Original Article

Risk factors for bleeding in patients with asymptomatic oesophageal varices secondary to schistosomal portal hypertension: a longitudinal hospital based study

Ibrahim SZ, FRCS, Shah T, FRCS, Arbab BM, MRCP, Abdel-Wahab O, DMRD

Departments of Surgery, Medicine and Radiology
Soba University Hospital, University of Khartoum, Sudan

Abstract

Objective
To determine the risk factors for bleeding from asymptomatic varices secondary to schistosomal portal hypertension.

Methods
This is a retrospective, prospective, longitudinal, hospital, based study in a specialised portal hypertension clinic. Clinical, biochemical, haematological, endoscopic and sonographic evaluation were performed. Data was collected prospectively in a special portal hypertension folder designed for the purpose.

Results
141 patients, 104 males and 37 females with an age range of 12 to 72 years (mean 33.7 +/- 13.7) were studied. They were followed-up for a minimum of 1 year and a maximum of 6 years (mean 27.6 months). 21 patients (14.9%) bled from their varices. 11 patients (7.8%) bled within one year and 10 within the subsequent 6 years. The interval between presentation and bleeding ranged from 4 days to 78 months (mean 19.9 +/- 21.6). Of the 21 who bled, 3 rebled (14.3%) within 1 year. The bleeders had significantly longer duration of schistosomiasis (p <0.05), more serum bilirubin above 2mg% (p<0.01), more thrombocytopenia (p <0.05), more grade III and IV varices (p <0.05) and more grade III periportal fibrosis (p <0.01).

Conclusion
It is suggested that patients with these risk factors should be considered for close follow-up and medical treatment.

Introduction
The prevalence of Schistosomiasis in the Gezira irrigated areas of Sudan was lowered from 53.6% in 1982 to 6.1% in 1989 by mass treatment with praziquantel under the Blue Nile Health project(1). During this same period Schistosomal periportal fibrosis was found to affect 13-18% of those afflicted with the disease(2). In field studies the prevalence of oesophageal varices in this population with periportal fibrosis was found to be 54% to 67% but only 3 to 4% of these bled from their varices(3). Eltoum and his colleagues(4), in a field study comparing patients with schistosomal periportal fibrosis who already bled from their varices to those who never bled, defined predictors of bleeding as a splenic longitudinal dimension of more than 11 cm, periportal fibrosis worse than grade I and varices more than grade I .

After the successful campaign of the Blue Nile Health Project in the eighties of the last century, the prevalence of Shistosomiasis is now again on the increase not only in selected endemic areas of Gezira, like Managil, where it reached 54.3%, but also in...
Southern Blue Nile (32.6%), Kassala province (45.2%), and White Nile (35.5%)[5]. This indicates that clinicians will again be faced with an increasing number of patients presenting with complications of the disease, especially the dreaded bleeding from oesophagogastric varices. This hospital-based retrospective prospective longitudinal study was undertaken to define the risk factors that may contribute to variceal rupture and bleeding in patients with asymptomatic varices. This may allow rational decisions on policies that address the treatment in these patients.

Patients and methods

Patients diagnosed as having Schistosomal portal hypertension, with history of bleeding, and or splenomegaly, and or hypersplenism were referred to a special portal hypertension clinic at Soba university hospital, University of Khartoum, Sudan. The clinic was established in 1980 and continued to function till 1996. Patients data were recorded in special portal hypertension folders. 141 patients with schistosomal portal hypertension and asymptomatic varices were included in the study. All patients underwent clinical, hematological, biochemical, and endoscopic evaluation. Oesophageal varices were graded endoscopically using Conn’s grading[6] into grades I to IV. Initially ultrasound was used for supporting diagnosis but later in the study, in 89 patients; it was used for both diagnosis and grading of periportal fibrosis. Grading was allotted three grades by modification of the original method described by Homeida et al[7], which was conducted in the same institution. Grade I: mild echogenic thickening of one or two portal vein radicles with little change in the walls of the portal vein. Grade II: moderate to severe periportal irregular thickening of most of the portal vein radicles, with marked narrowing of the central lucency, marked thickening at the bifurcation of the portal vein, and mild thickening of the main portal vein. Grade III: marked thickening of the walls of the portal vein radicles with obliteration of the central lucency in the peripheral branches forming thick irregular echogenic 10-20mm bands reaching the periphery of the liver with thickening down to main portal vein walls. In all grades the gall bladder wall is thickened.

The 141 patients with asymptomatic varices were followed up for a minimum of 1 year, and a maximum of 6 years. After the initial evaluation at presentation, they were re-evaluated at 6-12 months intervals, unless a complication occurs, specially bleeding, when they were offered prearranged immediate access to the hospital. A special emphasis was made on variceal bleeding and what risk factors could be defined as indicators of bleeding.

For statistical analysis the chi-square test was used to compare qualitative data and the student’s t-test to compare the means of quantitative data. Fisher exact test was used to compare qualitative data when the number of patients was small. The chi-square goodness of fit test was used to compare the duration from presentation to the time of bleeding. The chi-square test for percentages was used to compare the sonographic grades of fibrosis between the bleeders and the non-bleeders.

Results

The 141 patients with schistosomal periportal fibrosis and asymptomatic varices were followed up for a minimum of 1 year and a maximum of 6 years with a mean of 27.6 months. There were 104 males and 37 females. Their age ranged from 12 to 73 years with a mean of 33.7±13.7 years. 107 patients were child’s A (76%), 27 patients were Child’s B (19.1%), and only 7 patients were Child’s C (5%). Twenty one patients (14.9%) bled from their varices during the
follow up period. The time between initial presentation and variceal bleeding ranged from 4 days to 78 months (mean 19.9+/-.21.6 months). 15 patients (10.6%) bled from their varices within the first 2 years, of whom 11 (7.8%) did so within the first year. Of the 21 patients who bled in this study 11 (52.4%) did so within the first year, 4 within the 2nd year, 1 within the 3rd year, 4 within the 4th year, and 1 within the 6th year. Only 3 patients (14.3%) rebled from their varices and they did so within one year of their initial bleed. None of the bleeders died following his or her bleed. However while waiting for definitive treatment 7 patients were lost for follow-up 2 to 4 months after their initial bleeding episode.

There were no significant differences between those who bled (Bleeders) and those who did not bleed (Non-Bleeders) in relation to mean age (33.7+/-.13.7 versus 33.7+/-.13.8), or sex (M/F ratio 1.6:1 versus 3.1:1). There were no significant differences between the two groups in the presence of ascites, their haemoglobin level, white blood cells count, prothrombin time, or albumin levels (Table 1a).

**Table 1a: Comparison between bleeders and non-bleeders**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Ascites</th>
<th>Hb % mean±s.d.</th>
<th>WBC mean±s.d.</th>
<th>P.T (seconds above normal)</th>
<th>Albumin mean±s.d.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeders</td>
<td>N=21</td>
<td>38.1%</td>
<td>71.38±12.5</td>
<td>3207±1302</td>
<td>2.25±1.2</td>
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<tr>
<td></td>
<td></td>
<td>8 of 21</td>
<td></td>
<td></td>
<td>3.77±0.53</td>
</tr>
<tr>
<td>Non-Bleeders</td>
<td>N=120</td>
<td>30%</td>
<td>75.66±17.83</td>
<td>3210±2718</td>
<td>2.78±2.69</td>
</tr>
<tr>
<td></td>
<td></td>
<td>36 of 120</td>
<td></td>
<td></td>
<td>3.89±0.52</td>
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<td></td>
<td>N.S.</td>
<td>N.S.</td>
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(Hb: haemoglobin; WBC: total white blood cells count; P.T: Prothrombin time)

Compared to the non-bleeders, the bleeders had a significantly longer duration of schistosomal disease (11.3±10.1 versus 7.1±7.6 years, P<0.05), more serum bilirubin above 2mg% (80% versus 37.5% of patients, P<0.01), more thrombocytopenia below 75000 (60% versus 38% of patients, P<0.05), more grade III and IV varices (57.1% versus 30.8% - P<0.05) and more grade III periportal fibrosis (66.6% versus 21.2% - P<0.01) (Table 1b).

**Table 1b: Comparisons between Bleeders and Non-Bleeders**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Duration of Disease years mean±/s.d.</th>
<th>Bilirubin &gt;2mg%</th>
<th>Platelets &lt;75,000</th>
<th>Grade III &amp; IV Varices</th>
<th>Grade III periportal fibrosis N=89</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeders</td>
<td>N=21</td>
<td>11.3+/-.10.1</td>
<td>8 out of 10 (80%)</td>
<td>6 out of 10 (60%)</td>
<td>12 out of 21 (57.1%)</td>
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<td></td>
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<td></td>
<td>6 out of 9 (66.6%)</td>
</tr>
<tr>
<td>Non-Bleeders</td>
<td>N=120</td>
<td>7.1+/-.7.6</td>
<td>27 out of 72 (37.5%)</td>
<td>16 out of 42 (38.1%)</td>
<td>37 out of 120 (30.8)</td>
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<td></td>
<td></td>
<td></td>
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<td></td>
<td>17 out of 80 (21.2%)</td>
</tr>
<tr>
<td></td>
<td>P&lt;.05</td>
<td>P&lt;.01</td>
<td>P&lt;.05</td>
<td>P&lt;.05</td>
<td>P&lt;.01</td>
</tr>
</tbody>
</table>

Amongst the bleeders those with Grade I, II and III varices at presentation bled after an average of 22.4 months while those with grade IV varices bled after an average of 5 months (P<0.05). Moreover those bleeders with grade I fibrosis at presentation bled after an average of 22.5 months compared to those with grade II and III fibrosis who bled after an average of 7 and 8 months respectively (P<0.01).
Discussion

Schistosomiasis is the commonest cause of portal hypertension in the Sudan\(^8\). It is the commonest cause of upper gastrointestinal bleeding\(^9\). After a decline in its prevalence in the late eighties and nineties of the last century, following campaigns of mass treatment with praziquantel\(^1\), the problem is again on the rise\(^5\). Clinicians are again facing an increasing number of patients with complications of the disease. Bleeding oesophageal varices will need endoscopic or surgical treatment depending on the magnitude of the disease and the liver status. However asymptomatic varices present a problem as to what should be done about them. Prediction of bleeding or definition of risk factors for bleeding would identify a subset of patients who will need special attention.

In liver cirrhosis almost 30% of patients with asymptomatic varices will bleed within one to two years\(^{10,11,12}\) with over a 50% mortality rate\(^{13,14}\). Among those who survive 60% will rebleed within 1 year\(^{15,16,17}\). In this study 21 out of 141 patients (14.9%) with asymptomatic varices bled during the follow-up period, 15 patients (10.6%) bled within the first 2 years. Only 11 patients (7.8%) bled within the first year. The rebleeding rate was only 14.3% (3 patients), and all within 1 year of their initial bleed. These figures are evidently markedly less than those in cirrhotics. Of the 21 patients who bled, more than half (52.4%) bled within the first year and the rest bled within the following 6 years. This suggests that the risk of variceal bleeding declines precipitously if the patient does not bleed within the first year after diagnosis.

Variceal haemorrhage is well tolerated in Schistosomal portal hypertension, provided adequate resuscitative measures are instituted because liver function is well maintained for prolonged periods of time in the majority of patients\(^{18}\). In this study only 7 out of 141 patients (5%) were Child’s class C indicating good overall hepatocyte function in this group of patients. The survival rate after a first variceal bleed in patients with schistosomal portal hypertension is twice that from variceal bleeding in post-necrotic cirrhosis\(^{19}\). In this study all patients were given prearranged immediate access to the hospital in case of bleeding. No patient died from his or her first bleed. However 7 patients out of 21 bleeders were lost for follow-up 2 to 4 months after their first episode of bleeding while waiting for definitive treatment.

Studies conducted to predict variceal bleeding have shown that severity of liver disease and Child-Pugh score are significant risk factors\(^{11,20,21}\). In this study the chronicity of the disease appears to be a significant factor in that the bleeders had a longer duration of the disease than the non-bleeders (11.3±10.1 versus 7.1±7.6 years, P<0.05). However among the variables of Child’s score only a bilirubin level above 2mg% was significantly discriminant between bleeders and non-bleeders (80% versus 37.5%; P<0.01).

A low platelet count secondary to hypersplenism was shown to be one of the risk factors for variceal bleeding\(^{20,22}\). This has been a finding in this study where thrombocytopenia below 75000 was significantly more predominant in the bleeders (63.6%) versus 38%; P<0.05).

In cirrhotic patients the landmark study of Beppu et al, and other workers, have shown that detailed endoscopic characteristics of varices can be used to predict bleeding\(^{23,24,25}\). Medwar et al\(^{26}\) in a study on Schistosomal and non-Schistosomal portal hypertension found that endoscopic findings of cherry red spots and increased grade of varices were significant risk factors
for bleeding. In this study, although only simple grading of varices was used, it was shown that bleeders had significantly more grade III and IV varices than non-bleeders (57.1% versus 30.8%; P<0.05). In addition those with grade IV varices bled within a shorter period of time compared to the other grades (5 versus 22.7 months; P<0.05).

Ultrasound features of schistosomal periportal fibrosis were described by Abdel-Wahab and his colleagues in 1978(27). Fataar et al(28) were able to correlate the sonographic findings with macroscopic and microscopic changes of periportal fibrosis in liver biopsy specimens. Homeida et al(6) utilised ultrasound for diagnosis and grading of periportal fibrosis validated against liver wedge biopsies. In this study we graded periportal fibrosis by modification of the original technique of Homeida et al. This study clearly demonstrated that patients with grade III periportal fibrosis are more liable to bleed than those with grades I and II (66.6% versus 21.2%; P<0.01). Not only so, but patients with grade II and III fibrosis bleed in a shorter period of time than those with grade I (7 and 8 months versus 22.5; P<0.01).

This study is different from that of Eltoum et al(4) who compared a group of established bleeders to another with asymptomatic varices, in the Gezira endemic area, and found that a splenic longitudinal dimension of more than 11 cm, periportal fibrosis worse than grade I and varices more than grade I were independently associated with a significant risk of variceal bleeding. This study started with a group of patients with asymptomatic varices that were studied over a period of time prospectively. Thus the natural evolution of the disease and definition of the bleeding risk are more meaningful. Our study, however, supports the findings of Eltoum et al in that endoscopic and ultrasound parameters can predict the risk of bleeding. It differs in that additional parameters were identified like: chronicity of the disease, elevated serum bilirubin, and low platelets. Our findings support another longitudinal study on schistosomal patients in Brazil by Richter et al(29), where a score based on ultrasonographic findings of periportal fibrosis and portal vein dilatation was able to significantly predict variceal bleeding.

Prophylactic total shunt surgery for asymptomatic varices in cirrhotics have shown a very poor outcome and was abandoned(30,31). Prophylactic sclerotherapy, as well, did not reduce the incidence of a first variceal bleed(32) or alter survival in cirrhotic patients(33). Although nondecompression prophylactic surgery have shown improved survival in cirrhotics(34), yet this study have shown a significantly reduced bleeding risk and mortality in schistosomal portal hypertension compared to published findings in that of cirrhosis. The low bleeding rate and lack of mortality in our patient population do not justify prophylactic surgery or sclerotherapy in the high risk group by the criteria of this study. However studies have shown that medical treatment in the form of propranolol reduce the risk of a first variceal bleed, but did not alter survival, in cirrhotic subjects(35). In our patient population el Tourabi et al(36) have shown that propanolol reduces both rebleeding and mortality.

The findings of this study suggest that patients with asymptomatic oesophageal varices secondary to schistosomal portal hypertension with elevated serum bilirubin, low platelets, grade III and IV varices and grade III periportal fibrosis, should be considered for close follow-up and medical treatment. Further detailed studies are recommended to determine whether a subset of these patients can be offered endoscopic therapy or nondecompressive surgery on the basis of justifiable risk.
References


26. Madwar MA, Shaker MK, Atta MA, El Khashab TH, Mohamed MK. A prospective study: prediction of the first variceal haemorrhage in schistosomal and non
Original Article
Risk factors for bleeding Ibrahim SZ et al


