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Profile And Outcome of Variceal Bleeding Patients Referred for Endoscopy At A Tertiary Hospital in Kedah

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Abstract:
Introduction: *Variceal bleeding is a major complication of portal hypertension and is a leading cause of death in patients with cirrhosis.*
Objectives: *To determine the prevalence of variceal bleeding and to identify the etiology of cirrhosis. To assess the intervention during endoscopy and to determine the outcome of intervention.*
Methodology: *A retrospective observational study on 95 consecutive patients referred for endoscopy with the first episode of variceal bleeding was conducted in Hospital Sultan Abdul Halim, Kedah from 1st of January 2013 till 31st of December 2013. Data was analyzed using Microsoft Excel 2007.*
Results: *Majority of the patients were male, 63(66.3%) and Malay, 63(66.3%). The mean(SD) age was 59.1(10.8) years. Variceal bleeding was highest in the age group of 51 to 60 years old, 36(37.9%). From the endoscopic finding, 69(72.6%) cases were of oesophageal variceal bleeding. Among those with liver cirrhosis, 23(33.3%) were due to hepatitis C. 39(41.1%) patients underwent endoscopic variceal ligation, 4(4.2%) received sclerotherapy and 25(26.3%) received intravenous terlipressin. In-hospital mortality and re-bleeding rate were 2(2.1%) and 10(10.5%) respectively. The median (IQR) hospital stay was 1(1,2) day.*
Conclusion: *Relatively low in-hospital mortality and re-bleeding rates is most probably due to the smaller proportion of patients with severe liver dysfunction and management which adhered to clinical practice guideline.*
Keywords: *Cirrhosis, Outcome, Prevalence, Treatment, Variceal bleed*

I. Introduction

Variceal bleeding is a major complication of portal hypertension and is a leading cause of death in patients with cirrhosis [1]. Variceal bleeding accounts for 6.4% of upper gastrointestinal bleeding in Malaysia [1]. The most important predictive factors related to the risk of variceal bleeding are variceal size, the presence of red wale sign and the severity of liver dysfunction [2]. Nevertheless, new pharmacological, endoscopic, radiological and surgical therapies have led to an improvement in the management of variceal bleeding and decrease in the mortality rate over the past few decades [2]. Lately, there has been a rise in variceal bleeding cases in Hospital Sultan Abdul Halim (HSAH). Thus, our objectives are (1) To determine the prevalence of variceal bleeding (2) To identify the etiology of cirrhosis (3) To assess the intervention during endoscopy (4) To determine the outcome of intervention.

II. Materials And Methods

A retrospective observational study on 95 consecutive patients referred for endoscopy with the first episode of variceal bleeding was conducted in HSAH, Kedah from 1st of January 2013 till 31st of December 2013. We assessed database of the patients from a registry book in endoscopic unit and medical records. All endoscopies were performed by experienced endoscopists using the Olympus GIF-HQ 180 video endoscope. Data was analyzed using Microsoft Excel 2007. The protocol of this study was registered with the National Medical Research Register and approved by the Medical Research Ethics Committee, Malaysia.

III. Result

Majority of the patients were male, 63(66.3%) and Malay, 63(66.3%) (Table 1). The mean(SD) age was 59.1(10.8) years. Variceal bleeding was highest in the age group of 51 to 60 years old, 36(37.9%) (Table 1). From the endoscopic finding, 69(72.6%) cases were of oesophageal variceal bleeding (Table 1). Among those with liver cirrhosis, 23(33.3%) were due to hepatitis C (Table 1). 39(41.1%) patients underwent endoscopic variceal ligation, 4(4.2%) received injection sclerotherapy and 25(26.3%) received intravenous terlipressin (Table 1). In-hospital mortality and re-bleeding rate were 2(2.1%) and 10(10.5%) respectively (Table 1). The median (IQR) hospital stay was 1(1,2) day.

Table 1: Socio-demographic characteristics (n=95)

Variables	n(%)
Gender	
Male	63(66.3)
Female	32(33.7)
Age	
21 -40	4(4.2)
41-50	16(16.8)
51-60	36(37.9)
61-70	24(25.3)
71-90	15(15.8)
Ethnicity	
Malay	63(66.3)
Chinese	18(19.0)
Indian	14(14.7)
Endoscopic finding	
Oesophageal variceal bleeding	69(72.6)
Gastric variceal bleeding	8(8.4)
Oesophageal and gastric variceal bleeding	18(19.0)
Etiology of liver cirrhosis	
No liver cirrhosis	26(27.4)
Hepatitis B	17(17.9)
Hepatitis C	23(24.2)
Alcohol	11(11.6)
Cryptogenic	18(18.9)
Intervention during endoscopy	
Endoscopic variceal ligation (EVL)	39 (41.1)
Injection sclerotherapy (thrombovar, lipidol, histoacryl)	4(4.2)
Intravenous terlipressin	25 (26.3)
Antibiotic (ceftriaxone/ciprofloxacin)	15 (15.8)
Tablet propranolol (not for grade 1 or small varices)	80 (84.2)
Treatment outcome	
Re-bleeding (≤ 24 months from the first bleeding episode)	10 (10.5)
Mortality (≤ 24 months from the first bleeding episode)	2 (2.1)
Hospital stay (≤ 1 week)	91 (95.8)
Hospital stay (> 1 week)	4 (4.2)

IV. Discussion

The mean(SD) age of variceal bleeding patients in our study was similar to Yew *et al.* in Singapore and United States Nationwide Inpatient Sample database [2,3]. In our study and in Mallick and Mohammad Kamil's, majority of the patients with acute oesophageal variceal haemorrhage fell in the age group of 51 to 60 years old [4]. The similarity might be due to comparable population because both studies were done in Kedah. In contrary, Jamal *et al*. reported the incidence of varices, either bleeding or not bleeding, was highest in patients between 41 to 50 years old in the in the United States [3].

Majority of our variceal bleeding cases were male which is consistent with several other studies [2-11]. Variceal bleeding has correlation with the severity of liver disease, portosystemic shunting and continued alcohol abuse [1]. In our study, all alcoholic cirrhotic patients were male, 11(15.9%). Generally, male tend to consume more alcohols which leads to the formation of alcoholic liver cirrhosis and worsening of the liver disease, explaining why majority of the variceal bleeding cases occur in males. Child-Pugh grades which is used to determine the severity of liver disease was not assessed in our study. Nevertheless, we had 65.2% of male patients with cirrhosis in comparison to female which shows a higher possibility of male experiencing variceal bleeding.

According to Malaysia's statistic in 2007 and a Singaporean research done by Yew *et al.* in 2007 reported that majority of patients who presented with variceal bleeding were Chinese [1, 2]. However, in our study, variceal bleeding was common among Malays. The difference is because both the statistics were generated 6 years ago and does not portray the current scenario. Also, most Singaporeans are Chinese while Malay is the predominant race in Kedah [12]. Therefore, the discrepancies in the finding were also because of the different racial distribution. Another study conducted at Hospital Sultanah Bahiyah, Alor Setar which is located in the same state as our study showed that majority of the bleeding oesophageal varices were Malays (68.8%), followed by Chinese (18.7%) [4].

In our study, Yew et al. and Hadayat et al., variceal bleeding was mainly due to oesophageal varices while gastric (fundus and cardia) varices bleeding were less frequently observed [2, 11]. Oesophageal varices are the common cause of upper gastrointestinal bleeding compared to gastric varices in liver cirrhotic patients [5, 7, 9-11, 13 -15]. 72.6% of our study population were cirrhotic explaining the higher incidence of oesophageal varices bleeding cases.

Our study showed the commonest etiology of liver cirrhosis in variceal bleeding patients was chronic hepatitis C. This finding is consistent with several other studies [5, 7, 16]. The incidence rate per 100,000 populations in 2011 in Kedah for Hepatitis B and C were 1.01 and 2.48 respectively [17]. A higher hepatitis C case in Kedah explains the higher incidence of variceal bleeding among cirrhotic patients with hepatitis C. In contrary, Yew *et al.* reported the main causes of liver cirrhosis in variceal bleeding patients were chronic hepatitis B and alcohol consumption [2]. Etiology of liver cirrhosis varies within the region. In Western countries, alcohol and chronic hepatitis C are the leading causes of liver cirrhosis [18]. In the Asian Pacific region, chronic hepatitis B is highly endemic and appears to be the commonest cause of liver cirrhosis [1]. In Japan, hepatitis C is the most common cause of cirrhosis [19]. Alcohol related cirrhosis is not uncommon in China, Korea and Japan where consumption of alcohol is known to beheavy [20].

Although EVL of oesophageal varices is now regarded as the most effective method of endoscopic intervention, injection sclerotherapy is still widely used to control acute oesophageal variceal bleeding as well as to eradicate varices to prevent recurrent bleeding [6]. In our study, EVL was widely use in comparison to injection sclerotherapy. According to our local guideline, in order to control bleeding of acute oesophageal varices and gastric varices Type 1, EVL is recommended while sclerotherapy can be used if EVL is technically difficult [1]. In Yew *et al*., endoscopic procedures were performed for every patient (EVL for bleeding oesophageal varices and N-butyl-2-cryanoacrylate injection for bleeding gastric varices) and in Ouakaa-Kchaou *et al.,* EVL was performed in 92.0% of patients [2, 16]. The usage of monotherapy or combination of endoscopic and medical treatments such as somatostatin, octreotide or terlipressin depends on the types and severity of variceal bleeding. Concomitant EVL and medical treatment decreases the risk of re-bleeding [21]. Nevertheless, there was no significant difference in overall mortality in patients treated with combination therapies versus monotherapy in two meta-analyses [21, 22]. In the management of acute oesophageal and gastric variceal Type 1 bleeding, prophylactic antibiotic such as ciprofloxacin or ceftriaxone is recommended in patients with cirrhosis for duration of seven days and pharmacotherapy such as terlipressin, somatostatin or octreotide is given to prevent early re-bleeding [1]. Also, primary prophylaxis of tablet propranolol is prescribed for patients with medium (Grade 2) or large varices (Grade 3) with endoscopic red signs or Child's C cirrhosis [1]. Secondary prophylaxis of tablet propranolol is prescribed after the first episode of variceal bleeding [1].

In our study, in-hospital mortality was defined as death due to variceal bleeding within twenty four months from the first episode of variceal bleeding. Re-bleeding was defined as bleeding within twenty four months from the first episode of variceal bleeding. The in-hospital mortality and re-bleeding rates in our study were lower in comparison to other studies [2, 5, 16]. Decline in mortality was observed in Paris from 1980 to 2000 and in Ireland over 40 years [23, 24]. The mean(SD) hospital stay in our study was shorter as opposed to Yew *et al.*, 5.5(3.3) days in general ward [2]. The advancement in endoscopic procedures, medical care as well as wider use of primary and secondary prophylaxis which adhered to clinical practice guideline might have contributed to reduce in mortality and re-bleeding rates with shorter hospital stay. Also, shorter waiting time for undergoing endoscopy would have improved the mortality rate in patients with acute variceal bleeding which was not analyzed in our study. In a nationwide survival analysis in the United States, delayed time to endoscopy increases mortality in patients with acute variceal bleeding [25]. If endoscopy is delayed more than 15 hours after admission, in-hospital mortality raises around 3.5 folds (OR 3.67, 95% CI 1.27-10.39) [26]. Risk factors predictive of re-bleeding include the degree of hepatic decompensation, age greater than 60, severity of initial bleed, renal insufficiency, level of portal pressure, size of varices, active bleeding at the time of initial endoscopy and the presence of hepatoma [1].

There are some limitations in our study. Our study involved reviewing endoscopic records retrospectively, thus, some records have to be excluded due to incomplete data. Since Child-Pugh grades were not well documented, thus severity of liver dysfunction was unable to be assessed. Also, the time to endoscopy and grading of varices were not properly documented in the medical record making it impossible for us to determine the possible causes for lower in-hospital mortality and re-bleeding rates.

V. Conclusion

Relatively low in-hospital mortality and re-bleeding rates most probably due to the smaller proportion of patients with severe liver dysfunction and management which adhered to clinical practice guideline.

VI. Conflict Of Interest Statement

We declare that we have no conflict of interest.

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