Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: www.saspublishers.com

OPEN ACCESS

Medicine

Clinical Study of Non-Invasive Predictors of Esophageal varices in Chronic Liver Disease in a Teaching Hospital

Dr. Chaitanya Y[1*], Dr. P Veera Reddy[2]

[1]Assistant Professor, Department of General Medicine, Prathima Institute of Medical Sciences, Naganoor, Karimnagar Telangana India
[2]Consultant, Dr. PVR Multispeciality Hospital, Karimnagar India

DOI: 10.36347/sjams.2019.v07i07.050 | **Received:** 20.07.2019 | **Accepted:** 27.07.2019 | **Published:** 30.07.2019

***Corresponding author:** Dr. Chaitanya Y

Abstract **Original Research Article**

Portal hypertension commonly accompanies the presence of chronic liver disease, and the development of oesophageal varices is one of the major complications of portal hypertension. ***Aims:*** To study the ultrasonographic parameters, platelet counts and platelet count and spleen diameter ratio in prediction of severity of oesophageal varices in chronic liver disease. ***Methods:*** This cross-sectional observational study was done in the department of General Medicine, Prathima Institute of Medical Sciences Hospital, Naganoor, Karimnagar. A total of n=50 portal hypertensive patients were studied during the study period and n=50 normal age and sex-matched individuals were taken as controls. Exclusion criteria were Cases of portal hypertension who are on β blockers, Cases of portal hypertension who underwent EST or EVL. Cases of portal hypertension who underwent TIPS or shunt surgery. Routine biochemical investigations, liver function tests were done in every patient. Every recruited patient underwent Ultrasonography and Fiberoptic upper gastrointestinal endoscopy. Platelet count spleen diameter ratio was calculated. ***Results:*** Relationship of cases and controls based on *Child*-Turcotte-*Pugh Classification* for Severity of Cirrhosis score was calculated for all the patients with most of the patients with varices fall in group C and without varices in group B. Platelet count shows the highest sensitivity for the detection of oesophageal varices with 82.69% followed by platelet count/splenic diameter of 80.77%. Specificity is highest for splenic diameter and platelet count/splenic diameter. Platelet count/splenic diameter show the highest sensitivity of 88% and specificity is highest for splenic diameter with 69.23% for detection of large varices. ***Conclusion:*** Ultrasonography of abdomen is a simple, convenient and non-invasive method for assessing the severity of portal hypertension in patients and to predict the severity of esophagogastric varices indirectly.

Keywords: Non-Invasive Predictors, Esophageal Varices, Chronic Liver Disease.

INTRODUCTION

Chronic Liver Disease is a process of progressive destruction and regeneration of the liver parenchyma leading to fibrosis and cirrhosis [1]. Portal hypertension is the significant complicating feature of decompensated cirrhosis. It is responsible for the development of ascites and esophageal varices, which results in the development of collaterals to bypass the increased resistance to flow within the portal vein to the systemic circulation [2]. Portal hypertension is defined by a pathologic increase in portal pressure, in which the pressure gradient between the portal vein and inferior vena cava (the portal pressure gradient [PPG]) is increased above the upper normal limit of 5 mm Hg [3]. Portal hypertension becomes clinically significant when the PPG increases above the threshold value of 10 mm Hg (e.g., the formation of varices) or 12 mm Hg (e.g., variceal bleeding, ascites). PPG values between 6 and 10 mm Hg represent subclinical portal hypertension [4, 5]. Bleeding from ruptured esophageal or gastric varices is the main complication of portal hypertension and a major cause of death. Most cirrhotic patients develop esophageal varices, with a lifetime incidence as high as 90% [6]. As per existing guidelines in a case of cirrhosis of liver we are screening with upper gastrointestinal endoscopy to look for any esophagogastric varices present or not and grade the severity of varices. And then we start the prophylactic measures like propranolol to prevent the first bleed. A study was done by Brennan H. Spiegel *et al.* [7] concluded that empiric β blocker therapy for the primary prophylaxis of variceal hemorrhage is a cost-effective measure as the use of screening endoscopy to guide the therapy adds significant cost with an only

marginal increase ineffectiveness. If the severity of portal hypertension is predicted by a low cost and non-invasive method then one can use the upper gastrointestinal endoscopy for only high-risk patients. Although the occurrence of esophageal varices and the time of gastrointestinal bleeding in portal hypertension can't be exactly predicted, there are some endoscopic, ultrasonographic, laboratory parameters and clinical signs associated with a high risk of bleeding [8]. Some studies have shown a good correlation between ultrasonographic findings and platelet count and severity of esophagogastric varices. In the present study, an attempt is made to predict the oesophageal varices based on ultrasonographic findings, platelet count and platelet count spleen diameter ratio and its correlation with upper GI endoscopy.

MATERIAL AND METHODS

This cross-sectional observational study was done in the department of General Medicine, Prathima Institute of Medical Sciences Hospital, Naganoor, Karimnagar. Institutional Ethical committee permission was obtained for the study. Inclusion Criteria was Cases of portal hypertension admitted in the Department of General Medicine. A total of n=50 portal hypertensive patients were studied during the study period and n=50 normal age and sex-matched individuals were taken as controls. Exclusion criteria were Cases of portal hypertension who are on β blockers, Cases of portal hypertension who underwent EST or EVL. Cases of portal hypertension who underwent TIPS or shunt surgery. Hepatocellular carcinoma, Primary hematological disorders, active gastrointestinal bleeding on admission. A detailed clinical history was recorded regarding age, sex, duration of symptoms like jaundice, distension of abdomen, hematemesis, and Malena. All patients underwent complete clinical examination including a detailed examination of the gastrointestinal system. Routine biochemical investigations, liver function tests were done in every patient. Every recruited patient underwent Ultrasonography and Fiberoptic upper gastrointestinal endoscopy. Platelet count spleen diameter ratio was calculated. All variables which were found to be significant on univariate analyses were included as candidate variables for logistic regression analysis to identify independent predictors for the presence of esophageal varices and their size. Sensitivity, Specificity, Positive predictive value and negative predictive values were calculated for these parameters.

RESULTS

The age distribution (shown in table 1) median age among 50 cases was 43.18 years (range 24-86), and among 50 controls was 42.16 years (range 22-68), for large varices it is 44.46 years (range 29-86) and for small varices is 41.79 years (range 24-65). Out of 100 patients, 81 were males and 19 were females. Among cases 39 were males and 11 were females (no. of males/females in large varices is 20/6 and Small Varices is 19/5) and in controls 42 were males and 8 were females.

Table-1: Age distribution among cases and control

Age	Cases	Large Varices	Small Varices	Controls
20-30	6	3	3	10
31-40	24	12	12	15
41-50	12	6	6	14
51-60	4	3	1	07
61-70	3	1	2	04
>70	1	1	0	00
Total	50	26	24	50

Distribution of patients based on etiology: Alcoholic liver disease is the most common etiology in this study corresponding to 62 % of cases followed by hepatitis B with 10%.

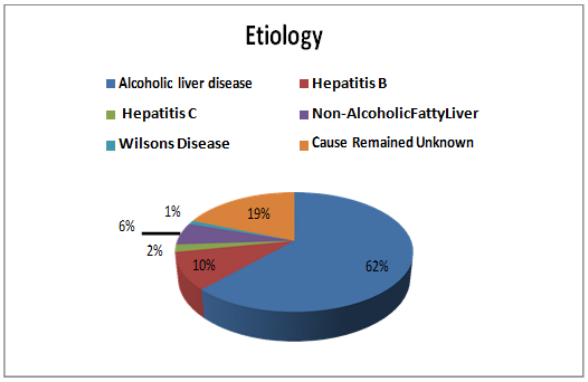

Fig-1: Pie diagram showing various etiologies among cases and controls

Relationship of cases and controls based on *Child*-Turcotte-*Pugh Classification* for Severity of Cirrhosis score was calculated for all the patients with most of the patients with varices fall in group C and without varices in group B.

Table-2: Distribution of cases and controls according to Child-Pugh score

Column1	Class A	Class B	Class C	total
Cases	4	18	28	50
Controls	7	23	20	50
Total	11	41	48	100
Large	3	10	13	26
Small	1	8	15	24
Total	4	18	28	50

On univariate analysis portal vein diameter, spleen diameter, platelet count and platelet count and spleen diameter ratio were found to be significantly associated with the presence of varices. On multivariate analysis the presence of esophageal varices was significantly associated with platelet count < 102,000/ µl (OR 6.65; 95% CI, 2.51- 17.6), spleen diameter > 154 mm (OR 5.78; 95% CI, 2.4-13.94), portal vein diameter > 13 mm (OR 2.49; 95% CI, 1.1-5.62) and platelet count /spleen diameter <815 (OR 10.92 ;95% CI 4.07-29.26).

Table-3: Relationship of various parameters with the presence or absence of esophageal varices on univariate analysis

VARIABLES	CASES	CONTROLS	P-VALUE
sex (M/F)	39/11	42/8	0.4444
Ascites	47(51.6%)	44(48.4%)	0.7532
Hepatic Encephaolpathy	6(66.7%)	3(33.3%)	0.3173
Total Bilirubin(Mg/Dl)	2.9(0.4-25.1)	2.3(0.3-26.9)	0.6027
Serum Albumin(Gm/Dl)	2.7(1.4-4.5)	2.8(1.6-4.2)	0.0692
Prothrombin Time(Sec)	17.7(11.6-38.5)	15.2(10.6-30)	0.0187*
Child Pugh Score			
Class A	4(36.4%)	7(63.6%)	0.2541
Class B	18(43.9%)	23(56.10%)	
Class C	28(58.33%)	20(41.67%)	
Platelet Count(/µl)	98000(45000-380000)	169000(78000-266000)	<0.0001*
Liver Size(Cm)	12.3(6.8-18)	12.5(8.9-18)	0.6391
Portal Vein Diameter(Mm)	13.9(8.0-18.0)	12.1(7.8-16)	0.0322
Spleen Diameter(Cm)	16.0(8.0-26)	13.8(9.0-19.6)	<0.0001*
Platelet Count /Spleen Diameter	608(264-2750)	1277(632-2611)	<0.0001*

***** Significant

On univariate analysis portal vein diameter, spleen diameter, platelet count and platelet count and spleen diameter were found to be significantly associated with the presence of large varices. On multivariate analysis the presence of large esophageal varices was significantly associated with platelet count < 93500/ µl (OR 4.8; 95% CI, 1.42-16.18), spleen diameter > 162 mm (OR 1.94; 95% CI 0.62-6.02), portal vein diameter > 14.4mm (OR 3.5;95% CI 1.05-11.66) and platelet count /spleen diameter <548 (OR 9.4;95% CI 2.46-36.19).

Platelet count shows the highest sensitivity for the detection of oesophageal varices with 82.69% followed by platelet count/splenic diameter of 80.77%. Specificity is highest for splenic diameter and platelet count/splenic diameter. Platelet count/splenic diameter show the highest sensitivity of 88% and specificity is highest for splenic diameter with 69.23% for detection of large varices.

Table-4: Relationship of various parameters with the presence or absence of esophageal varices on univariate analysis

Variables	Large Varices	Small Varices	P-VALUE
Sex (M/F)	20/6	19/5	0.8728
Ascites	25(53.2%)	22(46.8%)	0.6617
Hepatic Encephalopathy	3(50%)	3(50%)	1
Total Bilirubin(Mg/Dl)	2.5(0.4-25.1)	5.3(0.5-21.1)	0.1932
Serum Albumin(Gm/Dl)	2.6(1.4-3.6)	2.9(1.8-4.5)	0.1111
Prothrombin Time(Sec)	16.1(11.6-32)	19.2(12-38.5)	0.1065
Child Pugh Score			
Class A	3(75%)	1(25%)	0.6348
Class B	10(55.5%)	8(44.5%)	
Class C	13(46.5%)	15(53.5%)	
Platelet Count(/µl)	80500(45000-380000)	130500(46000-253000)	0.0021
Liver Size(Cm)	12.7(6.8-18)	11.4(7.5-16.2)	0.1132
Portal Vein Diameter(Mm)	14.7(8.5-16.8)	12.4(8-18)	0.0201
Spleen Diameter(Cm)	17.2(8-26)	14.3(8-22)	0.0021
Platelet Count /Spleen Diameter	445(279-1727)	910(264-2750)	0.0003

Table-5: Sensitivity, Specificity, Positive and Negative predictive values for significant parameters for presence of varices

Parameters for Presence of Varices				
Parameters	**Sensitivity**	**Specificity**	**Positive Predictive Value**	**Negative Predictive Value**
Portal Vein Diameter (>13.05mm)	65%	54%	55.58%	45.26%
Spleen Diameter(>15.4cm)	78.80%	64%	56.06%	44.63%
Platelet Count(<102000)	82.69%	58%	59.68%	41.03%
Platelet Count /Splenic Diameter (<815)	80.77%	64%	56.67%	44.01%
Parameters for the presence of Large Varices				
Portal Vein Diameter(>14.4mm)	79.17%	53.85%	60.43%	40.32%
Spleen Diameter(>16.25cm)	75%	69.23%	52.84%	47.85%
Platelet Count (<93500)	75%	65.38%	54.29%	46.42%
Platelet Count /Spleen Diameter (<548)	88%	65%	58.36%	42.28%

DISCUSSION

Cirrhosis is the most advanced form of liver disease and variceal hemorrhage is one of its lethal complications. Because cirrhotic patients with large esophageal varices are at high risk for bleeding, preventive efforts have concentrated on identifying cirrhotic patients with large varices [9]. Bleeding occurs in an insignificant proportion of patients with severe PHG which accounts for most non-variceal bleeding episodes in patients with cirrhosis and portal hypertension. PHG bleeding is a serious complication, which is usually chronic and insidious but occasionally massive and life-threatening [10]. Overt hemorrhage from the gastric mucosa occurred in 60% of patients with severe PHG with a cumulative risk of bleeding of 75% over a 5 year follow up period [11]. Several studies in the past have shown independent parameters like splenomegaly [12-14], ascites [12, 15], spider naevi [16], *Child*-Turcotte-*Pugh* grade [17], platelet count, prothrombin time/activity, portal vein diameter, platelet count/spleen diameter ratio [18], serum albumin [19], and serum bilirubin [20] as significant predictors for the presence of esophageal varices. Our study found that 50% of the cirrhotic patients had EV diagnosed by endoscopy. This result is similar to the range of 24% to 80% showed in literature [21] and reminds us that a significant part of cirrhotic patients is unnecessarily submitted to this procedure [22]. Fook-Hong NG et al; showed that Low platelet count and presence of ascites were the significant independent predictors for high-grade EGV [19]. In the present study ascites and hepatic encephalopathy were not significantly associated with the presence of varices. Similar results were obtained by Jijo V Cherian et al; in predicting oesophageal varices. Gennaro D'Amico *et al.* also showed that a serum albumin concentration of < 3.3 g/dL were predictors of oesophageal varices [21]. In a cross-sectional study done by Schepis F *et al.* has shown that prothrombin activity of 70% was used as an

independent predictor of oesophageal varices with odds of 9.85 [23]. In our study, we did not get significance for serum albumin and prothrombin activity in the prediction of oesophageal varices. Similar results were obtained by Jijo V Cherian *et al*. where no significance was obtained for the above parameters. No studies in the past have shown that total bilirubin as a predictor of oesophageal varices. The present study also did not show any statistical significance for the prediction of oesophageal varices based on total bilirubin levels. In our study child-pugh score was not significantly associated with the presence of oesophageal varices but most of the cases belong to class C and controls (no oesophageal varices) belong to class B. The study done by Jijo *et al.* shows significance and has a highest sensitivity of 95% for child-pugh class B and C in predicting oesophageal varices and postulated an algorithm where patients with child-pugh class B and C were given primary prophylaxis and for class A they have seen platelet count and spleen diameter and then initiated prophylaxis accordingly [24]. Pathogenesis of thrombocytopenia includes productive, consumptive or distributional mechanisms [25]. It is commonly believed to be due to pooling and destruction of platelets in the spleen which may be mediated by platelet-associated IgG. Reduced levels of thrombopoietin either due to impaired production or rapid degradation may also add to thrombocytopenia. Thomopoulos *et al*. [26] (184 patients) reported a low platelet count to be an independent risk factor for the presence of varices. Mohammad Khuram *et al.* [27] (200 patients) found OV in 146 with 121 having thrombocytopenia (94.5%). Present study shows that platelet count of <10200/mm^3 is 82.69 % sensitive and 58% specific predictor of OV with positive predictive value of 59.63 % and negative predictive value of 41.03 % in predicting presence of varices and a platelet count of 93500/mm^3 is 75% sensitive, 65.38% specific with 54.29 and 46.42 positive and negative predictive values respectively in predicting large varices. Similar results were obtained in a study done by Jijo.V.Cherian *et al*. with a platelet count of 90000/mm^3 with 59.3% sensitivity, 64.2 % specificity, and 47.5 PPV and 74.2 is NPV. Chalasani *et al*. [28] (346 patients) found that a platelet count < 88,000 was an independent risk factor for the presence of large varices. In our study, as the portal vein diameter and spleen size increased, gastro-oesophageal varices also transformed into higher grades. Median portal vein diameter and spleen size with the range in higher grade varices were 14.7 mm (8.5-16.8mm) and cm (8-26cm) respectively. In the present study, on univariate analysis, a platelet count-spleen diameter ratio of 608 was significantly associated with the presence of esophageal varices and it was found significant even in multivariate analysis with odds of 10.92 (CI-4.07-29.26).

CONCLUSION

Ultrasonography of the abdomen is a simple, convenient and non-invasive method for assessing the severity of portal hypertension in patients and to predict the severity of esophagogastric varices indirectly.

Patients having

- portal vein diameter >13.9mm,
- spleen size >16cm and
- platelet count of<98000/microL
- platelet count and spleen diameter ratio < 608

were found to have varices which were indirect evidence of the severity of portal hypertension. The above-said parameters tend to predict varices when they occur in combination than they occur individually. These predictors may be of help

- To the physicians practicing in rural areas where endoscopy facilities are not readily available, in helping them to initiate appropriate primary pharmacological prophylaxis in these patients.
- In an urban setting where the endoscopy workload is high, a noninvasive predictor, as in this study, can help one to initiate drug therapy while waiting for the endoscopy procedure.

REFERENCES

1. Jiang D. Care of chronic liver disease Prim Care. 2011 Sep; 38(3):483-98.
2. De Francis, Primignani M. Natural history of portal hypertension in patients with cirrhosis. Clin liver dis. 2001; 5:645-63.
3. Ashish Kumar, Praveen Sharma, Shiv Kumar Sarin. Hepatic venous pressure gradient measurement: Time to learn! Indian J Gastroenterol. 2008 Mar-Apr; 27: 74-80.
4. Garcia-Tsao G, Groszmann RJ, Fisher RL, Conn HO, Atterbury CE, Glickman M. Portal pressure, presence of gastroesophageal varices and variceal bleeding. Hepatology. 1985 May;5(3):419-24.
5. Viallet A, Marleau D, Huet M, Martin F, Farley A, Villeneuve JP, Lavoie P. Hemodynamic evaluation of patients with intrahepatic portal hypertension. Relationship between bleeding varices and the portohepatic gradient. Gastroenterology. 1975 Dec;69(6):1297-300.
6. Chang YW. Indication of treatment for esophageal varices: who and when?. Digestive Endoscopy. 2006 Jan;18(1):10-5.
7. Spiegel BM, Targownik L, Dulai GS, Karsan HA, Gralnek IM. Endoscopic screening for esophageal varices in cirrhosis: is it ever cost effective?. Hepatology. 2003 Feb;37(2):366-77.
8. Abby Philips C, Sahney A. Oesophageal and gastric varices: historical aspects, classification and grading: everything in one place. Gastroenterology report. 2016 Jun 19;4(3):186-95.
9. Boyer T. Natural history of portal hypertension. In: LaBreque D, ed. Clinics in liver diseases-Portal hypertension. Philadelphia: WB Saunder;

1997;1: 31-44.
10. Bosch J, Abraldes JG, Groszmann R. Current management of portal hypertension. Journal of hepatology. 2003 Jan 1;38(Suppl. 1):S54-68.
11. Perez-Ayuso RM, Pique JM, Bosch J, Quintero E, Valderrama R, Bordas JM, Rodés J, Panés J, Viver J, Gonzalez A, Esteban R. Propranolol in prevention of recurrent bleeding from severe portal hypertensive gastropathy in cirrhosis. The Lancet. 1991 Jun 15;337(8755):1431-4.
12. Thomopoulos KC, Labropoulou-Karatza C, Mimidis KP, Katsakoulis EC, Iconomou G, Nikolopoulou VN. Non-invasive predictors of the presence of large oesophageal varices in patients with cirrhosis. Digestive and liver disease. 2003 Jul 1;35(7):473-8.
13. Chalasani N, Imperiale TF, Ismail A, Sood G, Carey M, Wilcox CM, Madichetty H, Kwo PY, Boyer TD. Predictors of large esophageal varices in patients with cirrhosis. The American journal of gastroenterology. 1999 Nov 1;94(11):3285-91.
14. Sharma SK, Aggarwal R. Prediction of large esophageal varices in patients with cirrhosis of the liver using clinical, laboratory and imaging parameters. Journal of gastroenterology and hepatology. 2007 Nov;22(11):1909-15.
15. Sarwar S, Khan AA, Alam A, Butt AK, Shafqat F, Malik K, Ahmad I, Niazi AK. Non-endoscopic prediction of presence of esophageal varices in cirrhosis. Journal of the College of Physicians and Surgeons--Pakistan: JCPSP. 2005 Sep;15(9):528-31.
16. Pilette C, Oberti F, Aubé C, Rousselet MC, Bedossa P, Gallois Y, Rifflet H, Calès P. Non-invasive diagnosis of esophageal varices in chronic liver diseases. Journal of hepatology. 1999 Nov 1;31(5):867-73.
17. Zaman A, Becker T, Lapidus J, Benner K. Risk factors for the presence of varices in cirrhotic patients without a history of variceal hemorrhage. Archives of internal medicine. 2001 Nov 26;161(21):2564-70.
18. Madhotra R, Mulcahy HE, Willner I, Reuben A. Prediction of esophageal varices in patients with cirrhosis. Journal of clinical gastroenterology. 2002 Jan 1;34(1):81-5.
19. Ng FH, Wong SY, Loo CK, Lam KM, Lai CW, Cheng CS. Prediction of oesophagogastric varices in patients with liver cirrhosis. Journal of gastroenterology and hepatology. 1999 Aug;14(8):785-90.
20. Bressler B, Pinto R, El-Ashry D, Heathcote EJ. Which patients with primary biliary cirrhosis or primary sclerosing cholangitis should undergo endoscopic screening for oesophageal varices detection?. Gut. 2005 Mar 1;54(3):407-10.
21. D'amico G, Pagliaro L, Bosch J. The treatment of portal hypertension: a meta-analytic review. Hepatology. 1995 Jul;22(1):332-54.
22. De Franchis R, Dell'Era A. Diagnosis and therapy of esophageal vascular disorders. Current opinion in gastroenterology. 2007 Jul 1;23(4):422-7.
23. Schepis F, Cammà C, Niceforo D, Magnano A, Pallio S, Cinquegrani M, D'Amico G, Pasta L, Craxì A, Saitta A, Raimondo G. Which patients with cirrhosis should undergo endoscopic screening for esophageal varices detection?. Hepatology. 2001 Feb 1;33(2):333-8.
24. Cherian JV, Deepak N, Ponnusamy RP, Somasundaram A, Jayanthi V. Non-invasive predictors of esophageal varices. Saudi journal of gastroenterology: official journal of the Saudi Gastroenterology Association. 2011 Jan;17(1):64.
25. Wittels EG, Siegel RD, Mazu EM. Thrombocytopenia in the Intensive Care Unit Setting. J Int Care Med. 1990;5:224–40.
26. Thomopoulos KC, Labropoulou-Karatza C, Mimidis KP, Katsakoulis EC, Iconomou G, Nikolopoulou VN. Non-invasive predictors of the presence of large oesophageal varices in patients with cirrhosis. Digestive and liver disease. 2003 Jul 1;35(7):473-8.
27. Khuram M, Khan NY, Arif M, Irshad MM, Hammatul Bushra K, Hassan Z. Association of platelet count to splenic index ratio with presence of esophageal varices in patients with hepatitis C virus-related compensated cirrhosis. Pak J Gastroenterol. 2006; 20:37–42.