SciencePG
Science Publishing Group

Noninvasive Prediction of Esophageal Varices Grade (Size) in Sudanese Patients with Periportal Fibrosis

Mohammed Abdelrahim Hassan[1], Amin Mohammed Abass[2], Hyder Osman Mirghani[3, *], Elkhawad Osman[4], Mohammed Osman Elhassan Gadour[5]

[1]Sudan Medical Specialization Board, Khartoum, Sudan

[2]Department of Gastroenterology and Hepatology, Ibn Sina Teaching Hospital, Khartoum, Sudan

[3]Department of Internal Medicine, Faculty of Medicine, University of Tabuk, Tabuk, Saudi Arabia

[4]Depatment of Radiology, Ibn Sina Teaching Hospital, Khartoum, Sudan

[5]Department of Internal Medicine, Faculty of Medicine, Omdurman Islamic University, Omdurman, Sudan

Email address:
s.hyder63@hotmail.com (H. O. Mirghani)

*Corresponding author

Abstract: Endoscopy is an effective tool for variceal grading, but it is costly, invasive, and not always at hand. The study aimed to assess platelets count and ultrasonographic parameters of portal hypertension as predictors of esophageal grade. This, cross-sectional hospital based study conducted among100 patients with Schistosomal portal hypertension at Ibn Sina Teaching Hospital, Khartoum, Sudan during the period from November 2011 – August 2012. Patients with liver cirrhosis, previous treatment for esophageal varices or on β blockers were not included. Information collected were: socio-demographic data, history of and onset of variceal bleeding, ascites, SchistosomaMansoni Score (SMS), the spleen size, liver span, portal and splenic veins diameter, variceal grade, and platelets count. The ethical committee of the Sudan Medical Specialization Board approved the research and the Statistical Package for Social Sciences (SPSS, version 20, New York) was used for data analysis. Participants (76% males), Mean age (43.9 ± 14 years), liver span, spleen size below the costal margin, and portal vein diameter were, 10.34± 2.01, 6 ± 3.9, and 1.5 cm ± 0.27 cm respectively. Platelets count, SMS, the extent of periportal fibrosis, and portal vein diameter were significant predictors of esophageal grade,(P-value <0.05), while spleen size, portal vein diameter, platelets/spleen index were not. The study concluded that, non-invasive assessment of ultrasonographic parameters (ShistosomaMansoni Score, portal vein diameter, degree of periportal fibrosis) and platelets count could aid the detection of patients with large esophageal varies for the implementation of the needed intervention. The limitation was the small sample size.

Keywords: Predictors, Schistosomiasis, Esophageal Grade, Sudan

1. Introduction

It is estimated that 300 million people are infected with schistosomiasis worldwide, another 600 million are at high risk for infection, and 20 million have debilitating disease. Mortality from schistosomiasis was estimated at 11,000 deaths per year and the burden of disease at 1.7 million disability-adjusted life years lost per year [1]. The prevalence of schistosomaMansoni in Sudan varied from 80% to 10.1%

depending on endemicity and irrigation [2, 3]. Other non-irrigated areas are less affected

Periportal fibrosis of the liver is a serious consequence of Schistosoma mansoni infection that involves remodeling of the extracellular matrix and excessive deposition of collagen, primarily by hepatic stellate cells, along the branches of the portal tract leading to portal hypertension [4]

Portal hypertension is a necessary prerequisite for the development of varices, and variceal bleeding rarely occurs

below the pressure of 12mmHg [5].

Bleeding from varices is a frequent cause of mortality and morbidity [6]. Upper digestive endoscopy is the gold standard to diagnose and grade oesophagealvarices. However, endoscopy is an invasive procedure, not always available, and its cost-effectiveness for screening is also questionable. Moreover, schistosomiasis is endemic in poor areas where resources are limited and there is a particular need for noninvasive predictors of oesophagealvarices. Ultrasonography and platelets counts are simple, reproducible tools usually performed in the normal management of patients with chronic liver disease. Few researchers have studied ultrasonography grading for periportal fibrosis and platelets counts and relating them to esophageal grades. Thus, the present study was conducted to assess hematological and ultrasonographic feature of schistosomal periportal fibrosis as predictors of the presence oesophageal varices and their grades.

2. Materials and Methods

2.1. Design, Sample and Data Collection

This cross-sectional study was done at Ibn Sina Hospital and National Center of Gastrointestinal Bleeding, Sudan during the period from November 2011 to August 2012. One hundred Sudanese patients with the diagnosis ofschistosomal periportal fibrosis (PPF) with and without history of bleeding were included. The diagnosis of PPF was based on abdominal ultrasound. Patients were excluded If they have liver cirrhosis, hepatitis B or C virus infection, history of undergoing oesophageal band ligation or sclerotherapy. Patients who consume alcohol and those on beta blocker were not included.

For the purpose of this research the following was adopted

(1) A full medical history including the episode of upper gastrointestinal bleeding, the number, duration and amount of current episode of haematemesis or meleana, time of onset of bleeding and amount of vomited blood.

(2) Thorough clinical examination were undertaken including the size of the liver and spleen, and ascites, the patients were invited to sign a written informed consent, then interviewed using a structured questionnaire.

(3) The patients then underwent Oesophagogastroscopy using the PETAX video gastroscope, model EG-3490K. Prior to endoscopy, xylocaine spray was used as a local anesthetic but no other premedication were used. Oesophagealvarices were graded into four degree of severity according to the degree of severity. Surface change on the varices indicating recent bleeding or rupture such as cherry red spots were reported. Whenever feasible search for gastric varices was done with a careful look for gastric mucosa for evidence of portal hypertensive gastropathy.

(4) An ultrasound scan was done by a single investigator who was blinded to the endoscopic findings to avoid bias. Patients were examined while fasting in the supine position. The fibrosis was graded from one-four according to Homieda et al.[7] . The spleen size and portal vein diameter were also recorded according to the standard measures The platelets count was also estimated.

(5) S. mansoni sonographic score (SMS) was computed combining the degree of periportal fibrosis and the dilation of the portal vein and could vary from 0 to 4 points. The SMS score of a single patient is the sum of the score of the grade of periportal fibrosis plus the score of the degree of portal vein dilatation.

(6) Portal vein quotient = portal vein diameter in mm divided by the body height in meter.

2.2. Statistical Analysis

The Statistical Package for Social Sciences (SPSS, version 20, New York) was used for data analysis. The Wilicoxon matched-pair singed-rank test and Man-Whitney test were applied where appropriate. For linear association we use Mantel-Henszel. Significance of difference between relative frequencies was assessed by Mantel–Henszel or by Fisher exact test. Receiver operating characteristic (ROC) curves were used to identify the cut off point for parameter and for best sensitivity and specificity cutoff values of the significant variables for the presence of large oesophageal varices.

Ethical consideration:

The ethical committee of the Sudan Medical Specialization Board approved the research. All the participants signed a written informed consent.

3. Results and Discussion

There were 100 patients with periportal fibrosis, male dominance was obvious (76%), their ages ranged from 36-86 with a mean of 43.9 ± 14 years, the majority (79%) of the study sample were from Central Sudan. The spleen was 6 ± 3.9 cm below the costal margin, the liver span was 10.34 ± 2.01 cm, the portal vein diameter was 1.67 cm ± 0.26 cm, splenic vein diameter was 1.5 cm ± 0.27 cm, ascites was diagnosed in 9% of patients, grade 111 and 1V esophageal varices were found in 79%, while 41% had variceal bleeding. It is interesting to note that, the onset of the first bleeding was early morning in 82.9%. Table 1.

Table 2. Showed endoscopy grade with respect to periportal fibrosis (PPF) grade. The ultrasonographic grade of periportal fibrosis was found to correlate with the variceal grade (P =.0001).

Table 3. Correlated between platelet count and endoscopy grade. High correlation between the large grade of oesophagealvarices and low platelet count was found (2% vs. 38% in the platelets range 20000-90000, and 7% vs. 28% in the range 91000-150000 for small and large varices respectively), P = 0.0259.

Table 4. Depicted the relationship between the calculated SMS score and variceal grade, the SMS score was found to correlate significantly with the oesophagealvarices grade, with those with high SMS score having large varices at

endoscopy and vice versa (P = 0.00001).

Table 5. showed the sensitivity and specificity for each parameter of predictors in relation to detection of large oesophagealvarices. It shows that the SMS score had highest sensitivity at the level 2 (95.1%) whereas the splenic size by ultrasound at a cutoff point of 14.5cm and the splenic vein diameter at a cutoff point of 1.55 cm had the same high specificity which is 77.8%. The former had also high sensitivity (95.%) and the later had sensitivity of just 54.7%, whereas the portal vein diameter at a cutoff point of 1.55cm and the platelet count/ spleen size index at a cutoff point of 444 had the same sensitivity and specificity, 33.3% and 66.7% respectively.

Table 6. Illustrated the positive and negative predictive values among the predictors of the oesophageal grade. SchistosomaMansoni Score had the highest positive predictive value (90.6%) followed by splenic vein (90.2%), and portal vein diameter (89.1%), on the other hands, SMS reported the highest negative predictive value of 73.3%, followed by spleen size by ultrasound (50.0%), and portal vein diameter (33.3%).

Table 7. Showed the correlation between the oesophageal grade and most of the variables in the study. It shows that the correlation is very strong between the oesphageal grade and SMS score ($P= 0.00001$) and also it is very significant between OV grade and platelet count (P = 0.00002). Also portal vein diameter shows good correlation (P = 0.047). Whereas the age and sex show the least association with P. value of 0.116 and 0.449 respectively.

Figure 1. showed the relationship between the oesophageal grade and the platelets count/spleen size ratio. 62% of those who had large oesophagealvarices had platelet/spleen size ratio less than 1000, while this rate was found in 16% of those who had small varices, there is linear correlation between the platelets count/spleen size ratio and the variceal grade (P = 0.04).

Figure 2. illustrated the ROC curve between the oesophageal grade and the sonographic predictors in a form of spleen size, portal vein diameter, splenic vein diameter, the shistosoma mansoni score (SMS score) and platelet count, the parameters with the highest sensitivity and specificity being the SMS score followed by the platelet count then PVD, then the SVD, the least one is platelet count/spleen size ratio.

Table 1. *The basic and ultrasonographic characteristics of the study group.*

Character	No%
Sex	
Males	76 (76%)
Females	34 (24%)
Residence	
Central Sudan (Gazera& White Nile)	79(79%)
Khartoum	11 (11%)
Other areas	10 (10%)
Ascites present	9 (9.0%)
Large varices (111 and 1V)	79 (79%)
Variceal bleeding	41 (41%)
Morning onset of variceal bleeding	83 (83%)
Character	Mean± SD
Age	43.9 ± 14 years
Spleen size below the costal margin	6 ± 3.9cm
The liver span	10.34± 2.01 cm
The portal vein diameter	1.67 cm ± 0.26 cm
Splenic vein diameter	1.5 cm ± 0.27 cm

P = 0.0001
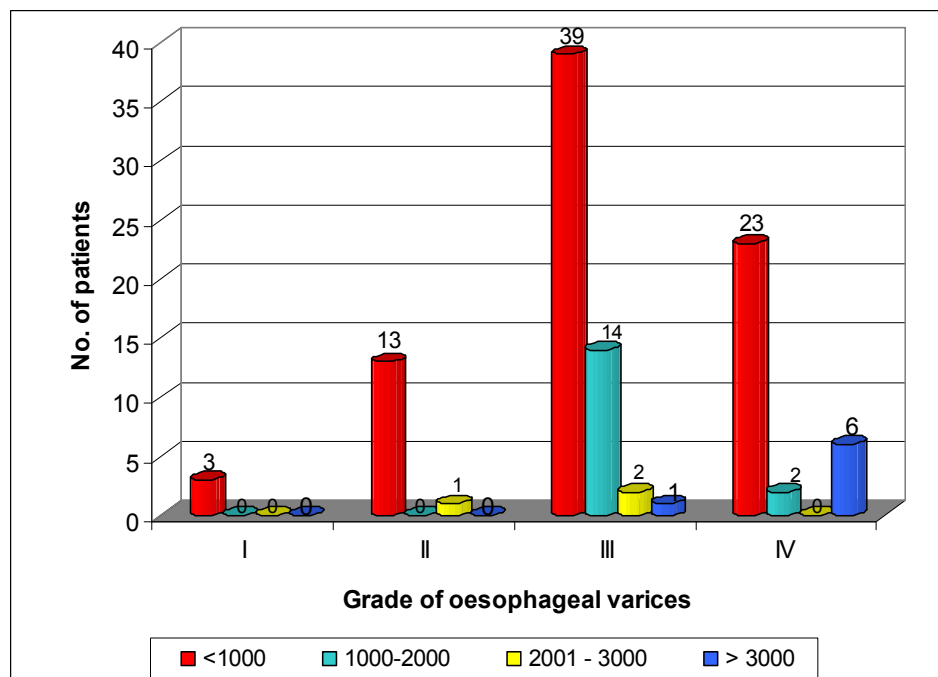
Figure 1. *Relationship between the oesophageal grade and the platelets /spleen size ratio in 100 Sudanese patients with periportal fibrosis.*
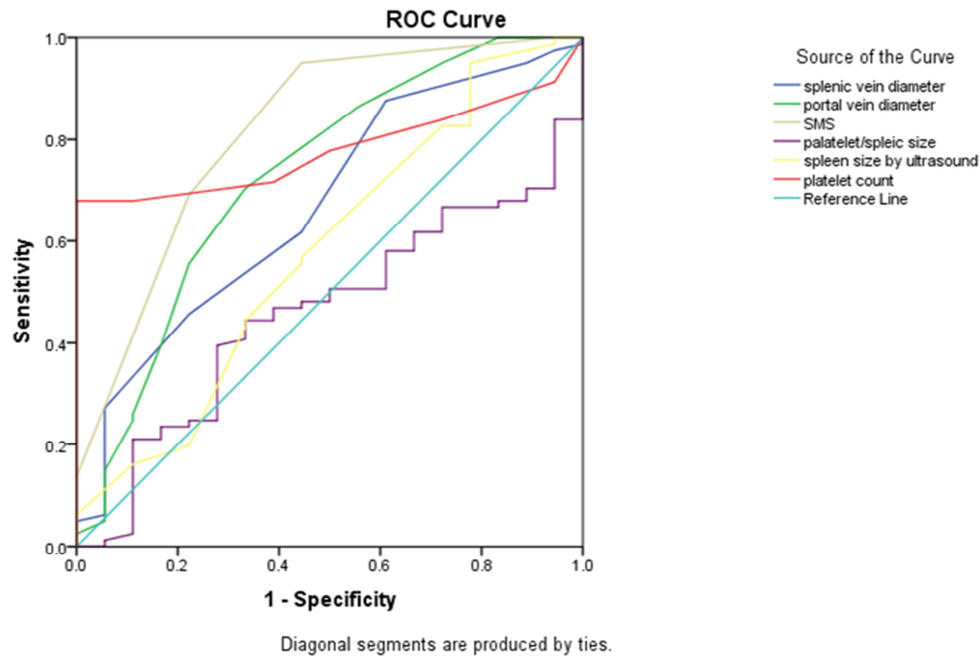
Figure 2. ROC curve demonstrate the cut of point for sensitivity and specificity for each sonographic variable and it is relation to the oesophageal grade.

Table 2. The endoscopy grade with respect to periportal fibrosis (PPF) grade in 100 Sudanese patients with periportal fibrosis.

Endoscopic grade	Periportal fibrosis grade				Total
	1	2	3	4	
I	1	1	1	0	3
II	0	10	4	2	16
III	1	11	34	10	56
IV	0	2	12	11	25
Total	2	24	51	23	100

P = 0.001

Table 3. Correlation between platelet count and endoscopy grade in 100 Sudanese patients with periportal fibrosis.

Platelets count (×109/L)	Endoscopic grade				Total
	1	2	3	4	
20-90	0	2	26	12	40
91-150	0	7	20	8	35
151-400	3	7	9	5	24
> 400	0	0	1	0	1
Total	3	16	56	25	100

P =0.026

Table 4. Relation between calculated SMS score andthe oesophageal grade.

Endoscopic grade	SMS score					Total
	0	1	2	3	4	
I	0	1	0	2	0	3
II	1	9	4	2	0	16
III	0	4	20	29	3	56
IV	0	0	1	16	8	25
Total	1	14	25	49	11	100

Table 5. Sensitivity and specificity for each variable as a predictors for detection of large varices (grade 3-4).

Variable	Cutoff point	Sensitivity	Specificity
SMS score	2	95.1%	57.9 %
Platelet count	121 ×109/L	42 %	73.7 %
Portal vein diameter	1.55 cm	33.3%	66.7%
Splenic vein diameter	1.55 cm	54.7 %	77.8 %
Spleen size by ultrasound	14.5	95.1%	77.8 %
Platelet count/spleen size index	444	33.3 %	66.7%

Table 6. *Showed the positive and negative predictive values among the predictors of large esophageal grades (3&4).*

Predictor	Cut of point	Negative predictive	Positive predictive
SMS score	2	73.3%	90.6%
Platelet count	121 ×109/L	12.8%	77.0%
Portal vein diameter	1.55 cm	33.3%	89.1%
Splenic vein diameter	1.55 cm	25.4%	90.2%
Spleen size by ultrasound	14.5 cm	50.0%	83.7%
Platelet count/spleen size index	444	19.2%	81.3%

Table 7. *Correlation between the oesophageal grade and the possible predictors among the study group.*

Variable	Chi square	Significance
SMS	0.0000	Significant
Platelet	0.004	Significant
Periportal fibrosis	0.001	Significant
Portal vein diameter	0.047	Significant
Spleen size clinically	0.311	Insignificant
Spleen size by ultrasound	0.612	Insignificant
Splenic vein diameter	0.201	Insignificant
Platelet /spleen size ratio	0.619	Insignificant
Ascites	0.472	Insignificant
Age	0.116	Insignificant
Sex	0.499	Insignificant

4. Discussion

In the present study, Scistosoma Mansoni Sonographic (SMS) score, platelets count, the extent of periportal fibrosis, and portal vein diameter were significant predictors of large variceal grade, while spleen size, splenic vein diameter (SVD), Platelet /spleen size ratio, ascites, age, and sex were not.

The current study showed that, the platelets count predict large varices, while splenic size was not , the present observation were in line with a recent study published by Akande et al. [8] who conducted a case-control study and concluded similar findings. The spleen size may be enlarged from various diseases in Sudan. Also it is well known that acute bleeding decompress the portal circulation leading to significant reduction in spleen size in the bleeders. The previous study reported that the platelets/splenic ratio predict large varices and no statistical significant difference between case and control regarding portal vein diameter in contradiction to the present findings in which, the portal vein diameter was a significant predictor of large varices. Plausible explanations could be the small size of the control group in the previous study and the fact that the study was conducted among patients with liver cirrhosis and the present study was among patients with Schistosoma portal hypertension in which the liver is rarely affected. A study conducted in Spain [9] concluded that platelets/spleen ratio would entail a risk of not diagnosing large varices in almost a quarter of patient with liver cirrhosis of different etiologies and in agreement with current result. Previous studies conducted among patients with Schistosomal chronic liver disease [10, 11] found that, platelets/spleen ratio predict large varices in spite of 25.3% may miss the necessary endoscopy in contradiction to the present findings. The differences in cut-off may explain the results. Manohar et al. [12] found that portal vein diameter is a predictor of large varices in agreement with the present observation. In the present study, ascites was not significantly associated with large esophageal varices, similar studies [13] showed that abundance of ascites predict large varices, in the current study we did not estimate if ascites is abundant or not. In the present study, sex and age were not predictor of large varices in similarity to Agha et al. [11] who found no association and in contradiction to a study conducted among black Africans in West Africa [14].

Our data revealed that, the degree of periportal fibrosis correlates well with the oesophageal varices grade. This result is similar to what has been obtained by Farid et al. [15]

In an attempt to relate the sonographic finding of hepatosplenic schistosomiasis to the clinical complication of disease, namely oesophageal varices *S. Mansoni* onongraphic (SMS) score was computed combing the degree of periportal fibrosis and the dilation of portal vein diameter.

The SMS score at the cut of point at 2 after applying the ROC curve shows high sensitivity for detecting LOV (95.1%) and high positive predictive value (90.6%). This result agrees with Rchter et al. [16].

Thrombocytopenia is the laboratory feature which is positively correlated with the grade of oesophageal varices and bleeding. Low platelet count can be explained by hypersplenism involved in the disease process. In the presence of portal hypertension, as much as 90% of the circulating thrombocytes are sequestered in the spleen, leading to a significant reduction in the circulating platelet count. In the current study after performing ROC curve for platelet and LOV, it seems that it is very good predictor (P=000). At cut off point of 121 it has sensitivity of 42% and specificity of (73.7%) and its positive predictive value in diagnosing LOV is (77%), which is similar to what was demonstrated by Mirghani et al.[17], and Zaman et al.[18].

5. Conclusions and Recommendations

Platelets count and ultrasound are simple, non-invasive measures for the prediction of large varices and hence variceal bleeding and may direct the need for endoscopy and prophylactic measures for portal hypertension. They will definitely reduce the need for endoscopy as screening tool and lower the medical expenditures. Larger multicenter studies assessing other non-invasive measures for the detection of large esophageal grades and bleeding are highly recommended.

References

[1] Lee Goldman, Dennis Ausiello, Chapter 376 – Schistosomiasis (Bilharziasis), 23 edition CECIL medicine , SAUNDERS ELSEVIER 2008.

[2] El Gadal AA. The Blue Nile Health Project: a comprehensive approach to the prevention and control of water associated diseases in irrigated schemes of the Sudan. Journal of Tropical Medicine and Hygiene.(1985); 88:57-63.

[3] Ahmed ES, Daffalla A, Christensen NO, Madsen H.. Pattern of infection and transsimision of Schistosoma haematobium in White Nile province. Ann Trop Med Parasitol. (1996); 90(2): 173-80.).

[4] Sherlock S, Dooly J. disease of the liver and biliary system, 11th edition ; chapter 29 , the liver in infection : (2002); pages 508-509.

[5] Viallet A, Marleau D, Huet M, Martin FA, Villeneuve JP, Lavoie P. Haemodynamic evaluation of patients with intrahepatic portal hypertension.. Relationship between variceal and portohepatic gradient. Gastroentrol (1995); 69: 1297 -1300.

[6] Rebouças G. Clinical aspects of hepatosplenic schistosomiasis: A contrast with cirrhosis. Yale J Biol Med. (1975); 48: 369–76.

[7] Homeida M, Abdelgader AF, Cheever AW, Bennet JI, Arbab BM, Ibrahim SZ, Nash TE. Diagnose of pathologically confirmed symmer periportal fibrosis by ultrasonography. AM J Trop Med Hyg (1988); 38(1): 86-91.

[8] Akande KO, Akere A, Otegbayo JA, Ola SO, Ousunmade D Accuracy of non-endoscopic predictors of oesophagealvarices in liver cirrhosis using platelet count, splenic size and portal vein diameter. Afr J Med Med Sci. (2016) ; 45(3): 243-251.

[9] Chiodi D, Hernández N, Saona G, Sánchez A, Berrueta J, Mescia G, Pollio C, Robaina G. [Noninvasive diagnosis of esophageal varices in cirrhotic patients]. Acta Gastroenterol Latinoam. (2014); 44(2):108-13. [Article in Spanish].

[10] Xu XD, Xu CF, Dai JJ, Qian JQ, Pin X. Ratio of platelet count/spleen diameter predicted the presence of esophageal varices in patients with schistosomiasis liver cirrhosis. Eur J Gastroenterol Hepatol. (2016); 28(5):588-91. doi: 10.1097/MEG.0000000000000584.

[11] Agha A, Abdulhadi MM, Marenco S, Bella A, Alsaudi D, El-Haddad A, Inferrera S, Savarino V, Giannini EG. Use of the platelet count/spleen diameter ratio for the noninvasive diagnosis of esophageal varices in patients with schistosomiasis. Saudi J Gastroenterol. (2011); 17(5):307-11. doi: 10.4103/1319-3767.84483.

[12] Manohar TP, Patil V, Salkar HR. Combination of non-endoscopic parameters as predictors of large esophageal varices. Trop Gastroenterol. (2014); 35(3): 173-9.

[13] Nada L, Samira el F, Bahija B, Adil I, Nourdine A Noninvasive predictors of presence and grade of esophageal varices in viral cirrhotic patients. Pan Afr Med J. (2015); 20:145. doi: 10.11604/pamj.2015.20.145.4320. eCollection 2015.

[14] Mahassadi AK, Bathaix FY, Assi C, Bangoura AD, Allah-Kouadio E, Kissi HY, Touré A, Doffou S, Konaté I, Attia AK, Camara MB, Ndri-Yoman TA. Usefulness of Noninvasive Predictors of OesophagealVarices in Black African Cirrhotic Patients in Côte d'Ivoire (West Africa). Gastroenterol Res Pract. (2012); 2012:216390. doi: 10.1155/2012/216390. Epub (2012).

[15] Farid M, Abdelwahab G, Thomas GS. Ultrasonographic prediction of oesophagealvarices in *Schistosomias ismansoni*. Am J Gastrol (1995); 88 (4): 560-563.

[16] Richter J, Correia AR, Vergetti JG. Sonographic prediction of variceal bleeding in patients with liver fibrosis due to *Schistosomaisis mansoni*. J Trop Med InteHealth (1998); 3(9): 728-735.

[17] Mirghani HO, Khamees H. Predictors of Bleeding of Esophageal Varices Among Patients with Portal Hypertension-Sudan. American Journal of Biomedical and Life Sciences (2016); 4(6): 103-106. doi: 10.11648/j.ajbls.20160406.14.

[18] Zaman, T. Becker, J. Lapidus, and K. Benner, "Risk factors for the presence of varices in cirrhotic patients without a history of variceal hemorrhage," Archives of Internal Medicine. (2001); 161 (21): 2564–2570.