Original Research Paper

Volume - 11 | Issue - 08 | August - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

General Medicine

"A STUDY OF NON INVASIVE MARKERS OF ESOPHAGEAL VARICES IN PATIENTS OF LIVER CIRRHOSIS"

Dr.D. Surya Kala Assistant Professor Of General Medicine, GMC & GGH Kadapa

Dr. J. Aparna* Assistant Professor Of General Medicine, GMC & GGH Kadapa. *Corresponding Author

ABSTRACT **INTRODUCTION:** Esophageal variceal bleeding is a life threatening complication of esophageal varices in patients with cirrhosis of liver. Subjecting all patients to screening endoscopy may not be cost effective and feasible in India. The present study has been undertaken to determine the appropriateness of the various clinical, biochemical and imaging parameters in predicting the existence of esophageal varices in cirrhosis of the liver. **METHODOLOGY:** This is a prospective, observational study on patients admitted in GGH, for a period of 1 year. In present study, 100 patients with cirrhosis of liver, fulfilling inclusion and exclusion criteria were included. Of which, 90 are male, alcohol(75%) is most common etiology, most common presentation ascites(74%), Varices are seen in 77% of patients, 91% patients in CTP group B &C. Presence of ascites and spleenomegaly are significantly associated with presence of varices. Biochemical parameters like platelet count, radiological parameters like splenic vein diameter, spleen size and ratio of Platelet count with spleen span are identified as independent predictors of esophageal varices. **CONCLUSION:** Presence of ascites, low platelet count, CTP group B & C, spleen span, platelet count to spleen span ratio can be used as predictors of presence of esophageal varices. Hence these parameters can be used as non invasive markers for presence of esophageal varices.

KEYWORDS : Liver Cirrhosis, Esophageal varices, Non invasive markers, Platelet count to spleen span ratio.

INTRODUCTION:

Esophageal varices are a major complication of portal hypertension in patients of cirrhosis. Esophageal variceal bleeding is a life threatening complication of esophageal varices. In patients with cirrhosis, the prevalence of varices is about 60- 80% and the lifetime risk of bleeding is 25-35%. They appear only after the hepatic venous pressure gradient (HVPG) has increased to at least 10 to 12 mmHg.[1, 2] The incidence of esophageal varices increases by nearly 5% per year, and the rate of progression from small to large varices is approximately 5 to 10 % per year [3]. Increasing size of varices is associated with an increase in variceal-wall tension to a critical level at which varices rupture and cause life-threatening bleeding.

Incidence of first variceal hemorrhage ranges from 20 to 40% within two years. Recurrent bleeding occurs in 30 to 40% of patients within the next two to three days and in up to 60% within one week. The mortality rate from variceal bleeding is about 20% when patients are treated optimally in hospital [4]. However, an appreciable proportion of patients with variceal bleeding die before reaching the hospital.[5] Thus, the true mortality rate from bleeding varices is considerably higher than relatively optimistic estimates based on hospitalized patients. Thus, prevention of esophageal variceal bleeding remains at the forefront of long-term management of cirrhotic patients. Two analyses of cost effectiveness[6, 7] suggested that the strategy of treating all cirrhotic patients without a history of bleeding with nonselective β-blockers, irrespective of the presence or size of varices is more cost-effective than the strategy of treating only patients with endoscopically proven risk-varices with β-blockers or banding ligation. However, third analysis, confirmed that this strategy is most cost-effective only for patients who have decompensated disease; for patients who have compensated disease screening and treating only those with large varices is more cost-effective.[8]

Because nonselective β-blockers and banding ligation prevent bleeding in more than half of patients with medium or large varices,[9, 10] the American Association for the Study of Liver Disease and the Baveno IV Consensus Conference on portal hypertension recommended that all cirrhotic patients should be screened for the presence of esophageal varices when liver cirrhosis is diagnosed.[11] It has been suggested that all patients should undergo endoscopic screening for varices at the time that cirrhosis is diagnosed, and every 2 to 3 years thereafter in those with compensated disease and no varices; the recommended time intervals between endoscopies for those with small varices was 1 to 2 years,[12] and 1 year for those with decompensated disease, with or without varices.[13] However, subjecting all patients with cirrhosis to screening endoscopy may not be cost effective and feasible in countries like India and it is a time consuming procedure. Furthermore, these recommendations imply a considerable burden of endoscopies and related costs; they require that patients repeatedly undergo an unpleasant procedure, even though up to 50% of them may still not have developed esophageal varices 10 years after the diagnosis of cirrhosis.[14] Therefore, these guidelines might not be ideal for clinical practice. A more affordable approach for screening would be possible if patients at low or high risk of having esophageal varices could be identified from easily obtainable clinical variables.

Investigators have attempted to identify characteristics that noninvasively predict the presence of varices. These studies have shown that biochemical, clinical and ultrasonographic parameters alone or together have good predictive power for noninvasively assessing the presence of esophageal varices.[16 -18] Overall, the most common result of these studies is that parameters such as splenomegaly, thrombocytopenia, Child Pugh score, ascites, portal flow patterns, and platelet count- splenic size ratio are predictors of esophageal varices.

Therefore, the present study has been undertaken to determine the appropriateness of the various clinical, biochemical and imaging parameters in predicting the existence of esophageal varices in cirrhosis of the liver.

AIMS AND OBJECTIVES

- To study the non invasive markers of esophageal varices in patients of cirrhosis like hemoglobin level, platelet count, prothrombin time, serum bilirubin, albumin, spleen size(clinical as well as ultrasound), splenic vein diameter, portal vein diameter and platelet count to splenic span ratio.
- To evaluate the usefulness of the above non invasive markers.
- To compare these markers with upper GI scopy for presence or absence of varices.

MATERIALS AND METHODS

Source of data: This study is conducted in Department of General Medicine, Government general hospital, over a period of 1 year.
Study population: Patients with liver cirrhosis were included in the study.

Study design: Prospective observational study

Sample size: 100

INCLUSION CRITERIA

a. Age >13yrs
b. Patients of liver cirrhosis with or without prior haematemesis at GGH, Kurnool will be included in the study.(Diagnosis of cirrhosis was based on clinical, biochemical and ultrasonographic findings)

EXCLUSION CRITERIA

a. Patients age <13yrs. All patients with platelet disorders like ITP, Dengue fever etc
b. Other causes of Spleenomegaly like malaria, hematological disorders, non cirrhotic portal hypertension, EHPVO etc.

c. Patients on treatment with beta blockers.
d. Patients with evidence of hepatocellular carcinoma on ultrasound.
e. Patients who have received endoscopic or surgical intervention for portal hypertension previously.

Methodology: Informed consent is taken. Each patient was subjected to detailed clinical history, clinical examination and investigations as mentioned in the proforma. Platelet count to spleen span ratio was calculated for each patient. Hepatic encephalopathy was graded from grade 0 to IV, as per the Conn's grading. For each patient, Child-Turcotte-Pugh score was calculated. Ascites was graded as none, mild (detectable only on ultrasound), moderate (visible moderate symmetrical abdominal distension) or severe (marked abdominal distension)

STATISTICS:

Data analysis done by using SPSS (Statistical package for social sciences) 19.0. Qualitative data variables expressed by using frequencies and percentage (%) Quantitative Data variables expressed by using descriptive statistics (Range, Mean, SD, Median) P-value < 0.05 considered as significant.

OBSERVATION & RESULTS

There were 90 male and 10 female patients out of 100population, which turn around to be 90% male and 10% female of study population

Table 1: Age wise distribution of patients

Age group	No of patients	Percentage (%)
≤ 30	3	3
31 - 40	15	15
41 - 50	30	30
51 - 60	32	32
61 - 70	15	15
> 70	5	5
Total	100	100.0

Table 2: Etiology wise distribution of patients

Etiology	No of patients	Percentage (%)
ALD	75	75
Cryptogenic	9	8
HBsAg	3	3
HCV	5	5
NASH	8	9
Total	100	100

Table 3: Distribution of patients according to signs.

Signs	No of patients	Percentage (%)
Pedal edema	70	70
Jaundice	71	71
Ascites	74	74
Palpable spleen	52	52

Table 4: Distribution of patients with respect to CTP group

CTP	No of patients	Percentage (%)
A	9	9
B	39	39
C	52	52
Total	100	100

Table 5: Distribution of patients according to grades of esophageal varices.

Esophageal Varices Grades	Number of patients	Percentage (%)
Grade 1	35	35
Grade 2	32	32
Grade 3	10	10
No Varices	23	23
Total	100	100

Table 6: Distribution of patients according to Laboratory parameters with presence of esophageal varices

Laboratory Parameters		Esophageal Varices		Total	P-Value
		Present	Absent		
Haemoglobin	Normal	3	5	8	0.0149*
	Abnormal	74	18	92	
WBC	Normal	45	17	62	0.179795
	Abnormal	32	6	38	
Platelet	Normal	14	13	27	0.000279*
	Abnormal	63	10	73	
Bilirubin	Normal	13	9	22	0.053815
	Abnormal	64	14	78	
SGOT	Normal	9	1	10	0.4464
	Abnormal	68	22	90	
SGPT	Normal	10	1	11	0.4487
	Abnormal	67	22	89	
Albumin	Normal	3	2	5	0.3241
	Abnormal	74	21	95	
Prothombin time	Normal	4	3	7	0.1968
	Abnormal	73	20	93	

Table 7: Distribution of patients according to CTP group for presence of esophageal varices

CTP group	Esophageal Varices		Total	P-Value
	Present	Absent		
A	4	5	9	0.042054*
B	30	9	39	
C	43	9	52	
Total	77	23	100	

Table 8: Distribution of patients according to palpable spleen and ascites with presence of esophageal varices.

Clinical Features		Esophageal varices		Total	P-Value
		Present	Absent		
Ascites	Present	64	10	74	0.000143*
	Absent	13	13	26	
Palpable Spleen	Present	44	8	52	0.009634*
	Absent	33	15	48	

DISCUSSION

Table 9: Comparison of number of cases, Median age, etiologies studied in various studies

Study	Male	Female	Median age group	Alcohol	NASH	HBsAG	HCV	Others
Cherian et al[19]	141	88	42 yrs	97	10	35	23	64
Sarangapani et al[20]	72	44	43.3yrs	62	-	23	-	21
My study	90	10	52yrs	75	8	3	5	9

Table 10: Comparison of patients of CTP group A,B,C between my study and other studies

	CTP A	CTP B	CTP C	Total
Cherian et al[19]	42	127	60	229
My study	9	39	52	100

Table 11 : Comparision between number of case with and without esophageal varices, platelet cutoff in various studies

Study	Esophageal varices		PLATELET COUNT CUTOFF
	Present	< 100,000/µl	Absent
Cherian et al[19]	178	< 150000/µl	51
Sarangapani et al[20]	77	< 12,5000/µl	29
My study	77		23

Study done by Cherian et al [19] showed that spleen diameter >160 mm was significantly associated with the presence of esophageal varices. Studies done by Cherian et al[(19)] and Sarangapani et al[(20)] showed that portal vein diameter > 13 mm was significantly associated with the presence of esophageal varices. Study by Zoli et al[(21)] suggested that splenic vein dimeter > 10 mm was 56% sensitive at specificity of 100% for presence of esohageal varices. Study done by Cherian et al[(19)] where on univariate analysis platelet count /spleen diameter ratio was significantly associated with the presence of esophageal varices. Giannini et al. study of 145 patients with cirrhosis found that the negative predictive value of platelet count/spleen diameter ratio was 100%. Agha A *et al*. studied 114 patients with compensated HCV related cirrhotics, 909 cut-off showed negative predictive value 100% and a positive predictive value of 93.8% for the diagnosis of EV. Baig *et al*. reported a cut-off value of 1014, which gave positive and negative predictive values of 95.4% and 95.1%, respectively.

CONCLUSIONS:

The present study was done in 100 patients of liver cirrhosis to study the noninvasive markers of esophageal varices. Attempt was made to predict the presence or absence of eosphageal varices , furthermore size (severity) of esophageal varices was predicted as large or small by various laboratory, clinical and ultrasonographical features.

1. Among the laboratory parameters low haemoglobin, low platelet count were significantly associated with presence of esophageal varices, along with them increased bilirubin, prolonged prothrombin time were associated with presence of large esophageal varices.
2. There was no association of WBC,SGPT,SGOT and albumin levels with presence of esophageal varices.
3. There is significant association between presence of ascites and palpable spleen with presence of esophagaeal varices.
4. CTP group B and C were associated with presence of esophageal varices.
5. The USG parameters like decreased liver span, increased spleen span, dilated portal vein and splenic vein diameter were significantly associated with both presence and severity of esophageal varices.

Platelet count to Spleen span ratio (PC/SS) was significantly associated with both presence and severity of esophageal varices and cut off of $\leq$ 1068 had better sensitivity, specificity and positive predictive value for presence of esophageal varices

REFERENCES

1. 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- Jun;5(3):419-24. PubMed PMID: 3873388.
2. Casado M, Bosch J, Garcia-Pagan JC, Bru C, Banares R, Bandi JC, et al. Clinical events after transjugular intrahepatic portosystemic shunt: correlation with hemodynamic findings. Gastroenterology. 1998 Jun;114(6):1296-303. PubMed PMID: 9609767.
3. D'Amico G, Morabito A. Noninvasive markers of esophageal varices: another round, not the last. Hepatology. 2004 Jan;39(1):30-4. PubMed PMID: 14752818.
4. D'Amico G, De Franchis R, Cooperative Study G. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. Hepatology. 2003 Sep;38(3):599-612. PubMed PMID: 12939586.
5. Nidegger D, Ragot S, Berthelemy P, Masliah C, Pilette C, Martin T, et al. Cirrhosis and bleeding: the need for very early management. Journal of hepatology. 2003 Oct;39(4):509-14. PubMed PMID: 12971959.
6. Saab S, DeRosa V, Nieto J, Durazo F, Han S, Roth B. Costs and clinical outcomes of primary prophylaxis of variceal bleeding in patients with hepatic cirrhosis: a decision analytic model. The American journal of gastroenterology. 2003 Apr;98(4):763-70. PubMed PMID: 12738453.
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. PubMed PMID: 12540787.
8. Arguedas MR, Heudebert GR, Eloubeidi MA, Abrams GA, Fallon MB. Cost-effectiveness of screening, surveillance, and primary prophylaxis strategies for esophageal varices. The American journal of gastroenterology. 2002 Sep;97(9):2441-52. PubMed PMID: 12358270.
9. D'Amico G, Pagliaro L, Bosch J. Pharmacological treatment of portal hypertension: an evidence-based approach. Seminars in liver disease. 1999;19(4):475-505. PubMed PMID: 10643630.
10. Imperiale TF, Chalasani N. A meta-analysis of endoscopic variceal ligation for primary prophylaxis of esophageal variceal bleeding. Hepatology. 2001 Apr;33(4):802-7. PubMed PMID: 11283842.
11. Grace ND. Diagnosis and treatment of gastrointestinal bleeding secondary to portal hypertension. American College of Gastroenterology Practice Parameters Committee. The American journal of gastroenterology. 1997 Jul;92(7):1081-91. PubMed PMID: 9219775
12. D'Amico G, Garcia-Tsao G, Cales P, Escorsell A, Nevens F, Cestari R, et al., editors. Diagnosis of portal hypertension: how and when. de Franchis R Portal Hypertension III Proceedings of the Third Baveno International Consensus Workshop on Definitions, Methodology and Therapeutic Strategies Oxford, UK: Blackwell Science; 2001.
13. Grace ND, Groszmann RJ, Garcia-Tsao G, Burroughs AK, Pagliaro L, Makuch RW, et al. Portal hypertension and variceal bleeding: an AASLD single topic symposium. Hepatology. 1998 Sep;28(3):868-80. PubMed PMID: 9731585.
14. D'Amico G, Pasta L, Madonia S, Tarantino IG, Mancuso A, Malizia G, et al. The incidence of esophageal varices in cirrhosis. Gastroenterology. 2001;120(5):A2.
15. Arguedas MR, McGuire BM, Fallon MB, Abrams GA. The use of screening and preventive therapies for gastroesophageal varices in patients referred for evaluation of orthotopic liver transplantation. The American journal of gastroenterology. 2001 Mar;96(3):833- 7. PubMed PMID: 11280560.
16. Paquet KJ. Prophylactic endoscopic sclerosing treatment of the esophageal wall in varices -- a prospective controlled randomized trial. Endoscopy. 1982 Jan;14(1):4-5. PubMed PMID: 7035153.
17. Wittels EG, Siegel RD, Mazur EM. Thrombocytopenia in the intensive care unit setting. Journal of Intensive Care Medicine. 1990;5(5):224-40.
18. Thabut D, Ratziu V, Trabut JB, Poynard T. Prediction of oesophageal varices with platelet count/spleen diameter ratio or platelets alone. Gut. 2004 Jun;53(6):913-4; author reply 4-5. PubMed PMID: 15138224. Pubmed Central PMCID: 1774084.
19. 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-Feb;17(1):64-8. PubMed PMID: 21196656. Pubmed Central PMCID: 3099085.
20. Sarangapani A, Shanmugam C, Kalyanasundaram M, Rangachari B, Thangavelu P, Subbarayan JK. Noninvasive prediction of large esophageal varices in chronic liver disease patients. Saudi journal of gastroenterology : official journal of the Saudi Gastroenterology Association. 2010 Jan-Mar;16(1):38-42. PubMed PMID: 20065573. Pubmed Central PMCID: 3023101.
21. Zoli M, Dondi C, Marchesini G, Cordiani M, Melli A, Pisi E. Splanchnic vein measurements in patients with liver cirrhosis: a case-control study. Journal of Ultrasound in Medicine. 1985;4(12):641-6.