

## THE SIGNIFICANCE OF VARICEAL HAEMORRHAGE IN GHANA: A RETROSPECTIVE REVIEW

T. N. A. ARCHAMPONG<sup>1,2</sup>, K. TACHI<sup>1,2</sup>, A. A. AGYEI<sup>1,2</sup> and K. N. NKURUMAH<sup>1,2</sup>

<sup>1</sup>Department of Medicine and Therapeutics, University of Ghana School of Medicine and Dentistry, Box 4236, Korle-bu, Accra, Ghana, <sup>2</sup>Department of medicine and Therapeutics, Korle-Bu Teaching Hospital, Box 77, Korle-Bu, Accra, Ghana

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Corresponding Author: Dr. Timothy N.A. Archampong

Email: [tnaa@doctors.net.uk](mailto:tnaa@doctors.net.uk)

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### SUMMARY

**Background:** This study describes the burden of bleeding oesophageal varices at the main tertiary referral centre in Accra.

**Design:** Retrospective design to describe the endoscopic spectrum and review mortality data following acute upper gastro-intestinal bleeding at the Korle-Bu Teaching Hospital. Endoscopic data was reviewed in the Endoscopy Unit between 2007 and 2010. Mortality data was collated from the Department of Medicine between 2010 and 2013.

**Interventions:** The study questionnaire compiled clinical and demographic characteristics, endoscopic diagnoses, length of hospital admission and treatment regimens.

Main outcome measures: Aetiology and time-trend analysis of mortality rates following acute upper gastro-intestinal bleeding; variceal bleeding treatment modalities.

**Results:** On review of the endoscopic diagnoses, gastro-oesophageal varices were identified in 21.9% of cases followed by gastritis 21.7%, duodenal ulcer, 17.0%, and gastric ulcer, 13.2%. Gastro-oesophageal varices were the predominant cause of death from acute upper gastro-intestinal haemorrhage from 46% in 2010 to 76% in 2013. Outcomes following acute upper gastro-intestinal bleeding were dismal with some 38% of fatalities occurring within the first 24 hours. Injection sclerotherapy was the dominant endoscopic modality for secondary prevention of variceal bleeding in comparison with band ligation, mainly as a result of cost and availability.

**Conclusions:** At the tertiary centre in Accra, variceal bleeding is an increasingly common cause of acute upper gastro-intestinal haemorrhage in comparison with previous reviews in Ghana. Its significantly high in-hospital mortality reflects inadequate facilities to deal with this medical emergency. A strategic approach to care with endoscopic services equipped with all the necessary therapeutic interventions will be vital in improving the outcomes of variceal bleeding in Ghana.

**Keywords:** gastro-oesophageal; varices; bleeding; gastro-intestinal, Ghana.

### INTRODUCTION

Acute upper gastro-intestinal bleeding (AUGIB) is defined as bleeding that results from lesions located above the ligament of Treitz, a thin suspensory muscle attached to the duodenum.<sup>1</sup> It is a common reason for emergency referral to hospital in patients with gastro-intestinal disease.<sup>1</sup>

AUGIB can be either variceal or non-variceal.<sup>2</sup> Sources of non-variceal bleeding include peptic ulcer disease (PUD), oesophagitis, Mallory-Weiss tear, vascular anomalies, gastric and oesophageal malignancy.<sup>3</sup> Gastro-oesophageal varices (GOV) are dilated tortuous anastomotic veins prominent at the lower oesophagus and gastro-oesophageal junction and are the most clinically relevant porto-systemic collaterals in cirrhosis and portal hypertension.<sup>4</sup>

They develop from connections between the short gastric and coronary veins and the oesophageal, azygous and intercostals veins<sup>5</sup>. Varices will be present in 40% of patients with clinically compensated cirrhotic liver disease<sup>2</sup>. This increases to 60% when decompensated with 90% developing oesophageal varices during the course of the disease.<sup>4</sup>

Variceal bleeding is a life threatening complication of portal hypertension<sup>6</sup>. It is a major cause of morbidity and death in patients living with liver cirrhosis<sup>7</sup> and accounts for 70% of all AUGIB episodes in the context of portal hypertension<sup>5</sup>. The risk of bleeding increases with increasing pressure and size of the varices as well as decreasing thickness of the variceal wall reflected by the red dot sign at endoscopy.<sup>3</sup>

Variceal haemorrhage carries a significant mortality of 20 – 30 %, therefore the identification and prophylactic treatment of patients at risk for esophageal bleeding is mandatory.<sup>8</sup>

This study describes the scope of the problem and the therapeutic options in Ghana, a country with a significant burden of liver cirrhosis.<sup>9</sup>

## METHODS

This study utilized a retrospective design to describe the endoscopic spectrum of disease following upper gastro-intestinal (GI) endoscopy for AUGIB at the Endoscopy Unit, Korle-Bu Teaching Hospital (KBTH) between June, 2007 and August 2010. Additionally, it reviewed mortality data from AUGIB in the Department of Medicine, KBTH from January, 2010 to November 2013.

These time periods were studied because endoscopy and mortality data were consistently archived and available for analysis. The study was conducted between September 2012 and December 2013. Korle-Bu Teaching Hospital (KBTH) is the premier Teaching Hospital in the capital city of Ghana, Accra, with an estimated population of 3.9 million people. It is the main tertiary referral centre in Accra serving the majority of the southern half of Ghana.

The hospital has a total bed capacity of one thousand six hundred (1600) with a daily out-patient department (OPD) attendance of about one-thousand-two-hundred (1200) and an annual turnover of about three hundred and fifty thousand (350,000) patients. The Endoscopy Unit runs two four-hour sessions per day on four days of the week. Approximately five patients attend each endoscopy session for upper-GI endoscopy.

Mortality data in the Department of Medicine, KBTH, was derived from monthly departmental records while endoscopic data was captured from the Endoscopy Unit Log-book. Departmental mortality records review captured demographic data, duration of illness, symptoms and subsequent diagnosis.

Endoscopically confirmed diagnoses of all mortality cases following AUGIB were recorded in this review. Where there was no prior documentation of endoscopic diagnosis, the aetiology was indicated as undetermined. Consenting patients with GOVs undergoing injection sclerotherapy during the study period were administered a structured questionnaire.

It included the sclerosant used, attendant complications such as pain, bleeding, dysphagia and endoscopic stric-

ture formation. Data were analyzed using Microsoft Excel and SPSS 16. Categorical data were expressed as proportions and presented in tables and bar charts.

## RESULTS

Six-hundred and ninety-five (695) cases of AUGIB were investigated at the Endoscopy Unit, KBTH between 2007 and 2010 presenting as haematemesis and/or melaena. Table 1 demonstrates the endoscopic diagnoses following upper GI endoscopy. On review of the common pathologies encountered, GOVs were identified in 21.9% of cases followed by gastritis 21.7%, duodenal ulcer (DU) 17.0%, and gastric ulcer (GU) 13.2%.

**Table 1** the aetiology of upper-GI haemorrhage following endoscopy at the Korle-Bu Teaching Hospital: 2007 – 2010, (n: 695)

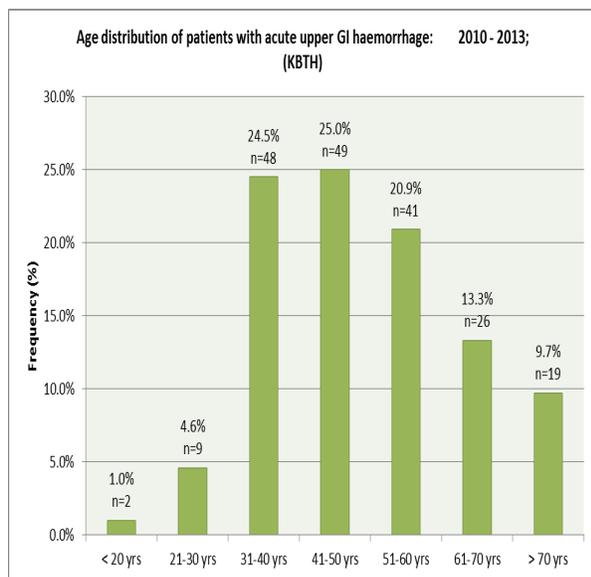
Endoscopic diagnosis	N	%
Gastro-esophageal varices	144	20.7
Intra-gastric varices	8	1.2
Esophagitis	41	5.9
Duodenal ulcer	118	17.0
Gastric ulcer	92	13.2
Gastric erosion	27	3.9
Gastritis	151	21.7
Gastric cancer	40	5.8
Normal	139	20.0

Table 2 shows the mortality patterns following AUGIB at the KBTH's Department of Medicine. One-hundred and ninety-six (196) mortality cases from AUGIB were recorded between 2010 and 2013 of which 70.1% were male and 29.1% female. AUGIB represented 3.8% (n=37) of all-cause mortalities in 2010, 4.3% (n=44), 2011; 6.7% (n=66), 2012 and 5.8% (n=52), 2013 respectively.

**Table 2** Mortality data on acute upper GI haemorrhage in the Department of Medicine, KBTH

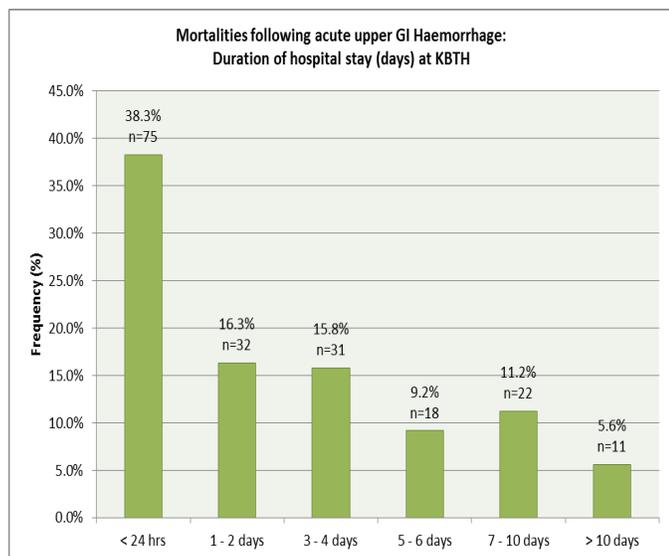
	2010	2011	2012	2013
Total Admissions	6735	6801	7501	7114
Total all-cause mortality cases	966	1014	981	890
Total deaths from AUGIB: (n)	37	44	66	52
- Deaths from variceal bleeding	17(45.9%)	28(63.6%)	51(77.3%)	40(76.9%)
- Deaths from bleeding PUD (DU+GU)	8(21.6%)	9(20.5%)	7, (10.6%)	4, (7.7%)
- Deaths from AUGIB (undetermined aetiology)	12(32.4%)	7(15.9%)	8, (12.1%)	8, (15.4%)

Figure 1 illustrates the age distribution of mortality cases from AUGIB with the commonest age group being 31 – 40 years, (24.5%) and 41 – 50 years, (25%). Bleeding GOVs were the predominant cause of death from AUGIB ranging from 45.9% (n=17) in 2010 to 76.9% (n=40) in 2013. In 2013, the GOV: PUD mortality ratio was as high as 10:1.



**Figure 1** The Age distribution of patients with Upper GI Bleeding

Figure 2 shows mortalities following AUGIB in relation to duration of hospital stay. Outcomes following AUGIB were dismal with some 38% (n=75) of fatalities occurring within the first 24 hours and a further 16.3% (n=32) in the subsequent 24 hours.



**Figure 2** Duration of hospital stay and Mortality following Acute Upper GI Bleeding

A cross-sectional review of endo-therapy for GOVs at the Endoscopy Unit, KBTH, demonstrated that the mainstay of treatment was injection-sclerotherapy, performed in 59 patients during the study period. However,

er, variceal rubber-band ligation therapy was also used when available.

The sclerosant used was 5% ethanolamine oleate with 2-3 (2.5ml) peri-variceal injections per sclerotherapy cycle.

All patients had large GOVs, North Italian Endoscopic Classification (NIEC) (10), with multiple columns of distended varices. Thirty-two percent (32%, n=19) of patients had dysphagia following injection sclerotherapy with a mean duration of 5.73 days; however no oesophageal strictures were recorded following endoscopy. Fifty-nine percent (59%, n=35) of patients had experienced post-procedure pain in the chest or abdomen which required either antacids or oral analgesia with paracetamol or tramadol.

**DISCUSSION**

Bleeding from the upper gastrointestinal tract is associated with significant morbidity and mortality. In the UK it accounts for 8% of emergency hospital admissions<sup>11</sup> with an incidence of 47 – 116 / 100,000 populations.<sup>12</sup> The aetiology of AUGIB and relationship with mortality varies across populations. A UK population-based multi-centre, prospective survey reviewed over 4,000 cases of AUGIB across 74 hospitals showing prevalence for GOVs, DU and GU as 4%, 18.6% and 12.3% respectively.<sup>13</sup>

Mortality was however inversely related to prevalence; (23%) in variceal and (12%) in peptic ulcer disease patients<sup>13</sup>. By contrast, in our study, GOVs were identified in 22% of cases in comparison to DU, 17.0%; and GU, 13.2%. It was second to peptic ulcer disease, which had an overall prevalence of 30.2% (DU+GU). This pattern was also demonstrated in a review of the clinical epidemiology of AUGIB in KBTH where there was a significant prevalence of bleeding GOVs amounting to 30%, almost equal to that for DU and GU cases which was 39.1%.<sup>14</sup> Gastro-oesophageal varices also remained the dominant cause of death from AUGIB ranging from 46% in 2010 to 76% in 2013 in our review. Similarly, a review at the Kenyatta National Hospital<sup>15</sup> demonstrated that GOVs were the commonest cause of AUGIB and were also responsible for the majority of its case fatalities.

However, this trend in GOV prevalence has not always been evident in previous endoscopic series at KBTH. A review of upper-GI endoscopies for AUGIB between 1981-1983 assessed 86 such patients with prevalence rates of GOV, 4.7%; DU, 31.4%; and GU, 8.1%<sup>16</sup>. In 1982, *Helicobacter pylori* were discovered<sup>17</sup> and the 1980s saw the advent of proton-pump inhibitors (PPI) for the treatment of acid-peptic diseases.<sup>18</sup>

It is likely that the relative increase in GOVs and concomitant reduction in prevalence of DU and GU may reflect the significant rise in PPI use and *H. pylori* therapy in dyspeptic patients prior to endoscopy. A pattern therefore emerges which shows that variceal bleeding is a much more common cause of AUGIB in Ghana and Sub-Saharan Africa in comparison with developed countries. However, its attendant mortality remains high irrespective of geographic location.

What seems alarming in our study is the high case fatality in the first 24 hours of emergency admission in patients with AUGIB (38%). Difficulties faced in resuscitation, availability of appropriate facilities such as Seng-staken Blakemore tubes, access to therapeutic endoscopy and delayed referral are likely reasons in the face of such a burden of disease at the Tertiary Centre.

Majority of sufferers were unfortunately relatively young, within the 30-50 year group, who are usually the backbone of the workforce and families in society. On the contrary, a similar sample population of patients with AUGIB in the UK was rather elderly, with a mean age of 66 years.<sup>13</sup> This may reflect the differing aetiologies geographically. In Ghana for instance there is a significant burden of Hepatitis B acquired predominantly in early life with a prevalence of approximately 12-15%<sup>19</sup> leading to cirrhotic liver disease and associated portal hypertension.<sup>20</sup> Liver cirrhosis is the commonest liver disease causing death in Ghana.<sup>20</sup>

Prevalence of Hepatitis B in patients with cirrhotic liver disease was found to be 42.9%.<sup>20</sup> Local data on other causes of liver injury such as alcohol and potentially hepatotoxic herbal medications are however lacking. In Europe, however, elderly patients tend to be more vulnerable to AUGIB particularly from peptic disease as a result of the higher incidence of multiple co-morbid conditions and use of non-steroidal anti-inflammatory drugs (NSAIDs).<sup>2, 21, 22</sup>

Injection sclerotherapy was the dominant endoscopic modality for secondary prevention of variceal bleeding in comparison with band ligation, mainly as a result of cost and availability. Over the study period, morbidity from the use of regular injection sclerotherapy was evident albeit temporary, with 32% of patients having reported dysphagia lasting approximately 5 days and some 60% experiencing post-procedure pain requiring analgesia. Both sclerotherapy and ligation can effectively arrest active bleeding from GOVs.<sup>23, 24</sup>

However, ligation is more-effective than sclerotherapy in decreasing the risk of re-bleeding from GOVs and can achieve variceal obliteration more rapidly with

fewer complications such as ulceration, bleeding or oesophageal stricturing.<sup>23</sup> In our study, the use of injection sclerotherapy was not associated with endoscopic stricture formation possibly as a result of the large varices encountered and therefore reduced para-variceal intimal injection and subsequent sclerosis.

In Ghana, bleeding GOVs are a significant cause of AUGIB, identified in some 22% of patients with a comparatively high mortality. Cases demonstrated a male preponderance with in-hospital mortality (in 24 hours) reflecting inadequate facilities to deal with this medical emergency. It is recommended that unstable patients are transfused with blood promptly, with platelets if counts are below  $50 \times 10^9/\text{ml}$  and fresh frozen plasma if INR above 1.5.<sup>25</sup>

Diagnostic and therapeutic endoscopy (e.g. band ligation) is essential in all unstable patients after resuscitation and to all other patients with AUGIB within 24 hours.<sup>25</sup> Octreotide or terlipressin in addition to prophylactic antibiotics with gram-negative cover also reduce morbidity and mortality in acute variceal bleeding.<sup>25, 26</sup>

It is therefore hoped that an orchestrated and strategic approach to care with endoscopic services equipped with all the necessary therapeutic interventions will be vital in improving the outcomes of patients with variceal bleeding in Ghana. Further study evaluating the impact of other potential causes of cirrhotic liver disease would be important as it gains prominence in Ghana.

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