



SEVERITY OF THROMBOCYTOPENIA WITH DIFFERENT GRADES OF ESOPHAGEAL VARICES IN CHRONIC LIVER DISEASE.

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ABSTRACT... Objectives: To correlate severity of thrombocytopenia with different grades of esophageal varices in chronic liver disease patients undergoing EGD in a tertiary care hospital. **Study Design:** Cross sectional study. **Setting:** Gastroenterology & Hepatology Department at Liaquat National. **Period:** Six months from Jan to June 2016. **Material and Methods:** Seventy six subjects of chronic liver disease were recruited and studied for correlation between platelet count and esophageal varices by gastroscopy while the data was analyzed in SPSS version 17. **Period:** From July 2016 to Dec 2016. **Results:** There were 55 (72.4%) males and 21 (27.6%) females. The mean age was 45.6 ± 14.7 years. 10 (13.2%) had Hepatitis B, 58 (76.3%) Hepatitis C, 01 (1.3%) Wilson's disease, 03 (3.9%) Autoimmune disease and 04 (5.3%) Alcoholic liver disease. 09 (11.8%) had Child-Pugh Class A, 41 (53.9%) Class B and 26 (34.2%) had Class C. The mean platelet count was $85/\mu\text{l} \pm 40.2/\mu\text{l}$. Out of 76 patients 70 (92.1%) had esophageal varices. 23 (30.3%) had grade III varices, 19 (25%) had grade II, 14 (18.4%) each had grade I & IV and 06 (7.9%) had grade 0 varices. **Conclusion:** thrombocytopenia can predict the occurrence of esophageal varices in cirrhotic population while gastroscopy has high yield for varices.

Key words: Esophageal Varices, Non Invasive Predictor of Varices, Portal Hypertension and Thrombocytopenia.

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INTRODUCTION

Esophageal varices are dilated collateral veins that project in the lumen and responsible for hemorrhage.¹ These are a result of portal hypertension secondary to cirrhosis.² The esophageal varices exists in 40% and 60% in compensated and de-compensated disease during the diagnosis of liver cirrhosis and ascites.³ The prevalence for esophageal varices (EVs) increases as 5% per year with 5-10% progression rate from small to large varices while mortality due to esophageal varices was reported as 30-35%.^{4,5} The screening of varices by esophagogastroduodenoscopy (EGD) is mandatory in all cirrhotic population and repeated follow up needed to prevent the sudden bleeding and hemorrhage.^{6,7} Patients with advanced cirrhosis have a complex haemostatic disturbance, and thrombocytopenia (platelet count < 150000/ul) observed in chronic liver disease (CLD) mainly due to splenic

sequestration by portal hypertension induced splenomegaly called as hypersplenism although other responsible parameters includes decreased interleukin-11 and thrombopoietin.^{8,9} The platelet counts with grading of esophageal varices were reported as inversely proportional.¹⁰

The rationale of this study was due to invasive nature and cost of endoscopic screening, there is need to explore noninvasive method that correlates with the grading of EV (i.e. Platelets counts which in range below 150000 will indicate grading of esophageal varices) that would decrease the number of EGDs performed.

PATIENTS AND METHODS

The six months cross sectional study was conducted in Gastroenterology and Hepatology department of Liaquat National Hospital Karachi. The inclusion criteria were

1. Age 25 to 70 years

2. Diagnosed patients with liver cirrhosis (as defined in operational definition).
3. Child-Pugh class A, B and C (as defined in operational definition).
4. Either gender
5. Thrombocytopenia (platelet count < 150,000/ μ l)

The exclusion criteria were:

1. Antibodies against human immunodeficiency virus (HIV)
2. Hepatoma and portal vein thrombosis evident on ultrasonography
3. Previous or present treatment with beta blockers
4. Patients with history of esophageal variceal band ligation
5. Idiopathic thrombocytopenia
6. Non cirrhotic portal hypertension
7. Variceal upper gastrointestinal bleeding

LIVER CIRRHOSIS

Cirrhosis of liver was diagnosed on the basis of clinical (Ascites), hematological (platelets counts <150,000, prothrombin time >3seconds of control) and ultrasound findings (i.e. shrunken or altered echo-texture of liver, ascites) regardless of their duration of illness. The esophageal varices were graded while thrombocytopenia was defined as platelet count < 150,000/ μ l whereas the severity of thrombocytopenia as Group 1 with platelet count of < 20000/ μ l, Group 2 with platelet count of 21000 to 50000/ μ l, Group 3 with platelet count of 51000 to 99000/ μ l, and Group 4 with platelet count of 100000 to 150000/ μ l.

Patients in each subgroup according to severity of thrombocytopenia would be assessed for the presence or absence of esophageal varices and esophageal varices if present would be graded according to operational definition.

The study was conducted in Gastroenterology and Hepatology Department of Liaquat National Hospital. Patients with diagnosed cases of liver cirrhosis was inducted from endoscopy suite where they are referred for screening EGD. Demographic data such as age, gender and

etiology of liver cirrhosis was recorded. Platelet counts were noted if done recently (within 1 week), if platelet count done older than 1 week then were repeated before EGD. A verbal and consent was taken from patients and/or their attendants after explaining the intention of procedure. Endoscopic findings were noted (presence or absence of varices) and grading of varices also noted. All the endoscopies were performed by the consultant and senior fellows having at least 5 and 2 years experience respectively. Statistical analysis was done (SPSS) version 17. Frequencies and percentages were computed for sex, etiology of chronic liver disease, child class, E.V and grading of varices. For quantitative variables the mean and standard deviation (SD) was calculated. Effect modifiers were controlled while the correlation of thrombocytopenia with grading of EV was analyzed by applying Kendall's tau-b test. P-value of <0.05 was considered as significant.

RESULTS

Total 76 patients were studied with 55 (72.4%) males and 21 (27.6%) were females the mean \pm standard deviation age of study population was 45.6 \pm 14.7 years. The results are presented in Table-I to VI.

On analysis of etiology of CLD it was observed that 10 (13.2%) had Hepatitis B, 58 (76.3%) had Hepatitis C, 01 (1.3%) had Wilson's disease, 03 (3.9%) had Autoimmune disease and 04 (5.3%) had Alcoholic liver disease.

On analysis of Child-Pugh classification of study population it was observed that 09 (11.8%) had Child-Pugh Class A, 41 (53.9%) had Child-Pugh Class B and 26 (34.2%) had Child-Pugh Class C.

The mean platelet count was 85/ μ l \pm 40.2/ μ l
Out of 76 patients 70 (92.1%) had esophageal varices

On analysis of grading of esophageal varices it was observed that 23 (30.3%) had grade III varices, 19 (25%) had grade II, 14 (18.4%) each had grade I & V and 06 (7.9%) had grade 0 varices.

Mean age and platelet count of patients having

esophageal varices was 45.3 ± 14.8 years and $76.1/\mu\text{l} \pm 27.3/\mu\text{l}$ respectively as compared to this mean age and platelet count of patients do not have esophageal varices was 48.3 ± 13.8 years ($p=0.028$) and $188.2/\mu\text{l} \pm 7.5/\mu\text{l}$ ($p=0.001$)

Mean age and platelet count of patients having grade II varices was 41.8 ± 14.7 years and $78.5/\mu\text{l} \pm 9.4/\mu\text{l}$, followed by grade IV mean age was 46 ± 15 years ($p=0.015$) and mean platelet count was $48.9/\mu\text{l} \pm 3.5/\mu\text{l}$ ($p<0.05$).

Out of 55 male patients 50 (90.9%) had esophageal varices and 05 (9.1%) do not had varices as compared to this out of 21 female patients 20 (95.2%) had varices and 01 (4.8%) do not had varices ($p=0.531$).

On analysis of grading of esophageal varices among the gender it was observed that out of 55 males 05 (9.1%) had grade 0, 09 (16.4%) had grade I, 11 (20%) had grade II, 18 (32.7%) had grade III and 12 (21.8%) had grade V esophageal varices as compared to this out of 21 females 01 (4.8%) had grade 0, 05 (23.8%) had grade I, 08 (38.1%) had grade II, 05 (23.8%) had grade III and 02 (9.5%) had grade IV esophageal varices ($p=0.348$).

On analysis of frequency of esophageal varices among the etiology of CLD it was observed that 09 (90%) patients having Hepatitis B had esophageal varices, 53 (91.4%) patients having Hepatitis C, 01 (100%) having Wilson’s disease, 03 (100%) having Autoimmune disease and 04 (100%) having Alcoholic liver disease had esophageal varices ($p=0.940$).

Out of 10 patients having Hepatitis B, 01 (10%) had grade 0 esophageal varices, 03 (30%) had grade I, 03 (30%) had grade II, 02 (20%) had grade III and 01 (10%) had grade IV esophageal varices as compared to this out of 58 patients having Hepatitis C 05 (8.6%) had grade 0 esophageal varices, 09 (15.5%) had grade I, 16 (27.6%) had grade II, 17 (29.3%) had grade III and 11 (19%) had grade IV varices ($p=0.795$).

07 (77.8%) Child-Pugh class A patients had esophageal varices, 40 (97.6%) Child-Pugh class

B patients had varices and 23 (88.5%) Child-Pugh class C patients had esophageal varices ($p=0.096$).

Out of 09 CP class A patients 02 (22.2%) had grade 0, 02 (22.2%) had grade I, 03 (33.3%) had grade II and 02 (22.2%) had grade III.

Out of 41 CP class B patients 01 (2.4%) had grade 0, 05 (12.2%) had grade I, 15 (36.6%) had grade II, 12 (29.3%) had grade III and 08 (19.55) had grade IV esophageal varices.

Out of 26 CP class C patients 03 (11.5%) had grade 0, 07 (26.9%) had grade I, 01 (3.8%) had grade II, 09 (34.6%) had grade III and 06 (23.1%) had grade IV ($p=0.046$).

Esophageal Varices		Age	Platelet Count
Yes	Mean	45.34	76.10/ μl
	Std. Deviation	14.8	27.29/ μl
No	Mean	48.33	188.17/ μl
	Std. Deviation	13.77	7.49/ μl
P-value		0.028	0.001/ μl

Table-I. Analysis of mean age & platelet count among frequency of esophageal varices

Grades of Esophageal Varices		Age	Platelet Count
Grade 0	Mean	48.33	188.17/ μl
	Std. Deviation	13.765	7.494/ μl
Grade I	Mean	47.36	122.07/ μl
	Std. Deviation	17.649	17.916/ μl
Grade II	Mean	41.84	78.47/ μl
	Std. Deviation	14.736	9.43/ μl
Grade III	Mean	46.61	62.70/ μl
	Std. Deviation	13.412	7.707/ μl
Grade IV	Mean	46.00	48.93/ μl
	Std. Deviation	14.946	3.496/ μl
p value		0.015	<0.05

Table-II. Analysis of mean age & platelet count among frequency of grades of esophageal varices

Gender	Esophageal Varices	
	Yes	No
Male	50	5
	90.9%	9.1%
Female	20	1
	95.2%	4.8%

Table-III. Analysis of frequency of esophageal varices among the gender $p=0.531$

Gender	Grades of Esophageal Varices				
	Grade 0	Grade I	Grade II	Grade III	Grade IV
Male	5	9	11	18	12
	9.1%	16.4%	20.0%	32.7%	21.8%
Female	1	5	8	5	2
	4.8%	23.8%	38.1%	23.8%	9.5%

Table-IV. Analysis of frequency of grades of esophageal varices among the gender
p=0.348

Etiology of CLD	Esophageal Varices	
	Yes	No
Hepatitis B	9 90.0%	1 10.0%
Hepatitis C	53 91.4%	5 8.6%
Wilson's Disease	1 100.0%	0 0.0%
Autoimmune Disease	3 100.0%	0 0.0%
Alcoholic Hepatic Disease	4 100.0%	0 0.0%

Table-V. Analysis of frequency of esophageal varices among the etiology of CLD
p=0.940

Child-Pugh Class	Grades of Esophageal Varices				
	Grade 0	Grade I	Grade II	Grade III	Grade IV
Child-Pugh Class A	2	2	3	2	0
	22.2%	22.2%	33.3%	22.2%	0.0%
Child-Pugh Class B	1	5	15	12	8
	2.4%	12.2%	36.6%	29.3%	19.5%
Child-Pugh Class C	3	7	1	9	6
	11.5%	26.9%	3.8%	34.6%	23.1%

Table-VI. Analysis of frequency of grades of esophageal varices among the child-pugh classification
p=0.046

DISCUSSION

Thrombocytopenia in cirrhotic population is due to portal hypertension induced splenomegaly, platelet sequestration and correlates with oesophageal varices.^{11,12} Zaman A, et al. studied eight nine subjects without varices bleeding underwent gastroscopy and observed platelet count of <88,000/mm³ associated with existence of large varices.¹³ Chalasani N et al. assessed 346 liver transplant patients and factors responsible for existence of varices and reported 28% cirrhotic population with a platelet count <88,000/mm³ had esophageal varices.¹⁴ Gue CS, et al. in their study reported that the diagnostic yield of varices grade 2 and 3 was 6.3% if platelet count was > 150,000/mm³, 25% if platelet count was 100,000

to 150,000/mm³, 38.9% if platelet count was 50,000-99,000/mm³ and 100% if platelet count was <50,000/mm³.¹⁵ Tanweer S, et al¹⁶ in their study reported that mean age was 48.55 ± 13.88 years. 59.1 % were male and 40.9% were female. The platelet count varied from 22000 to 385000/mm³. Esophageal varices were detected in 102 cases. Seventeen cases were of grade I varices, 25 cases were of grade II varices, 40 cases were in grade III varices and 4 cases were in grade IV varices. Maximum number of grade-III (22 patients) and grade IV (3 patients) esophageal varices occurred in patients having platelet count less than 50000/mm³. As compared to these studies, in present study we observed that there were 55 (72.4%) males and 21 (27.6%) females.

The mean age was 45.6 ± 14.7 years. 10 (13.2%) had Hepatitis B, 58 (76.3%) Hepatitis C, 01 (1.3%) Wilson's disease, 03 (3.9%) Autoimmune disease and 04 (5.3%) Alcoholic liver disease. 09 (11.8%) had Child-Pugh Class A, 41 (53.9%) Class B and 26 (34.2%) had Class C. The mean platelet count was $85/\mu\text{l} \pm 40.2/\mu\text{l}$. Out of 76 patients 70 (92.1%) had esophageal varices. 23 (30.3%) had grade III varices, 19 (25%) had grade II, 14 (18.4%) each had grade I & IV and 06 (7.9%) had grade 0 varices.

CONCLUSION




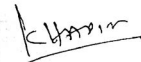
It has been observed that thrombocytopenia can be used to assess the existence of esophageal varices in cirrhotic population and when platelet count $\leq 100/\mu\text{l}$ the gastroscopy has high yield for diagnostic and therapeutic tool of esophageal varices.

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REFERENCES

- Abbasi A, Butt N, Bhutto AR, Munir SM. **Correlation of thrombocytopenia with grading of esophageal varices in chronic liver disease patients.** J Coll Physicians Surg Pak 2010; 20:369-72.
- Sharma SK, Aggarwal R. **Prediction of large esophageal varices in patients with cirrhosis of the liver using clinical, laboratory and imaging parameters.** J Gastroenterol Hepatol. 2007 Nov; 22(11):1909-15.
- Sarangapani A, Shanmugam A, Kalyanasundaram M, Rangachari B, Thangavelu P, Subbarayan JK. **Noninvasive prediction of large esophageal varices in chronic liver disease patients.** Saudi J Gastroentero. 2010; 16(1):38-42.
- Barrera F, Riquelme A, Soza A, Contreras A, Barrios G, Padilla O, et al. **Platelet count/spleen diameter ratio for non-invasive prediction of high risk esophageal varices in cirrhotic patients.** Ann Hepato. 2009; 8(4):325-30.
- Qamar AA, Grace ND, Groszmann JR, Tsao GG, Bosch J, Burroughs AK, et al. **Platelet count is not a predictor of the presence or development of gastroesophageal varices in cirrhosis.** Hepatology. 2008; 47(1):153-9.
- Dite P, Labrecque D, Fried M, Gangl A, Khan GA, Bjorkman D, et al. **Esophageal varices.** World Gastroenterology Organisation practice guideline: June, 2008.
- Grace ND. **Diagnosis and treatment of gastrointestinal bleeding secondary to portal hypertension.** Am J Gastroenterol. 1997; 92:1081-91.
- de Franchis R. **Updating consensus in portal hypertension: Report of the Baveno III consensus workshop on definitions, methodology and therapeutic strategies in portal hypertension.** J Hepatol 2000; 33:846-52.
- de Franchis R. **Evolving consensus in portal hypertension report of the baveno IV consensus workshop on methodology of diagnosis and therapy in portal hypertension.** J Hepatol 2005; 43:167-76.
- Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W; **Practice Guidelines Committee of the American Association for the Study of Liver Diseases; Practice Parameters Committee of the American College of Gastroenterology.** **Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis.** Hepatology. 2007 Sep; 46(3):922-38.
- Merli M, Nicolini G, Angeloni S, Rinaldi V, De Santis A, Merkel C, et al. **Incidence and natural history of small esophageal varices in cirrhotic patients.** J Hepatol. 2003 Mar; 38(3):266-72.
- Rye K, Scott R, Mortimore G, Lawson A, Austin A, Freeman J. **Towards noninvasive detection of oesophageal varices.** Int J Hepatol. 2012; 2012:343591.
- Zaman A, Hapke R, Flora K, Rosen HR, Benner K. **Factors predicting the presence of esophageal or gastric varices with advanced liver disease.** Am J Gastroenterol 1999; 94(11):3292-6.
- Chalasani N, Kahi C, Francois F, Pinto A, Marathe A, Bini EJ, et al. **Improved patient survival after acute variceal bleeding: A multicenter, cohort study.** Am J Gastroenterol. 2003 Mar; 98(3):653-9.
- Gue CS, Yap CK, Ng HS. **The correlation between cytopenia and esophageal varices in patients with liver cirrhosis.** Med J Malaysia. 2004 Dec; 59(5):604-8.
- Tanweer S, Khan AQ, Pervez T, Arshad M, Taseer IH. **Hepatic cirrhosis association of platelet count, splenomegaly and esophageal varices in patients.** Professional Med J. July-Sep 2011; 18(3):426-9.

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author's Signature
1	Raj Kumar Lohana	Contributions conception and design, acquisition of data, analysis and interpretation of data.	
2	Riaz Hussain Awan	Drafting the article and shares its expert research and experience in finalizing the manuscript.	
3	Seema Nayab	Contributed in conception and interpretation of data and give his expert view of for manuscript designing.	
4	Khadim Hussain Awan	Collection and acquisition of data, analysis and interpretation of data and make it suitable for final revision and a corresponding author.	
5	Faqir Muhammad Awan	Data collection and analysis.	