoms	16 (8.9)	
<b>GBS Score</b>		10.71 (3.3)
<6	7 (4)	
≥6	173 (96)	
<b>Total RBC unit transfused</b>	500	2.8 (1.5)
1	38 (21.1)	
2	59 (32.8)	
3	20 (11.1)	
4	38 (21.1)	
5	18 (10.0)	
6	7 (3.9)	
<b>Forrest Classification</b>		
Spurting Bleeding (Ia)	8 (4.4)	
Non-spurting active bleeding (Ib)	26 (14.4)	
Visible Vessels (IIa)	22 (12.2)	
Non-Bleeding Ulcer with Overlying Clot (IIb)	26 (14.4)	
Ulcer with Hematin Covered Base (IIc)	41 (22.8)	
Clean Ulcer Ground (Forrest III)	65 (36.1)	

units with a mean (SD) of 2.78 (1.5) units. The majority of NVUGIB patients received two RBC units which accounted for 32.8% (Table I). Hence, the intended variables were being evaluated. The association between aetiologies and number of unit of RBC transfusion was analysed with Mann-Whitney U test because it was skewed data. It showed that gastric erosion had a significant association with the number of units of RBC transfusion ( $p = 0.023$ ). There was no significant association in other aetiologies (Table II). The other variable assessed was presenting symptoms. There were no significant association between melaena ( $p = 0.436$ ), haematemesis ( $p = 0.979$ ) and anaemic symptoms ( $p = 0.081$ ) with the number unit of RBC transfusion. However, haematochezia was strongly associated with the number of unit of RBC transfusion ( $p < 0.001$ ) (Table III). Anaemic symptoms ( $p = 0.081$ ) were included in further statistical analysis with Regression Analysis considering the medically significant variable to the study (Table V). Regarding the GBS score, the mean GBS (SD) was 10.71 (3.3) (Table I). According to Pearson's Correlation, there was a significant correlation between GBS and number unit of RBC transfusion,  $r = 0.922$  with  $p$ -value  $< 0.001$  (Table IV).

**Table II: Association between aetiologies and unit of RBC Transfusion (n=180)**

Aetiology	Frequency (%)	RBC Units (SD)	Mean Difference (95% CI)	p-value
<b>*Gastric Erosion</b>				
Yes	118 (65.6)	2.96 (1.5)	0.52 (0.08, 0.97)	0.023*
No	62 (34.4)	2.44 (1.3)		
<b>*Duodenitis/Duodenal Ulcer</b>				
Yes	47 (26.1)	2.64 (1.4)	-0.19 (-0.67, 0.30)	0.458
No	133 (73.9)	2.83 (1.5)		
<b>*Oesophagitis/ Oesophageal Ulcer</b>				
Yes	14 (7.8)	2.79 (1.8)	0.09 (-0.79, 0.81)	0.746
No	166 (92.2)	2.78 (1.4)		
<b>*Malignancy</b>				
Yes	9 (5.0)	2.25 (1.5)	0.47 (-0.51, 1.45)	0.311
No	171 (95.5)	2.83 (1.4)		

<sup>a</sup>Mann-Whitney U Test  
\*Significant if  $p < 0.05$

**Table III: Association between presenting symptoms and unit of RBC transfusion (n=180)**

Symptoms	Frequency (%)	RBC Units (SD)	Mean Difference (95% CI)	p-value
<b>*Melaena</b>				
Yes	113 (62.8)	2.82 (1.4)	0.12 (-0.32, 0.56)	0.436
No	67 (37.2)	2.70 (1.5)		
<b>*Haematemesis</b>				
Yes	69 (38.3)	2.75 (1.4)	-0.04 (-0.48, 0.40)	0.979
No	111 (61.7)	2.79 (1.5)		
<b>*Haematochezia</b>				
Yes	19 (10.6)	4.53 (1.1)	1.96 (1.32, 2.59)	$< 0.001^*$
No	161 (89.4)	2.57 (1.3)		
<b>*Anaemic Symptoms</b>				
Yes	16 (8.9)	2.25 (1.5)	-0.58(-1.33,0.17)	0.081**
No	164 (91.1)	2.83 (1.4)		

<sup>a</sup>Mann-Whitey U Test  
\*Significant if  $p < 0.05$   
\*\*Significant if  $p < 0.25$

**Table IV: Correlation between GBS and number unit of RBC transfusion**

Variable	Correlation Coefficient, r No unit of RBC transfusion	r <sup>2</sup>	p value
<sup>b</sup> GBS	0.922	0.850	$< 0.001^*$

<sup>b</sup>Pearson Correlation  
\*Significant if  $p < 0.05$

The significant factors (haematochezia, anaemic symptoms, peptic ulcer and GBS) were analysed using multiple linear regression. This statistical analysis was used to determine factors that independently predict RBC transfusion units in these subjects. The final model showed that two factors, hematochezia ( $p = 0.022$ ) and GBS ( $p < 0.001$ ), were independently associated with the number of units of RBC transfusion among NVUGIB patients (Table V).

**Table V: Association of variables to number of RBC transfusion by Multiple Linear Regression in NVUGIB patients**

Predictors	Unstandardized B Coefficient	p value	95% CI	
			Lower	Upper
Haematochezia	-0.339	0.022*	0.049	0.629
Anaemic Symptoms	-0.036	0.811	-0.265	0.337
Gastric Erosion	0.011	0.904	-0.193	0.171
GBS	0.396	$< 0.001^*$	0.369	0.424

Enter Method  
\*Significant if  $p$ -value  $< 0.05$   
There was no issue of multicollinearity or interaction between the significant predictors

## DISCUSSION

Appraisal of clinical characteristics of NVUGIB in this study were demographic data, risk factor, aetiology, presenting symptoms, Glasgow-Blatchford Score (GBS), RBC unit transfusion and endoscopic findings according to Forrest Classification. Three demographic factors were analysed, including age, gender and ethnicity. There were an estimated 2000 patients with NVUGIB from 2012 to 2017 in Putrajaya Hospital, of which 180 (9.0%) were transfused in this study period. Likewise, about 10-13% of RBC being used to treat acute UGIB in the UK and Europe (13, 14). Comparing to a Western Australia study, RBC transfusions for UGIB treatment accounted for 21% of RBC usage (15). This could be explained by the fact that the rate of UGIB at Australian Hospitals was about 140 per 100000 hospitalisations. The hospitalisation rate was double compared to the Malaysian and UK populations leading to higher RBC usage among NVUGIB among the Australian patients (16).

The mean age for NVUGIB patients at Putrajaya Hospital was 63.9. In a local study done in 2000, the mean age was 51.9 years (17). This is comparable to another study done in Europe wherein the sample mean age was 60.5; and in the Republic of Korea, 60.9 (18, 19). The incidence of UGIB was found to be two times higher in men than in women (20). A similar study done locally

in Sultanah Bahiyah Hospital, Kedah, involved a sample of 61.8% male and 38.2% female (12). In this particular study, the sample consists of 65.6% males. This finding was anticipated as male patients make up the highest number of UGIB admission. Besides, data from Putrajaya Hospital showed that 60-70% of NVUGIB patients were male. This trend is in line with a local study carried out by Lakhwani et al., wherein 88.2% of the patients were male, and this is possibly due to higher prevalence of smoking and alcohol consumption (17).

Concerning ethnic distribution, the majority in this study was Malays (76.1%), followed by Chinese (13.9%), Indians (6.1%) and others (3.9%). This distribution is similar to that of a local study done in Sultanah Bahiyah Hospital, in which 70.4% were Malays, 12.0% Chinese, 9.5% Indians and 8.1% other races (12). However, the ethnic distribution in this study differs from a study done in HKL where the highest proportion of the patient was Chinese (47.7%), followed by Malays (25.8%), Indians (23.8%) and other races (3.1%) (17). The finding in HKL was consistent with an audit done in Seremban Hospital (21). The higher Malay ethnicity percentage in the Putrajaya Hospital cohort could be attributed to the predominant Malay ethnicity living in the surrounding areas compared to HKL and a study in Seremban. Interestingly, in an international study done in Texas involving 2196 patients, the highest percentage of the patients were Hispanic (40%), followed by the Whites (29%), the Blacks (28%), and other ethnicities (3%)(12).

Patients with NVUGIB are initiated by trends and behavioural characteristics. Six risk factors were identified in this study. Among them, anticoagulant therapy contributed to 41.1%, smoking 35.0%, NSAIDs use 27.3%, alcohol consumption 12.2%, traditional drug use 10.0% and steroid use 7.8%. These observations differ to a great extent from that of a local study done by Lakhwani et al. and Dewan KR et al., in which smoking contributed to 50.1%, alcohol consumption 37.5%, NSAIDs use 17.2%, traditional drug use 5.5%, anticoagulant therapy 2.3% and steroid use 0.8% (17, 22). The contributive trend found in this study runs parallel to that of a study done in Thailand, wherein the highest contribution of 21.6% was due to anticoagulant therapy, followed by smoking (16%), alcohol consumption (14.6%), and NSAIDs use (15%) (23). In contrast, the contributive trend observed in a study done in Europe found that the factors were reversed: alcohol use contributed to 36.7%, NSAIDs use 34.5%, smoking 26.7% and anticoagulant therapy 7.1% (19). The difference might be contributed by the inappropriate use of oral anticoagulants among the Asian population compared to their European counterparts (24). Meanwhile, in Europe, alcohol consumption is higher among Europeans compared to Asians. Thus, it is not unexpected as alcohol consumption contributed to the higher risk of developing UGIB (25). The aetiologies of NVUGIB analysed in this study comprised gastric erosion

65.6%, duodenitis/duodenal ulcer 26.1%, malignancy 7.8%, other aetiologies 2.2%, Mallory-Weiss tear 1.7%, and angiodysplasia 0.6%. These findings were almost similar to a study done by Lakhwani et al. and Dewan KR et al. with peptic ulcer 61.7%, erosive gastritis/duodenitis 21.9% and others with 5.5% (17, 22). In an RCT by Villaneuva et al., peptic ulcer constitutes 51.0%, erosive gastritis/duodenitis 9.0%, Mallory Weiss Tear 6%, and malignancy 4% (9).

Melaena was the most common presenting symptom in this study with 62.8%, followed by haematemesis 38.3%, haematochezia 10.6% and anaemia 8.9%. This observation paralleled to a study done in the Republic of Korea, in which melaena accounts for 60%, haematemesis 27%, haematochezia 7% and others 6% (18). A similar finding was obtained by Garrido A. et al, in which melaena contributed 53.9%, haematemesis 50.2%, others 13.7% and haematochezia 2.6% of NVUGIB patients (19). Anaemia accounts for the least presenting symptom in this study. The reason is those anaemic patients, particularly iron deficiency anaemia, with no clinical evidence of UGIB, will be investigated by the endoscopic procedure; OGDS, colonoscopy, enteroscopy and/or capsular endoscopy (26).

GBS is a regular scoring tool used for patients presenting with UGIB. In this study, the mean GBS (SD) score was 10.71 (3.3) and comparable to a similar study done in Iran and the Republic of Korea, in which the mean GBS (SD) were 10.71 (4.2) and 12.1 (2.7), respectively (18, 27). GBS score also had a strong correlation to RBC unit transfusion (Table IV). According to an analysis, GBS > 10 combined with other scoring tools can accurately predict the RBC transfusion requirement, and GBS was also found to be more accurate than the other two scoring systems; Modified Early Warning Score and Pre-Endoscopic Rockall Score (28). In a study conducted by J Stevenson et al., patients with GBS < 6 were unlikely to have RBC transfusion, but patients with a score of 7 or more required an average of 3 units of RBC transfusion. In addition to this, 86% of patients with GBS of 7 or more required emergency endoscopy within 24 hours of admission (29). Therefore, GBS is superior and presents an essential tool in managing gastrointestinal bleeding and estimating transfusion procedures.

In this study, Forrest Classifications among NVUGIB patients were analysed. These findings were compared to a study done in the Republic of Korea and Nigeria, and the results were depicted in Table VI (30, 31). Results in column 1 and 3 are almost parallel, ascending from top to bottom with the slight exception of Forrest IIa of the current study (12.2%). There is no apparent pattern for column 2. In general, the findings were similar to the Korean study in Forrest IIb classification. Besides that, Forrest IIc and Forrest III findings were comparable to the Nigerian study. There were no apparent similarities in other Forrest classification.



**Table VI: Comparison of the Forrest Classification findings in NVUGIB patients**

Forrest Classification	Current Study (%)	Kim <i>et al.</i> , 2009 (%) (31)	Akande <i>et al.</i> , 2014 (%) (30)
Spurting Bleeding (Forrest Ia)	4.4	7.8	5.8
Non-spurting active bleeding (Forrest Ib)	14.4	28.0	5.8
Visible Vessels (Forrest IIa)	12.2	17.2	9.6
Non-Bleeding Ulcer with Overlying Clot (Forrest IIb)	14.4	16.0	19.2
Ulcer with Hematin Covered Base (Forrest IIc)	22.8	4.6	25.0
Clean Ulcer Ground (Forrest III)	36.1	26.7	34.6

Regression Analysis of this study revealed that haematochezia and GBS score were significantly associated with a higher number of units of RBC transfusion (Table V). This finding was supported by a study conducted by Wilcox *et al.*, whereby it concluded that haematochezia had been associated with higher transfusion requirement, a necessity for surgery and mortality compared to those without haematochezia. They also suggested that haematochezia was associated with more severe bleeding and worse outcome (32). In another study in Europe, haematochezia was associated with greater transfusion requirement for RBC units (19). Besides, patients with severe haematochezia with a reduction in Hb level at least two (2) g/dl or RBC transfusion requirement for at least two units warranted for endoscopic intervention to control bleeding (33, 34). It was attributed to the fact that haematochezia was linked to a larger blood loss volume with haemodynamic repercussions. Thus, the presence of haematochezia is a predictive sign of massive haemorrhage. Therefore, early recognition of the clinical presentations allows clinicians to classify the patient as having a mild or severe haemorrhage. They can also take necessary interventions accordingly, including emergency endoscopy, blood volume replacement, resuscitation, and RBC transfusion to those patients (19).

Concerning the GBS score, a study compared it to Rockall Score about predicting specific clinical end-point in UGIB and discovered that GBS was more superior to Rockall Risk Score in predicting blood transfusion, endoscopic or surgical intervention (35). Another study by Shahrami *et al.*, summarised that GBS was found to be an accurate scoring system in a patient with UGIB to predict the probability of rebleeding, transfusion demands, endoscopic intervention, emergency surgery, intensive care unit admission and mortality (27).

A simple linear regression has been used to analyse the association between GBS and the number of unit of RBC transfusion. Its result showed there was a statistically significant linear association ( $p < 0.001$ ). For each RBC unit transfused, there was an increase of 0.408 unit of GBS. The equation below explained this linear association.

$$\text{Number of RBC units} = -1.59 + (0.408 * \text{GBS})$$

Based on the B value of 0.408, a higher GBS would result in a higher number of units of RBC transfused in NVUGIB patients.

Subsequently, factors consist of anaemic symptoms, haematochezia, gastric erosion and GBS were analysed using multiple linear regression. In the final model, only haematochezia and GBS were independent predictive factors to the number of units of RBC transfusion in NVUGIB patients. Garrido *et al.* gave a similar result that haematochezia was associated with higher transfusion requirement (19). This is also reinforced in another study in Iran, which shows a significant correlation between higher GBS and the increased risk of an intervention, which includes blood transfusion (36).

## CONCLUSION

This study concluded that the clinical characteristic of NVUGIB in Putrajaya Hospital, which consists of demographic patient's data, risk factors, aetiologies, GBS score and endoscopic findings based on Forrest Classification, showed almost similar findings with other studies worldwide. The new additional local data resulting from this study is the RBC utilisation rate in NVUGIB patient and its rate, which remains comparable to the global transfusion rate. Besides, the essential new predictive factors to the RBC transfusion, which represent this cohort, were haematochezia and higher GBS score.

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