

Predictors of Bleeding of Esophageal Varices Among Patients with Portal Hypertension-Sudan

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Abstract: Esophageal varices develop in more than one third in patients with liver cirrhosis with a high rate of mortality due to bleeding. We aimed to study predictors of bleeding in esophageal varices in Sudan. This retrospective cross-sectional study conducted at the National Gastrointestinal bleeding Center in Sudan, during the period March-September 2007. The record of 236 patients with bleeding esophageal varices was reviewed for: Demographic data, the presence of jaundice, fever, ascites, splenomegaly, and splenectomy full blood count, liver function tests, ultrasonographic report, endoscopic finding. Ethical clearance was obtained from both ethical committees of Sudan Medical Specialization Board, and the National Gastrointestinal bleeding Center. Out of 236 patients their age ranged from 18-79 years with a mean of 52.1 ± 14.3 , male dominance was apparent (80%). The majority were from Gazera region (62.3%). Splenomegaly, thrombocytopenia, and raised prothrombin time were found to predict esophageal variceal bleeding P-value < 0.05 , while fever and splenectomy were not P-value > 0.05 . Splenomegaly, thrombocytopenia, and raised prothrombin time were predictors of bleeding in esophageal varices.

Keywords: Predictors, Bleeding, Varices, Sudan

1. Introduction

Esophageal varices are very common in patients with liver cirrhosis amounting to 50% of patients and correlate with severity of liver cirrhosis, depending on hepatic venous pressure gradient, esophageal varices develop at a rate of 8% per year [1, 2]

The mortality rate of an episode of hemorrhage is 8% at six weeks [3, 4].

Varices develop due to increasing in vascular resistance aggravated by increased collateral blood flow, the resistance is intra-hepatic in the case of liver cirrhosis but can be pre-hepatic (schistosomiasis) and post-hepatic in Budd-Chiari syndrome [5].

The primary two causes of portal hypertension worldwide are liver cirrhosis and schistosomiasis; the former is commoner in Western countries while the latter is the most common cause in other nations [6]

All patients with liver cirrhosis develop portal hypertension

and gastroesophageal varices. Bleeding esophageal varices is a serious complication leading to death in about one-third of patients, a considerable proportion of patients are prone to re-bleeding with a mortality of 50-60% [7].

It is estimated that near eight hundred million people are at risk of schistosomiasis worldwide 200 million are infected with the majority residing in Africa, In Sudan about 7 million are suffering from the disease with deleterious consequences on the patients, families, and the whole community [8]

The diagnosis of portal hypertension relies on the clinical picture (splenomegaly, caput medusae, and ascites, and investigations (ultrasonography, upper gastrointestinal endoscopy) of at-risk patients. If the diagnosis is doubtful, the hepatic venous pressure gradient can guide prophylactic therapy (β blockers, nitrates, and band ligation). The portal venous pressure can be measured directly, but the test is even more invasive [9, 10]. A life threatening complication of portal hypertension is bleeding from large esophageal varices, prophylactic therapy for such large varices could considerably reduce the bleeding rate, morbidity and mortality. The current

guidelines recommend upper gastrointestinal endoscopy for the detection of gastroesophageal varices, but such invasive methods of investigation is not available in peripheral areas necessitating a search for a non-invasive methods for the detection and intervention when indicated [11] Sudan is a vast country amounting to 2% of the world surface; the health facilities are not well-equipped when present and investigations like imaging and gastro duodenoscopy are not available in remote out-reaching areas. Thus we conducted this research in which we thought to study predictors of bleeding of esophageal varices in Sudan.

2. Subjects & Methods

A retrospective cross-sectional study carried out at the National Center for Gastrointestinal Bleeding (the reference center accepting the referral from all parts of Sudan), during the period March 2007 to-September 2007. The medical record of 236 patients with esophageal varices was reviewed from a well-organized statistic office. The rules of privacy and confidentiality were strictly followed. Information collected included: Demographic data, liver and renal function tests, ultrasound report for the diagnosis of liver cirrhosis or bilharzial periportal fibrosis endoscopic finding including the size of varices, the presence of the red sign, clots, gastropathy, gastric varices. Full blood count for hemoglobin, white cell count and platelets was recorded. The ethical committee of the Sudan Medical Specialization Board and the local committee approved the research, and the Statistical Package for Social Sciences (SPSS) was used (the chi-square for comparison of categorical variable) with P-value of <0.05 considered significant.

3. Results

Out of 236 patients with bleeding esophageal varices near to half of them were in the productive age range (18-44 years). The majority were from Gazira region (62.1%), followed by Khartoum state in 11.9%, and White Nile in 6.4%, male dominance was apparent (80%), the vast majority (91.9%) were due to intestinal schistosomiasis. Table (1) illustrated demographic characteristics of patients.

Table (2) depicted clinical characteristic of the study group in which: Fever was evident in 10.6% of patients with no significant statistical difference (P-value=0.06), splenomegaly was found in 53.3%, 3.3% of patient were splenectomized P-value=0.08, while ascited was detected in 21.6% P-value=0.000.

Table No (3) depicted the endoscopic finding of patients with esophageal varices in which: gastropathy was evident in 75 (31.8%), fundal varices were found in 9 (3.8%) of patients, while red signs were detected in 28 (11.9%) of patients.

The majority of patients (71.7%) had grade 3 varices at bleeding P-value=0.000 followed by grade four in 16.5%, grade two in 8.4%, while grade one was evident in 3.4 of patients, thrombocytopenia was concluded in 75.4% P-

value=0.000, leucocytosis was found in 22.8%, leucopenia in 19.4% P-value=0.000. The majority of patients (62.2%) had prolonged prothrombin time P-value=0.000. Table (4)

The commonest grade of esophageal varices was grade 111 (71.4%), followed by grade 1V (16.5%). Figure No (1) illustrated the variceal grades among the study group.

Table 1. Demographic features of patients with variceal bleeding.

| Character | % |
|-------------------------------|--------|
| Age range years | |
| 18-45 | 42.10% |
| 46-65 | 48.50% |
| > 65 | 9.40% |
| Sex | |
| Males | 80% |
| Females | 20% |
| Residence | |
| Gazera | 62.30% |
| Khartoum | 11.90% |
| White Nile | 6.40% |
| North Sudan | 4.20% |
| Western Sudan | 4.20% |
| Eastern Sudan | 3.80% |
| Blue Nile | 3.80% |
| Southern Sudan | 3.40% |
| Underline diagnosis | |
| Bilharzialperiportal fibrosis | 91.90% |
| Liver cirrhosis | 7.20% |
| Unknown | 0.90% |

Table 2. The clinical characteristics of Sudanese patient with bleeding esophageal varices.

| Character | % | P-value |
|--------------|------|---------|
| Fever | 10.6 | 0.060 |
| Splenomegaly | 53.3 | 0 |
| Splenectomy | 3.3 | 0.080 |
| Ascites | 21.6 | 0 |

Table 3. Endoscopic findings of the study group.

| Character | No% |
|--------------------|------------|
| Esophageal varices | 236 (100%) |
| Gastropathy | 75 (31.8%) |
| Fundal varices | 9 (3.8%) |
| Red signs | 28 (11.9%) |

Table 4. Investigations of Sudanese esophageal varices patients.

| Investigation | % | P-value |
|------------------------------------|------|---------|
| Hemoglobin | | |
| <5gm/dl | 25 | 0 |
| 5-10gm/dl | 59.7 | |
| 10-11gm/dl | 14.3 | |
| Thrombocytopenia | 75.4 | 0 |
| White cell count | | |
| Leucocytosis | 22.8 | 0 |
| Leucopenia | 19.4 | |
| Prothrombin time seconds > control | | |
| 1-3 | 45.3 | 0 |
| 4-6 | 11.4 | |
| > 6 | 5.5 | |
| Vrceal grade | | |
| Grade 1 | 3.4 | 0 |
| Grade 2 | 8.4 | |
| Grade 3 | 71.7 | |
| Grade 4 | 16.5 | |

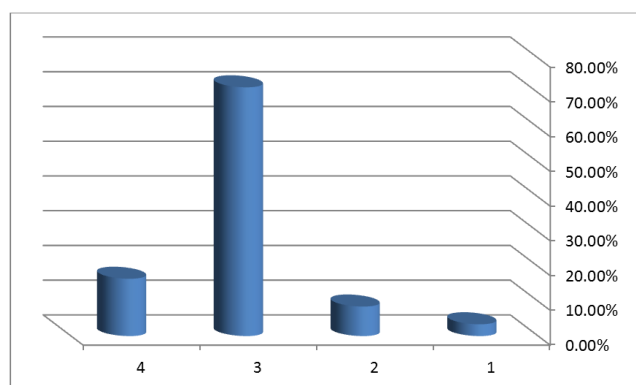


Figure 1. Grades of esophageal varices among the study group.

4. Discussion

In the present study the majority of patients with esophageal varices were in the age group 18-65 years and the majority were male, our findings were in accordance to Chofle who conducted a study among patients with portal hypertension in Tanzania and concluded similar findings [12].

The current data concluded that the majority (91.9%) of portal hypertension was associated with bilharziasis, the present data were higher than a study conducted in Sudan [13] and found schistosomiasis in 42% of the study sample, the present data were higher than Chofle [12] finding who observed schistosomiasis in 62% among patients with portal hypertension.

In the current study the majority of patients were men because the males are more prone to be infected with bilharzias as the majority were farmers (data not shown), similarly previous researchers concluded that bilharzial portal hypertension was commoner among men [13].

In the current study splenomegaly, thrombocytopenia, prolonged prothrombin time, and grade 3 esophageal varices were predictors of hemorrhage.

In the present study, splenomegaly was observed in 53.3% of patients and related to esophageal bleeding P-value <0.05 similar to previous studies [14-16] in which low platelets and splenomegaly were independent predictors of esophageal bleeding.

The current data showed that large varices were commoner than small ones in contradiction to Manohar et al. [17] who concluded small varices in 60% this can be explained by the advanced disease at the presentation to the hospital.

In the present study grade three esophageal varices were present in more than two-thirds of patients (71.7% (P-value <0.001), a study published in Sudan [16] among patients with bilharzial periportal fibrosis showed a similar result.

The Child class and size of varices can be used to quantify the risk of variceal bleeding [18], in the current study prothrombin time was prolonged in 62.2% of patients, and ascites was concluded in 21.6% in accordance with the previous finding.

The prolonged prothrombin time observed in the current study may be due to co-infection with hepatitis B virus as patient infected with hepatosplenicschistosomiasis had up to

10 fold infection with this virus compared to normal counterparts [19].

Persistent antigenemia [19] and other co-infection may in part explain the high rate of leucocytosis observed in our sample.

The fact that Varices occur in 25-40% of cirrhotic patients [20], combined with the invasiveness and cost of endoscopy, also the prophylactic drug therapy is not without hazards, it is of value to restrict upper gastrointestinal endoscopy and protective measures to patients at high risk of bleeding, thus avoiding them in 60-75% of patients who are not at risk of bleeding. Furthermore, detection of portal hypertension at an earlier stage by the noninvasive transient elastography [21] is increasingly used making noninvasive predictors of bleeding a valuable stratification measure for referring patients for endoscopy. The present study has many limitations: first, it is a retrospective, second is the small sample, and it was conducted at a single center. Further larger multicenter prospective studies are needed.

5. Conclusion

Low platelets count, splenomegaly, larger variceal size, and high prothrombin time were associated with variceal bleeding and may predict those at risk of bleeding for prophylactic therapy, avoiding the more invasive investigations like endoscopy, while fever and splenectomy were not.

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