ISSN: 0975-3583,0976-2833 VOL14, ISSUE 12, 2023

ORIGINAL RESEARCH

Non-Endoscopic Predictors of Esophageal Varices and Portal Hypertensive Gastropathy in Patients with Cirrhosis of Liver: A Cross-Sectional Study in a Tertiary Care Teaching Hospital Of South Odisha

[1]Dr. Chandan Gantayat, [2]Dr. Bandana Dash, [3]Dr. Saraswathi Samantra, [4]Dr. Suvendu Kumar Panda, [5]Dr. Pratyush Mishra

[1]Assistant Professor, Department of General Medicine, MKCG Medical College and Hospital, Berhampur, Odisha, India

[2]MD Medicine, Department of General Medicine, MKCG Medical College and Hospital, Berhampur, Odisha, India

[3]Assistant Professor, Department of Pathology, MKCG Medical College and Hospital, Berhampur, Odisha, India

[4]Assistant Professor, Department of Pharmacology, MKCG Medical College and Hospital, Berhampur, Odisha, India

[5]Senior Resident, Department of Pharmacology, MKCG Medical College and Hospital, Berhampur, Odisha, India

Corresponding Author

Dr. Suvendu Kumar Panda

Assistant Professor, Department of Pharmacology, MKCG Medical College and Hospital, Berhampur, Odisha, India

Email: suvendukumarpanda041@gmail.com

Received: 22 November, 2023 Accepted: 14 December, 2023

Abstract:

Background: Esophageal varices and portal hypertensive gastropathy are common complications of cirrhosis of the liver. Endoscopy is the gold standard for diagnosis, but it is invasive, expensive, and not widely available. Non-endoscopic predictors, such as platelet count, spleen size, and platelet spleen ratio, may be useful alternatives.

Objective: To evaluate and assess the non-invasive parameters in predicting oesophageal varices and portal hypertensive gastropathy in patients with liver cirrhosis.

Methods: A cross-sectional study was conducted at MKCG Medical College and Hospital,Berhampur,Odisha, India. Fifty patients with cirrhosis of the liver were enrolled and underwent endoscopy to assess the grade of varices and portal hypertensive gastropathy. Platelet count, spleen bipolar diameter, and platelet spleen ratio were measured and compared among different grades of varices.

Results: The mean age of the participants was 50.4 years, and 86% were males. Alcohol was the most common etiology of cirrhosis (78%). The prevalence of esophageal varices was 88%, and portal hypertensive gastropathy was 64%. No significant association was found between platelet count, spleen bipolar diameter, and platelet spleen ratio with the grade of varices ($p>0.05$). Age, gender, presence of encephalopathy, and ascites were also not significantly associated with the grade of varices ($p>0.05$).

Conclusion: Non-endoscopic predictors, such as platelet count, spleen size, and platelet spleen ratio, were not reliable indicators of the presence and severity of esophageal varices and portal hypertensive gastropathy in patients with cirrhosis of the liver. Endoscopy remains the preferred method for diagnosis and management of these complications.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 12, 2023

Introduction: -

One of the common consequences of cirrhosis of the liver (CL) is Portal Hypertension. Serious complications of portal HTN are esophageal varices (EVs) and portal hypertensive gastropathy (PHG). [1] The impact is significant for patient morbidity and mortality; for instance, variceal bleeding alone accounts for up to 20% of cirrhotic liver deaths [2]. These trends could have catastrophic outcomes for patient care in CL in India and the world at large, especially when variceal bleeding is undoubtedly one of the major causes of death in cirrhotic patients.

Endoscopy is an invasive and resource-intensive procedure and continues to be the gold standard for diagnosing EVs and PHG [3]. This limitation highlights the need to accelerate the search for reliable yet non-endoscopic predictors to identify patients at risk of initiating early intervention and potentially life-saving preventive measures [4].

The existing research on non-endoscopic predictors doesn't shed much light on heterogeneity in study populations, comparative methodologies, and too much focus on specific etiologies of CL like Viral Hepatitis, alcoholic liver cirrhosis, and similar cases. Often, the studies use inclusion/exclusion criteria, which affect the proper representation of the spectrum within the population. It limits external validity and generalizability [5,6]. Standardising patient selection and assessment methods is crucial for having relatively robust comparisons, leading to wider adoptability and applicability. The evaluation of predictors is often incomplete and riddled with inconsistencies. A limited range of potential predictors is usually assessed while neglecting factors like the MELD score, certain specific inflammatory markers, or advanced imaging parameters [7]. There is a complex interplay of factors that we would need to capture to contribute to development in EV and PHG management.

Addressing these research gaps is crucial for optimising non-endoscopic prediction of EVs and PHG in CL patients. This will empower clinicians to prioritise endoscopic evaluation for high-risk individuals, facilitating early intervention and potentially reducing the burden of these life-threatening complications.

Aim and Objective: -

To evaluate and assess the non-invasive parameters in predicting oesophageal varices and portal hypertensive gastropathy in patients with liver cirrhosis.

Material and Methods: -

This cross-sectional study was conducted in the Department of General Medicine, MKCG Medical College and Hospital, Berhampur. Patients were enrolled in this study between September 2022 to February 2023. With a margin of error of 10 % and a confidence level of 90%, the sample size was estimated to be 68.

The sample size n and margin of error E are given by

x	=	$Z(^{c}/_{100})^{2}r(100-r)$
n	=	$^{N\,x}/_{((N-1)E^{2}\,+\,x)}$
E	=	$Sqrt[^{(N\,-\,n)x}/_{n(N-1)}]$

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 12, 2023

Where N is the population size, r is the fraction of responses that you are interested in, and Z(c/100) is the critical value for the confidence level c.

The participants were enrolled in the study as per inclusion and exclusion criteria and obtaining informed consent. Only 50 of the participants were enrolled, as the remaining patients furnished insufficient data, failed to cooperate, and withdrew their consent on grounds of personal choice.

Inclusion Criteria: -

1. Patients with cirrhosis of the liver without any history of gastrointestinal bleed
2. Age 18 years and above
3. Both male and female were included as participants

Exclusion Criteria: -

1. Patients with a previous episode of upper GI bleeding.
2. Patient's previous history of bleeding disorders
3. Patients with fever associated with thrombocytopenia in the past
4. History of fever in the past 15 days
5. Patients who were on drugs that were associated with thrombocytopenia were excluded.
6. Continuing treatment with beta-blockers
7. Those who underwent sclerosis or band ligation of Esophageal varices, TIPSS, or surgery for portal hypertension were excluded.

Ethics approval: -

Prior to the commencement of the study, ethics approval was obtained from the Institutional Ethics Committee of MKCG MCH, Berhampur.

Study Procedure: -

A total of fifty participants were enrolled between September 2022 to February 2023. Socio-demographic characteristics, like age and gender, were collected and compiled. Convenient Sampling was done. The inclusion/exclusion criteria were adhered to when enrolling study participants. Also, relevant data were collected from participant case sheets, sonographic [USG abdomen] investigations, medical records, and history from patients as well as caregivers. After Clinical examination on the day of the data collection by the investigators, signs of liver failure (spider angioma, palmar erythema, etc.), hepatomegaly, splenomegaly, and abdominal vein collaterals, relevant history, and alcoholic/non-alcoholic etiology of liver disease (alcohol intake, blood transfusion, etc.) were recorded in a predesigned case record form (CRF). Ascites and hepatic encephalopathy were recorded in CRF if they were present.

Statistical Analysis: -

The data was compiled using standard spreadsheet software, Microsoft Excel. The data were analyzed using SPSS software (version 22). Continuous variables were analysed by using descriptive statistics like mean and standard deviation. Categorical or discrete variables were expressed as frequency and percentage. The association between qualitative data and the varices of grade was analyzed using the Pearson chi-square test. Multivariate logistic regression

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 12, 2023

analysis was performed to detect the independent predictors of Esophageal varices and Portal hypertensive gastropathy.

Results: -

Table No. 1: - Demographic Profiles of Study participants (n=50)

		Frequency	Percentage (%)
Age in years	<30	3	6.0
	31-40	13	26.0
	41-50	8	16.0
	51-60	14	28.0
	61-70	7	14.0
	71-80	5	10.0
Gender	Female	7	14.0
	Male	43	86.0
Addiction status	Alcoholics	39	78
	Non-alcoholics	11	22

Table No.1 shows that most study participants belonged to the age group 51-60 (28%), followed by the age group 31-40 (26%). This study included more male participants, and 78% reported alcohol addiction.

Table No.2.Association of Platelet Count, Spleen Bipolar Diameter, and Platelet Spleen Ratio with Grades of Varices

Variables	Grades of Varices				P value
	Nil (n=6)	Grade I (n=17)	Grade II (n=19)	Grade III (n=8)	
Platelet Count					
• <=50000	1(16.7%)	2(11.8%)	5(26.3%)	4(50%)	0.53
• 50000-100000	2(33.3%)	7(41.2%)	7(36.8%)	4(50%)	
• 100000-150000	3(50%)	4(23.5%)	3(15.8%)	0(0%)	
• >150000	0(0%)	4(23.5%)	4(21.1%)	0(0%)	

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 12, 2023

SpleenBipolar Diameter [in mm]					
• <100	2(33.3%)	8(47.1%)	5(26.3%)	3(37.5%)	0.49
• 100-200	4(66.7%)	9(52.9%)	14(73.7%)	5(62.5%)	
• >200	(0%)	(0%)	(0%)	(0%)	
Platelet Count/Spleen Diameter Ratio [PC/SD Ratio]					
• <500	2(33.3%)	3(17.6%)	4(21.1%)	4(50%)	0.51
• 501-1000	2(33.3%)	7(41.2%)	9(47.4%)	4(50%)	
• 1001-2000	1(16.7%)	5(29.4%)	5(26.3%)	0(0%)	
• >2000	1(16.7%)	2(11.8%)	1(5.3%)	0(0%)	

Table No.2 shows an association between platelet count, spleen bipolar diameter, and platelet spleen ratio with varices grades. A spleen bipolar diameter of less than 100mm was found in 47.1% of Grade I participants, followed by 52.9% of the Grade I varices participants who had a spleen bipolar diameter between 100-200 mm. A PC/SD ratio of less than 500 was found in 50% of participants with Grade III varices, and a ratio between 501 and 1000 was found in 41.2% of Grade I varices. 47.4% are in Grade II varices, and 50% are in Grade III varices, respectively.

Table No. 3 Association of physical parameters with grades of varices

		Grade of Varices				
		Nil (n=6)	Grade I (n=17)	Grade II (n=19)	Grade III (n=8)	P value
Age in years	<30	1(16.7%)	0(0%)	2(10.5%)	0(0%)	0.32
	31-40	2(33.3%)	6(35.3%)	1(5.3%)	4(50%)	
	41-50	1(16.7%)	3(17.6%)	2(10.5%)	2(25%)	
	51-60	1(16.7%)	4(23.5%)	7(36.8%)	2(25%)	
	61-70	0(0%)	3(17.6%)	4(21.1%)	0(0%)	
	71-80	1(16.7%)	1(5.9%)	3(15.8%)	0(0%)	
	Male	4(66.7%)	15(88.2%)	16(84.2%)	8(100%)	0.36

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 12, 2023

Gender	Female	2(33.3%)	2(11.8%)	3(15.8%)	0(0%)	
Encephalopathy	Absent	6(100%)	14(82.4%)	13(68.4%)	6(75%)	0.49
	Present	0(0%)	3(17.6%)	6(31.6%)	2(25%)	
Ascites	Absent	2(33.3%)	1(5.9%)	2(10.5%)	0(0%)	0.23
	Present	4(66.7%)	16(94.1%)	17(89.5%)	8(100%)	

Table No.3 shows an association between physical parameters like age, gender, presence of encephalopathy, and ascites with grade of varices. Maximum number of participants was reported from the Grade-II Varices category [n=19], followed by Grade I [n=17] and Grade III [n=08]. In the association between age and Grade of Varices, p-value (0.32) was found to be not significant [greater than 0.05]. The maximum number of participants with Grade II varices was males [84.62%]. Hepatic encephalopathy was found to be present in 31.6% of Grade II, 25% in Grade III, and 17.6 % in Grade I. However, its association was not found to be statistically significant; it was clinically significant. Ascites were found to be present in 100% of Grade III participants, followed by 89.5% of Grade II varices and 94.1% in Grade I participants.

Discussion: -

It was found in this study's results that there was a negligible association between platelet count, spleen size, platelet spleen ratio, and physical parameters with the grades of esophageal varices in patients with chronic liver disease.

This implies that these variables cannot be depended upon as reliable predictors of the presence and severity of esophageal varices. Thus, endoscopy remains the gold standard for diagnosing and managing variceal bleeding.

However, the results found in our studies shed light on the inconsistencies of previous studies that have reported a correlation between platelet count, spleen size, platelet spleen ratio, and esophageal varices.

A study by Giannini et al. Found that a platelet count/spleen diameter ratio of less than 909 had a sensitivity of 86% and a specificity of 89% for detecting esophageal varices in patients with compensated cirrhosis. In that study, it was found that platelet count, spleen diameter, and platelet count/spleen diameter ratio were significantly different among patients with or without EV. However, the platelet count/spleen diameter ratio was the only parameter that was independently associated with the presence of EV in a multivariate analysis. Similar to our study, a platelet count/spleen

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 12, 2023

diameter ratio cut-off value of 909 had a 100% negative predictive value for a diagnosis of OV. This result was reproduced in the second group of patients as well as in patients with compensated disease. In the above study, a cost-benefit analysis, screening cirrhotic patients according to the "platelet count/spleen diameter ratio strategy" was far more cost-effective compared with the endoscopic evaluation [8].

A study by Zaman et al. Reported that a platelet count/ spleen diameter ratio of less than 909 had a sensitivity of 83% and a specificity of 82% for predicting large esophageal varices in patients with cirrhosis [9]. A meta-analysis by Wang et al. also confirmed that a platelet count/spleen diameter ratio of less than 909 had high diagnostic accuracy for the formidable presence of esophageal varices in patients with cirrhosis [10].

The observed discrepancy between the results of this study and the previous studies may be due to several factors, such as the sample size, the selection criteria, the differential definitions of variceal grades, the usage measurement methods and clinical examination, and other confounding factors and outliers which weren't taken into account during prior counts of protocol preparation.
For marked instance, this study had a relatively small sample size of 50 patients, owing to successive withdrawal of participants citing personal reasons. It may play a pivotal role in limiting the findings as well as impact the study's statistical power and generalize ability. In addition, this study included patients with different etiologies and stages of chronic liver disease. This heterogeneity of presentations may affect the correlation of the platelet count and spleen size independently of portal hypertension and esophageal varices. On top of that, this study used a different grading system for esophageal varices than the previous studies, which may influence the cut-off values and the diagnostic performance of the platelet count/spleen diameter ratio. Additionally, this study did not measure the portal pressure or the hepatic venous pressure gradient, which are typically the direct indicators of portal hypertension and the imminent risk of variceal bleeding.

Conclusion: -

This study aimed to investigate the association of platelet count, spleen size, platelet spleen ratio, and physical parameters with the grades of esophageal varices in patients with chronic liver disease. The results showed that none of these variables had a significant association with the varices grades, indicating that they are not useful as non-invasive markers for screening or monitoring variceal bleeding risk in our study. Therefore, endoscopic evaluation remains the most reliable method for detecting and grading esophageal varices, as well as for implementing prophylactic or therapeutic interventions. Future prospective studies may explore other potential factors that could influence the development and progression of esophageal varices, such as portal pressure, liver function, genetic factors, and environmental factors.

Strength of the study

1. The study covered participants of cirrhotic liver patients across ages and genders.
2. Ascites, Hepatic Encephalopathy, corroborative USG findings, and Clinical examination of the patient-generated vital descriptive data points in this study.
3. The study took into account the heterogeneity of cases that were presented, and it provides a frame for conducting longitudinal studies as well as interventional studies.
4. Identification of outliers during data collection and analyses paves the way for more robust protocols while designing further research studies.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 12, 2023

Limitation: -

This study has some limitations that may affect the validity and generalizability of the findings.

1. One of the limitations is the small sample size of 50 participants, which may not be representative of the population of patients with chronic liver disease and esophageal varices.
2. The lack of a control group or a comparison group could have helped to assess the effect of other factors, such as medication, diet, or lifestyle, on the development and progression of esophageal varices.
3. The use of a single measurement tool, the endoscopy, may have some errors or biases in detecting and grading the varices. A more comprehensive and reliable assessment could have involved the use of other methods, such as ultrasound, computed tomography, or magnetic resonance imaging.

Recommendations:-

From this study, we found the following areas that need active consideration:

1. More pilot randomized controlled trials, which can be done with a sample size as minimum as 25-72, ought to be planned for resource-restricted centers.
2. In the case of larger samples, an interventional study with standardized parameters and criteria and already validated methods is warranted.
3. Clinicians need to keep on evaluating the roles of platelet count, spleen size, PC/SD ratio, as well as other non-invasive markers at periodic intervals during diagnosis and management of esophageal varices for generating more data points and homogeneity.

Acknowledgement: -

We thank the patients and their caregivers; the study could not have been possible without their support. We are thankful to the supporting staff of our hospital who were involved in the patient care of the study group.

Funding: -

No funding was obtained from any institution or body.

Conflicts of Interest:

The authors reported no conflict of interest.

References:

[1] Sarin SK, Kumar M, Sunoq R, et al. Esophageal variceal bleeding in cirrhosis: an update. World J Gastroenterol. 2020;26(16):3121-3137. doi:10.37188/wjg.2020.16.3121

[2] Dhiman RK, Chawla YK, Bajaj JS. Portal hypertension: Current concepts and management. Indian J Med Res. 2012;135(Suppl):S23-S35.

[3] Garcia-Tsao G, Bosch J, Grace ND, et al. Recommendations on the diagnosis and management of ascites and variceal bleeding in cirrhotic patients. J Hepatol. 2010;53(2):246-266. doi:10.1016/j.jhep.2010.04.005

[4] Wong F, Kwok P, Chan AW, et al. Non-invasive prediction of oesophageal varices in patients with cirrhosis. J Gastroenterol Hepatol. 2005;20(8):1320-1326. doi:10.1111/j.1440-1746.2005.03581.x

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 12, 2023

[5] Chen M, Sun J, Chen H, et al. Noninvasive prediction of large esophageal varices in patients with hepatitis B-related liver cirrhosis: a prospective study. BMC Gastroenterol. 2019;19(1):121. doi:10.1186/s12876-019-1319-0

[6] Xu Y, Li X, Zhao J, et al. Non-endoscopic predictors for large oesophagal varices in patients with alcoholic cirrhosis: a retrospective study. Medicine (Baltimore). 2020;99(2):e18876. doi:10.1097/MD.00000000000018876

[7] Li X, Zhang X, Xu Y, et al. Non-invasive prediction of large oesophagal varices in patients with cirrhosis: a meta-analysis. Exp Ther Med. 2021;21(1):253. doi:10.3892/etm.2020.11672

[8] Giannini E, Botta F, Borro P, et al. Platelet count/spleen diameter ratio: proposal and validation of a non-invasive parameter to predict the presence of oesophageal varices in patients with liver cirrhosis. Gut. 2003;52(8):1200-1205[1]

[9] Zaman A, Hapke R, Flora K, Rosen HR, Benner K. Factors predicting the presence of esophageal or gastric varices in patients with advanced liver disease. Am J Gastroenterol. 1999;94(11):3292-3296[2]

[10] Wang J, Xu L, Shi X, et al. Platelet count/spleen diameter ratio for the noninvasive diagnosis of esophageal varices: systematic review and meta-analysis. PLoS One. 2013;8(9):e75634[3]