A Study of Correlation between Platelet Count and Severity of Esophageal Varices in Patients with Chronic Liver Disease

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Abstract:
Background:
Esophageal varices are one of the most dreadful complications of cirrhosis of liver. They are diagnosed using endoscopy which is invasive and not easily available. There is a need for a more affordable parameter to screen for esophageal varices. One of the other manifestation of portal hypertension is thrombocytopenia.
Objectives:
1.   To determine the correlation between platelet count and severity of esophageal varices in chronic liver disease patients.
2.   To assess the clinical profile of patients with chronic liver disease
Materials and methods:
This was a retrospective record based studyconducted in a tertiary care hospital with a sample size of 77. History, physical examination findings, endoscopic and laboratory findings were taken from patient's records. Child Pugh and MELD Score were used to assess the severity of liver disease patients. Spearman's correlation test was used to find out correlation between platelet count and severity of esophageal varices.
Results
Among 77 participants,83.1% were male and 16.9% were females. Mean age was 46.68±8.86 years. About 59.7% had history of jaundice, 76.6% are regular alcohol consumers, and 77.9% had ascites. According to Child Pugh score, 11.7% belonged to Class A and 50.6% belonged to Class C. Nearly 40.3% and 31.1% had grade 2 and grade 3 varices respectively. Inverse correlation was found between platelet count and severity of esophageal varices (r-0.306, p value-0.007).
Conclusion
Severity of esophageal varices correlates inversely with platelet count. Hence, platelet countmaybe usedas a cost effective screening tool for varices assessment.
Keyword: *Thrombocytopenia, Endoscopy, Correlation, Cirrhosis*

I.   Introduction

Cirrhosis of liver causesportal hypertension which leads to dilatation of portal vein, splenomegaly, ascites and formation of porto-systemic collaterals.[1-3]Around 60%-80% of such patients develop esophageal varices which has high mortality rates.[4,5]Prevention of esophageal variceal bleeding is the prime objective in Cirrhosis management. Upper gastrointestinal endoscopy is considered as the best screening tool for varices. But endoscopy is an expensiveand invasive procedure.[6] In order to overcome these issues, platelet count can be used as a non-invasive screening tool.[7]

With this background, this study was conducted to correlate whether thrombocytopenia is a good indicator of large esophageal varices in chronic liver disease patients.

II.   Materials and methods

Study Design: Retrospective record based study
Study Location: This study was carried out in the Departments of General Medicine and Gastroenterology of Sri ManakulaVinayagar Medical College and Hospital, located in the rural Pondicherry.
Study Duration: This study included patients who were admitted from January 2019 to January 2020.

Study Population: Study population includedchronic liver disease patients with esophageal varices who got admitted in the Departments of General Medicine and Gastroenterology,fulfilling the following criteria.

Sample size: 73 Patients.

Sample size calculation: The sample size for the study was calculated to be 73, using the software N Master version 2.0 taking the sensitivity of platelet count in detecting esophageal varices as 95% based on the previous study by Nouh MA in the year 2018, with absolute precision of 5% and at confidence interval of 95%. But, the final samples included were 77.[8]

Sampling method: Chronic liver disease patients with esophageal varices, meeting the inclusion and exclusion criteria were selected using convenient sampling method, from the available records maintained in the medical records department.

Inclusion criteria: Inclusion criteria for the study were all admittedChronic liver disease patients of age more than 18 years and less than or equal to 60 years with esophageal varices.

Exclusion criteria: Patients with previous history of variceal bleed and who have undergone band ligation or sclerotherapy were excluded from the study.

Procedure Methodology

Medical records department of the hospital was approached with the permission of the Medical Superintendent and the detailed list of chronic liver disease patients with esophageal varices, who got admitted during the study period was collected. From that list, 77 samples who met the inclusion and exclusion criteria were chosen. Details about sociodemographic variables (Age, sex and socioeconomic status), clinical history (history of fever, jaundice, alcohol usage, intake of drugs causing thrombocytopenia, pervious history of thrombocytopenia, history of transfusion for thrombocytopenia and previous history of ascites), physical examination findings, laboratory parameters like hemoglobin, platelet count, serum albumin, serum creatinine, total bilirubin, direct bilirubin, SGOT, SGPT, GGT, Child Pugh score and MELD (Model for End Stage Liver Disease) score were collected from the medical records.Gastroscopyreports were used to document grading of the varices.

Ethical clearance: Ethical clearance was obtained from Institutional Ethical Committee (IEC).

Statistical analysis plan:Data was entered in software Epi   Data Version 4.2 and analysed using SPSS (Statistical Package for the Social Sciences) version 24.0 . Description of categorical variables was done in frequency and percentage.   Description of continous variables was done in median and interquartile   range. Association between platelet count and severity of esophageal varices was determined using Kruskal Wallis non-parametric test at the significance level of 0.05. The correlation between platelet count and severity of esophageal varices was analysed using Spearman's correlation test at the significance level of 0.01.

Operational definition

1.   **Grading of esophageal varices[9]**

Paquet classification was used to grade esophageal varices.

- Grade 1- Micro capillaries located in distal esophagus or esophagogastric junction.
- Grade 2-1 or 2 small varices located in distal esophagus.
- Grade 3-Medium sized varices of any number.
- Grade 4-Large sized varices in any part of the esophagus.

2. **Grading of thrombocytopenia[10]**

- Grade 1- Platelet count 75,000-1,50,000/μl.
- Grade 2- Platelet count 50,000-74,999/μl.
- Grade 3- Platelet count 25,000-49,999/μl.
- Grade 4- Platelet count < 25,000/μl.

3. **Child Pugh Turcotte classification[11]**

Based on the Child Pugh scores calculated using the parameters Total Bilirubin, Serum albumin, Prothrombin Time, Ascites and Hepatic encephalopathy, the following classification for assessing the severity of the disease was made.

- Class A- 5 to 6 points (least severe disease)
- Class B- 7 to 9 points (moderately severe disease)
- Class C- 10 to 15 points (most severe disease)

III. Results

Table 1: Sociodemographic characteristics of study population(N=77)

S.No	Character	Frequency	Percentage
1.	Age 20-30 years	4	5.1%
	31-40 years	15	19.5%
	41-50 years	28	36.4%

	50-60 years	30	39%
2.	Sex		
	Male	64	83.1%
	Female	13	16.9%
3.	Socioeconomic status		
	Upper class	8	10%
	Upper middle	23	29.9%
	Lower middle	31	40.2%
	Upper lower	15	18.9%

A total of 77 chronic liver disease patients with esophageal varices were included in this study. There were 64 males (83.1%) and only 13 females (16.9%). Mean age of the participants was 46.68±8.86 years and about 39% belonged to 50-60 years of age. Socioeconomic status was calculated using modified BG Prasad classification 2019 and majority (40.2%) of them fall into lower middle socioeconomic status (Table 1).

Table 2: Clinical characteristics of the study population (N-77)

S.No	Character	Frequency	Percentage
1.	History of fever		
	Yes	7	9.1%
	No	70	90.9%
2.	History of jaundice		
	Yes	46	59.7%
	No	31	40.3%
3.	Alcohol consumption		
	Yes	59	76.6%
	No	18	23.4%
4.	Years of alcohol consumption (N-59)		
	< 5 years	1	1.6%
	5-10 years	7	11.9%
	11-20 years	32	54.2%
	> 20 years	19	32.3%
5.	Ascites		
	Present	60	77.9%
	Absent	17	22.1%

From the records, only 9.1% (7) of them had history of fever and 59.7% (46) had history of jaundice. Around 76.6% were regular alcohol consumers and the mean years of alcohol consumption was 19.06±7.25 (Table 2). Among the Chronic liver disease patients, 7.8% (6) were positive for HBsAg and in 77.9% of them ascites was present.

Table 3: Laboratory parameters of the study population

S.No	Parameter	Median	Inter Quartile Range (IQR)
1.	Hemoglobin (g/dl)*	10.2	8-11.9
2.	Platelet count (μl)	1,15,000	87,000-1,61,500
3.	Total bilirubin (mg/dl)	3.2	1.2-6.85
4.	Direct bilirubin (mg/dl)	1	0.3-3.75
5.	Serum Creatinine (mg/dl)	0.8	0.7-1
6.	Serum Albumin (g/dl)	3.4	3.-4.15
7.	SGOT (U/l)	42	33.5-101.5
8.	SGPT (U/l)	26	36.5
9.	GGT (U/l)	60	30-184.5
10.	INR	1.4	1.2-1.6
11.	Prothrombin time (seconds)	19	17-22
* Hemoglobin is with a minimum of 4gdl and maximum of 14g/dl			

Laboratory parameters are represented in Table 3. Hemoglobin had a median of 10.2 with minimum of 4g/dl and maximum of 14g/dl. Median platelet count was 1,15,000.INR had a median of 1.4 (Table 3). Thrombocytopenia is a platelet count < 1,50,000 and was graded into 4 categories. In this study, about 74% (57) had thrombocytopenia and among them 15.8% had grade 1 thrombocytopenia,29.8% had grade 2 thrombocytopenia,35.1% had grade 3 thrombocytopenia and 19.3% had grade 4 thrombocytopenia (Figure 1).
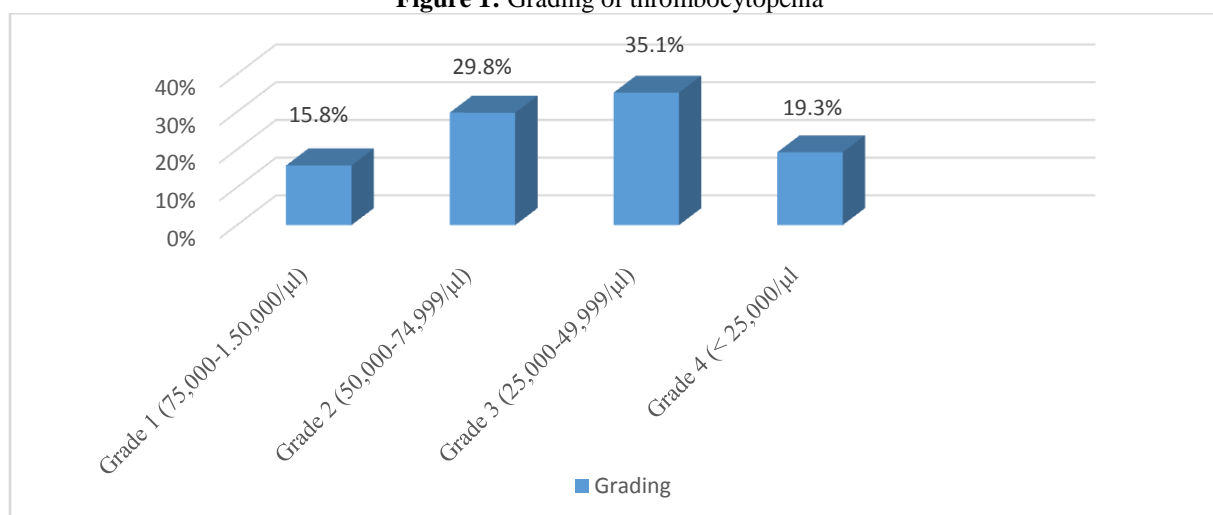
Figure 1: Grading of thrombocytopenia

Table 4: Severity of the liver disease based on scoringsystems (N=77)

S.No	Child Turcotte Pugh (CTP) class	Frequency	Percentage	Severity of liver disease
1.	Class A	9	11.7%	Mild
2.	Class B	29	37.7%	Moderate
3.	Class C	39	50.6%	Severe
S.No	Model for End Stage Liver Disease (MELD) Score	Frequency (N-77)	Percentage	Mortality risk in 3 months
1.	< 9	11	14.3%	1.9%
2.	10-19	46	59.7%	6%
3.	20-29	19	24.7%	19.6%
4.	30-39	1	1.3%	52.6%

Severity of the liver disease and the risk of mortality was assessed using Child Pugh and MELD scoring systems. According to Child Pugh scoring system, 11.7% belonged to Class A (Mild disease) category and majority of them 50.6% belonged to Class C (severe disease) category. About 59.7% of the participants had a MELD score 10-19 and only 1.3% had MELD score of 30-39.

Figure 2 - Grading of Esophageal varices
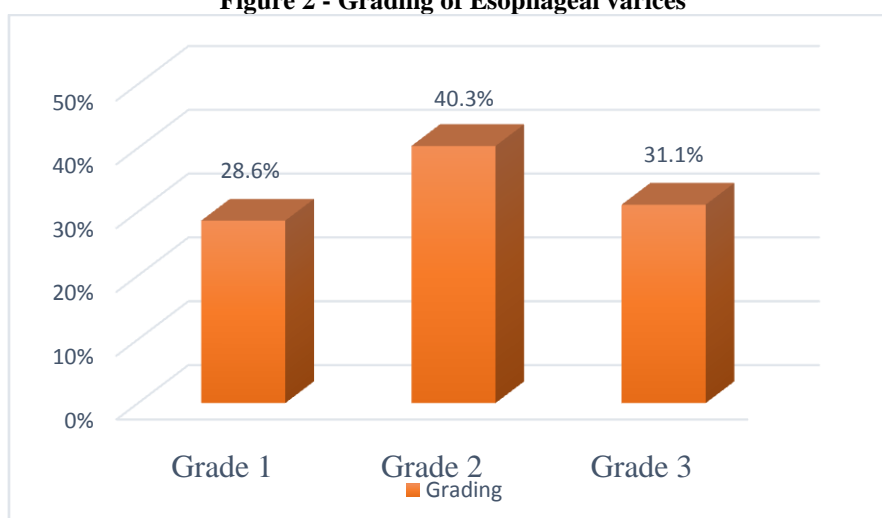
Esophageal varices were visualized using a Gastroscope and were graded using Paquet classification. As per the above classification 40.3% of them had grade 2 varices and 31.1% had grade 3 varices. None of the study participants had grade 4 esophageal varices (Figure 2).

Table 5: Association between grading of esophageal varices and platelet count

Esophageal varices grading	Platelet count		
	N	Median (IQR)	P Value*
Grade 1	22	1,30,000 (1,04,500-1,82,750)	**0.029**
Grade 2	31	1,15,000 (99,000-1,61,000)	
Grade 3	24	90,000 (42,000-1,53,500)	
* P value is calculated using Kruskal Wallis Non parametric test			

As the variables did not follow normal distribution, non-parametric test was used, and based on the test significant association was present between platelet count and severity of esophageal varices (p value < 0.029). Spearman's correlation test revealed that there is an inverse correlation between platelet count and severity of esophageal varices (r-0.306, p value 0.007). This implies that, as the platelet count decreases, there is increase in the severity of esophageal varices. (Table 5)

Table 6: Correlation between grading of esophageal varices and platelet count

Grading of variceal bleed	R	P value
Grade 1 Grade 2 Grade 3	-0.306*	**0.007**
* Spearman's correlation test was used at 0.01 level of significance (Two tailed)		

IV. Discussion

In our study 83.1% were males and 16.9% females, male preponderance was present as alcohol consumption was more in males and it was an important etiology for chronic liver disease. Similar to our study male preponderance (68.3%) was seen in Zaman et al and Abbasi A study (males 60.8% and females 39.2%). Conversely, Gue C S performed a study in Singapore in which there was no sex preponderance as the etiology for liver disease was other than alcohol usage.[12,13,14]

Mean age of the participants was 46.68±8.86 years in our study as liver cell failure usually sets in with increasing age and alcohol consumption rates are also higher in the middle of adulthood. This finding was comparable to studies by Zaman et al, Cherian JV and Abbasi A in which the mean age was 48 years, 42 years and 49.49±14.3 years respectively.[12,13,15]

In the present study, 76.6% use alcohol regularly and ascites was present in 77.9% of them. Results of Kleber G study indicate that 62.3% of the chronic liver disease patient had alcohol as the etiology and ascites was present in 47.9% of them.[16]On the contrary, alcohol was the etiology for liver disease among 26% of the participantsin a study by Gue C S.[14]

According to child Pugh classification,majority of the participants 50.6% belonged to Class C and 37.7% belonged to Class B in our study as the study setting is a tertiary care hospital. In Cherian J V's hospital based study, 178 participants had esophageal varices and among them 53.3% belong to Child Pugh class B and 32.5% Child Pugh class C.[15] Whereas Zaman et al study noted that majority were in Class B (51%) and only 15% are in Class C this contradiction might be due to differences in the study setting.[12]

Endoscopic examination revealed that 28.6% had grade one varices,40.3% had grade 2 varices and 31.1% had grade three varices in our study as the study setting was a tertiary hospital more severe cases are referred and admitted. About 29% had grade two esophageal varices in a study by Oberoi K.[1] Chiodi D conducted an analysis on 125 cirrhosis patient and concluded 42.4% had large varices (Grade three & four) and the remaining had small varices (Grade one & two) findings of these two studies indicate that higher grades of varices are detected, supporting the observations of our study.[17]

About 74% of the participants had thrombocytopenia and among them majority (35.1%) belonged to grade 2 thrombocytopenia followed by grade 3 thrombocytopenia (29.8%) as none of the study participants had a previous history of thrombocytopenia or intake of drugs causing thrombocytopenia. Abbasi A study found out that 54.9% had grade 3 thrombocytopenia and 32.3% had grade 2 thrombocytopenia.[13]

Inverse correlation between platelet count and severity of esophageal varices (r-0.306 and p value 0.007) was present in our study. Similarly, in Abbasi A study conducted in Karachi inverse correlation between platelet count and severity of esophageal varices (r-0.321, p value < 0.01) and in Nouh MA study negative correlation was present between platelet count and severity grading of esophageal varices (r-0.756 and p value < 0.001).[8,13]B.P.Priyadarshistudy revealed a positive significant association between thrombocytopenia and esophageal varices grading (p value, < 0.0001).[18] In studies by Sherief Abd-Elsalam andMadhotra, platelet count was an independent predictor of esophageal varices.[19,20] On the contrary, platelet count was not a predictor of gastroesophageal varices in a study by Amir A and the finding supports the current guideline used for screening of gastroesophageal varices which does not include platelet count as a predictor.[21]

V. Conclusion

Platelet count was inversely correlated with severity of esophageal varices. As the platelet count decreases, the severity of esophageal varices increases. From the results it is inferred that in rural and hard to reach areas, where facilities for endoscopy were not readily available, platelet count can guide the physician in management and initiation of prophylactic therapy for esophageal varices. Platelet count is also highly cost effective compared to endoscopy and hence can be considered as a screening tool for esophageal varices.

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