Prevalence of Bleeding Esophageal Varices among patients with Upper Gastrointestinal Bleeding in Calabar, South-South Nigeria


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Abstract

Introduction: Bleeding from esophageal varices (EV) is an important complication of portal hypertension and a major cause of death in patients with chronic liver disease. In Nigeria, hepatitis B and C viral infection and alcohol are the leading causes of portal hypertension and EV arising from liver cirrhosis. The study aimed to present data on bleeding EV during esophagogastroduodenoscopy (EGD) in Calabar, Cross River State (CRS).

Methodology: This was a descriptive retrospective study of patients with bleeding EV who had EGD performed at two health facilities in Calabar, CRS, from November 2012 to May 2024. Patients’ demographics and endoscopy findings were obtained from the endoscopy registers into a spreadsheet and analyzed statistically using Statistical Package for the Social Sciences (SPSS) version 20 software. The continuous variables were summarized using means ± standard deviation, whereas frequencies and percentages were used for the categorical variables.

Results: A total of 165 patients who presented with upper gastrointestinal bleeding had EGD performed during the study period. Fifty-five (33.3%) of these patients had EV. The age range of patients with bleeding EV was 24-78 years, with a mean age of 45.1 years (SD ± 14.6) and a male: female ratio of 5.9:1. All the patients with bleeding esophageal varices had background chronic liver disease.

Conclusion: Bleeding esophageal varices are a significant cause of upper GI bleeding in our study population, especially among those with chronic liver disease.

Keywords: Calabar, Esophagogastroduodenoscopy, Esophageal Varices, Upper Gastrointestinal Bleeding
Introduction

Esophageal varices (EV) are one of the most common causes of acute upper gastrointestinal bleeding (UGIB) with varying global prevalence. Upper gastrointestinal bleeding from EV is a leading cause of death. Acute variceal bleeding is a potentially fatal complication of clinically significant portal hypertension (PH) and represents an important economic and public health issue. Esophageal varices are the seventh most common cause of GI bleeding in the United States, with alcohol and chronic hepatitis C virus (HCV) being the major risk factors for chronic liver disease (CLD). In Africa, the prevalence of EV is relatively high due to the significant role schistosomiasis, HBV, and HCV play in the etiology of CLD. Liver cirrhosis is the most common cause of EV in the Western world, with up to 85% of cirrhotic patients developing EV at some point in their lives, with the incidence varying with disease severity. In compensated cirrhosis, EV develops at an annual rate of 8%, with higher rates in decompensated cirrhosis. Hematemesis, melena, and rarely hematochezia may indicate gastroesophageal variceal bleeding. Variceal bleeding is an important complication of PH arising from liver cirrhosis. It is associated with significant mortality and morbidity figures in patients with CLD.

Esophageal varices are dilated submucosal distal esophageal veins connecting the portal and systemic circulations. Liver cirrhosis is a major cause of PH, leading to resistance to portal blood flow and ultimately increased portal venous blood inflow. An average of 30% (i.e., 1.5L/min) of blood circulation is found in the portal vein. If there is an obstruction here, this results in raised portal venous pressure. The body responds to this rise by forming collaterals. These portosystemic collaterals divert blood from the portal venous system to the inferior and superior vena cava. At the same time, one important system is the gastroesophageal collaterals that drain into the aygos vein and lead to the development of esophageal varices. When these varices get enlarged, they rupture, producing severe hemorrhage. Esophageal varices develop due to PH, which is usually assessed indirectly by determining the hepatic venous pressure gradient (HVPG). PH is defined as an HVPG > 5 mmHg, while clinically significant portal hypertension (CSPH) is defined in the presence of a gradient > 10 mmHg (CSPH manifests as acute variceal bleeding).

The mortality rate for each bleeding episode of EV is about 30%; however, if left untreated, as many as 70% of patients who bleed die within one year of the initial bleeding episode. Studies have shown the mortality from any episode of bleeding in decompensated cirrhosis with Child-Pugh class C is usually greater than 70%, and the risk of re-bleeding is as high as 80%. Hence, the early detection and prevention of EV in patients with liver cirrhosis is crucial in lowering complications. In a study conducted in Pakistan, about two-thirds of patients with liver cirrhosis had EV found during EGD, with a male preponderance. In Jos, Nigeria, Achinge et al. reported that 75% of patients with liver cirrhosis had EVs found during EGD. Several local-based studies have reported EV's significant role in UGIB in Nigeria.

Given that EGD's diagnostic yield is significant, the clinical relevance of this procedure in evaluating patients presenting with either liver cirrhosis or UGIB is compelling. This preliminary report seeks to demonstrate the role of EGD in the University of Calabar Teaching Hospital. There is currently no study that describes the role of EGD in evaluating patients presenting with bleeding EV in Calabar. Hence, there is a need to fill this knowledge gap in our environment.

Materials and Methods

This was a 12-year (from November 2012 to May 2024) descriptive retrospective study of patients referred to the endoscopy unit of the University of Calabar Teaching Hospital and a private clinic based in Calabar metropolis (JIL Specialist Clinic) in South-South Nigeria. These health facilities provide specialist care in Gastroenterology and Endoscopy. The University of Calabar Teaching Hospital (UCTH) is a 780-bed capacity tertiary center providing tertiary-level health care within Cross
River State (CRS) and its environs. The hospital is a major referral center in the state, offering a wide range of specialist healthcare, including Gastroenterology and Endoscopic services. JIL Specialist Clinic is a private clinic in the Calabar metropolis that also offers Gastroenterology, Surgical, and Endoscopic services. An Olympus 190 series video gastroscope system was used for patients in the endoscopy unit of the UCTH.

In comparison, an Olympus 140 series video gastroscope was used for patients who had their endoscopy at the JIL specialist clinic. The procedures were performed as day cases in both facilities. All patients were duly counseled about the procedure, and informed consent was obtained. The patient's vital signs and oxygen saturation were routinely monitored before, during, and shortly after the procedure. Patients had an overnight fast before the procedure, with an occasional few having a minimum of 6-8 hours of fast. Local anesthesia was achieved using 10% xylocaine pharyngeal spray. In a few selected cases, conscious sedation by an Anesthetist was provided. Esophagogastroduodenoscopy was carried out with the patient lying in the left lateral position. Endoscopic evaluation of esophageal varices was classified according to Paquet grading of esophageal varices, i.e., I-IV. Data was obtained from the endoscopy suite register of UCTH and JIL Specialist Clinic from the inception of endoscopy services in both centers, i.e., November 2012 to May 2024.

Patient identifiers were removed. No patients were involved in developing the research process and informed consent forms were not required for this retrospective study. The study was approved by the Health Research Ethics Committee (HREC) of the University of Calabar Teaching Hospital. The HREC protocol assigned number was UCTH/HREC/33/Vol.III/342. Trained research assistants retrieved the required data (on age, sex, and endoscopic diagnosis).

Data entry and analysis were carried out using SPSS version 20. The variables of interest included patients' Socio-demographic data, clinical presentation, and endoscopic findings. Univariate analysis was carried out on all the socio-demographic, clinical, and endoscopic findings of patients presenting with bleeding esophageal varices.

**Results**

A total of 165 patients presenting with UGIB had EGD performed during the study period. Fifty-five (55, 33.3%) of these patients had esophageal varices. The age range of patients with bleeding esophageal varices was 24-78 years, with a mean age of 45.1 years (SD±14.6). Males constituted 85.5% of patients, with a male-to-female ratio of 5.9:1 (see Table 1).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Bleeding esophageal varices N=55</th>
<th>Bleeding esophageal varices (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-45</td>
<td>27</td>
<td>49.1</td>
</tr>
<tr>
<td>46-64</td>
<td>22</td>
<td>40</td>
</tr>
<tr>
<td>&gt;65</td>
<td>6</td>
<td>10.9</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>47</td>
<td>85.5</td>
</tr>
<tr>
<td>Female</td>
<td>8</td>
<td>14.5</td>
</tr>
</tbody>
</table>

Table 1. Socio-demographic characteristics of patients with Bleeding Esophageal Varices (n=55)
All the patients with bleeding esophageal varices had CLD. Hepatitis B virus-induced chronic liver disease was a leading etiology in all but one patient (at the time of the study, the exact etiology could not be determined in the patient). The varices were worse in the lower esophagus. There was associated gastric fundal varix in three patients (5.5%). The largest proportion of the patients (16, 29.1%) had grade 3 varix, while nine patients (16.4%) had grade 2 and six (10.9%) had grade 1 varix. The red whale sign was seen in most patients (80%). Five (9.1%) patients had both the presence of EV and PUD (duodenal ulcer, gastritis, gastric erosion) see Table 2. Hematemesis, passage of melena, and ascites were the major modes of presentation in these patients. All the patients were in Child-Pugh class C. Eight (14.5%) of these patients had Endoscopic Variceal Band Ligation (EVL) performed as a therapeutic intervention in addition to medical therapy.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Bleeding esophageal varices</th>
<th>Bleeding esophageal varices</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=55</td>
<td>(%)</td>
</tr>
<tr>
<td>Grading of esophageal varices</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade I</td>
<td>6</td>
<td>10.9</td>
</tr>
<tr>
<td>Grade II</td>
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<td>EV and coexisting PUD*</td>
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</tr>
<tr>
<td>Gastric erosion</td>
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<td>1.8</td>
</tr>
<tr>
<td>Gastritis</td>
<td>3</td>
<td>5.5</td>
</tr>
<tr>
<td>Duodenal ulcer (Forrest class 3)</td>
<td>1</td>
<td>1.8</td>
</tr>
<tr>
<td>Gastric varices</td>
<td>3</td>
<td>5.5</td>
</tr>
<tr>
<td>EVL*</td>
<td>8</td>
<td>14.5</td>
</tr>
</tbody>
</table>

*EVL: Endoscopic Variceal Ligation, PUD: Peptic Ulcer Disease

Table 1. Socio-demographic characteristics of patients with Bleeding Esophageal Varices (n=55)

Discussion
Variceal bleeding is a life-threatening complication of PH and a major cause of death in patients with CLD. It is a leading cause of UGIB in Calabar. This is in keeping with other local reports in the country. In Western countries, bleeding from EV is responsible for 5-11% of all cases of UGIB. Whereas in our study, it constituted 33.3% of cases. This disparity may be due to late disease presentation and geographical variation in the prevalence of CLD. Chronic hepatitis B virus infection was the cause of CLD in most of our patients. This reflects the high burden of HBV infection in our environment and sub-Saharan Africa, as well as its significant role in the etiology of CLD. This is in sharp contrast to what is obtained in North Africa and the Western world, where chronic hepatitis C virus infection, schistosomiasis, and alcohol are the major etiological agents of CLD. All of our patients with
variceal bleeding were in Child-Pugh class C. Studies have shown that up to 85% of patients with liver cirrhosis will develop EV at some time in their lives, with the incidence varying with disease severity. In compensated cirrhosis, EV develops at an annual rate of 8%, with higher rates in decompensated cirrhosis (70%)\textsuperscript{1,15}. This supports the observation that patients with CLD in our environment present late with evidence of complications.

In our study, bleeding esophageal varices were found mostly in males (85.5 %%) with a male:female ratio of 5.9:1. Ajayi et al. in Ekiti also reported a male preponderance (73.3%) in their series on liver cirrhosis patients with bleeding EV, whereas 26.7% (8/30) were females\textsuperscript{19}. In another study carried out in Jos, the majority of patients presenting with EV from liver cirrhosis were also males\textsuperscript{3}. Another report in Pakistan also had a similar finding\textsuperscript{5}. The reason for this may not be unconnected with the high prevalence rate of CLD in males compared to females, and this is in keeping with documentation in the literature\textsuperscript{14}. Male predominance seen in CLD has been linked to the role of the male sex hormone (testosterone) and socio-cultural practices common among men\textsuperscript{14}. We found the mean age of patients diagnosed with bleeding EV in the fifth decade of life. Ajayi et al. found that most of their patients with EV are in their sixth decade of life\textsuperscript{19}. In Nepal, Panta et al. reported that EVs occur more often in patients in their seventh decade of life\textsuperscript{20}. The older age demographics seen in our studies and others may suggest how particularly the aging population is more at risk of developing chronic illness while having a reduced capability to regenerate healthy tissue\textsuperscript{21}. Age-related liver diseases include non-alcoholic fatty liver disease, alcoholic liver disease, hepatitis, fibrosis, and cirrhosis. These insults lead to the elaboration of signaling pathways driving liver pathologies, such as inflammation, steatosis, and fibrosis, which activate positive feedback mechanisms that further worsen the symptoms of liver disease\textsuperscript{21}.

In our study, the varices were worse in the lower esophagus, and gastric fundal varices were associated in only three patients (5.5%). More than a quarter of the patients (29.1%) had grade 3 varix with evidence of a red wale sign. The distal third of the esophagus is the most commonly affected by esophageal varices, but proximal varices can occur in conditions affecting extra-portal venous circuits\textsuperscript{1}. The risk of having high-risk varices rises when liver function deteriorates and hepatic decompensation occurs (i.e., presence of ascites, hepatic encephalopathy)\textsuperscript{22}. High-risk esophageal varices are those large in size or of any size and with red signs (e.g., red wale markings, erythematous raised spots)\textsuperscript{22}. The observation of our patients who had bleeding EV in the presence of advanced liver cirrhosis supports the literature as discussed above. Additionally, our study reflects the underutilization of endoscopy in the management of CLD, probably due to the high cost of the procedure, which is often unaffordable for most patients. Various evidence-based guidelines are available in developed countries to reduce the high morbidity and mortality associated with bleeding EV, using key indicators such as transient elastography/fibroscan values of ≥20 kPa or platelet count ≤150,000/mm\textsuperscript{3} or just the mere presence of compensated/decompensated liver cirrhosis\textsuperscript{18}. Endoscopic ultrasound is another minimally invasive innovative tool that has been developed to screen for varices, especially for the detection of gastric and paraesophageal varices\textsuperscript{18}.

Our study also showed the poor utilization of therapeutic interventions such as EVL was less than a quarter of our patients (14.5%) could afford this intervention, which improves outcomes in liver cirrhosis patients. In the past decades in Nigeria, the landscape of the endoscopic management of EV, though suboptimal, has evolved from injection sclerotherapy to EVL, which has become a game changer in the management of CLD patients with portal hypertension and its complications. Endoscopic variceal band ligation, though more expensive (hence less affordable) than injection sclerotherapy, is a superior endoscopic hemostatic technique due to the lower risk of re-bleeding episodes and adverse events\textsuperscript{1}. As recommended by international guidelines, all our patients with bleeding EV had secondary prophylaxis with non-selective beta-blockers (e.g., propranolol or carvedilol) and in combination with EVL where they could afford the procedure. However, these patients could not be referred for liver
transplantation because of the unavailability of such services in our environment and were treated conservatively. In 20% of acute EV bleeding, patients can be refractory to standard therapy, and this is associated with high death rates (30% to 50%). In this instance, bridge therapy, including balloon tamponade, esophageal stent placement, or transjugular intrahepatic portosystemic shunt, has been used with variable outcomes. In Nigeria, few centers offer advanced therapeutic endoscopic and interventional radiologic techniques, and where available, they are usually very expensive.

Another interesting finding in our study was the presence of peptic ulcer disease (PUD), i.e., gastritis, gastric erosion, and duodenal ulcer Forrest class in our patients with bleeding EV. Although EV is a leading cause of UGIB in liver cirrhosis. Bleeding peptic ulcer disease has been implicated in UGIB in a relatively small proportion of cirrhotic patients. Liver dysfunction, medications, helicobacter pylori infection, and coagulation disorders further increase the risk of UGIB in EV patients, worsening the clinical outcome of patients. Therefore, considering that the management of bleeding EV and PUD are very distinctive, it is pertinent to establish the cause of UGIB in liver cirrhosis, especially when the diagnosis of bleeding PUD can be easily overlooked.

Conclusion
Bleeding EV remains a grave complication of chronic liver disease, and endoscopic evaluation is the gold standard. A definitive diagnosis and treatment of this condition are now possible in our center. The uptake of EVL as a treatment modality was below par owing to financial constraints our patients face.

Study limitations
Due to the manual entry of data, we encountered missing fields/data during entry into the SPSS spreadsheet. The manual entry also did not follow the standardized endoscopic description of the lesions, e.g., Sarin's classification of gastric varices was not used, while some entries were made without further classifying EV using Paquet classification. We also were unable to correlate laboratory and radiological findings typically seen in liver cirrhosis with the presence/size and class of EV.

Recommendations
The scaling up of funding support through health insurance schemes needs to be considered to enable liver cirrhosis patients to benefit from EVL in our environment. Further studies (prospective) need to be done to correlate laboratory and radiological findings typically seen in liver cirrhosis with the presence/size and class of EV. Gastroenterologists in the country need to design and adopt evidence-based guidelines (tailored to our environment) that encourage the use of EGD in compensated liver cirrhosis patients to mitigate the poor clinical outcomes arising from this condition. The use of modern digital reporting and the entry of endoscopic findings using validated endoscopy software in keeping with international best practices is strongly recommended. This will ensure appropriate entry and retrieval of data for future comprehensive analysis.

Acknowledgment
I wish to thank all the members of the Endoscopy unit for the teamwork and professionalism they display, as well as the team of Biomedical Engineers who ensure that our endoscopy machines work optimally. I sincerely thank my colleagues in the Anesthesia department who have continued to support our unit in delivering expert care to our patients.

Conflict of Interest
None
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The authors of this original research paper hereby declare no competing interest.

**References**


