

Study of Etiology and Prevalence of Esophageal Varices in Patients of Liver Cirrhosis

SYEDA ZAINAB, HAMID JAVAID QURESHI*, SYED MUHAMMAD RIZWAN BUKHARI**

ABSTRACT

Objective: To determine the cause and prevalence of esophageal varices in patients suffering from liver cirrhosis

Design: Cross-sectional study

Setting: Department of Physiology, University of Health Sciences Lahore, Gastroenterology Department, Shaikh Zayed hospital, Lahore from March 2010 to October 2010.

Methods: Two hundred diagnosed patients of liver cirrhosis were recruited. On the basis of history, clinical examination and biochemical parameters, patients were categorized according to Child Pugh classification as A, B and C. After that, every patient underwent esophagogastroduodenoscopy (EGD) for presence and grading of esophageal varices.

Results: Out of 200 patients, 79(39.5%) were female and 121(60.5%) were male. The mean±SD age was 46.79±7.59 years and mean±SD duration of disease was 31.18±29.72 months. Majority of the patients, 182(91%) were HCV+, 10(5%) were HBV+, 6(3%) were having HCV and HBV co-infection and 2(1%) were alcoholics. On child pugh classifications, 89(44.5%) were class A, 71(35.5%) were class B and 40(20%) patients were in class C. On endoscopy, 141 were having varices and 59 were without varices. Out of 141 having varices, 30 were with small varices, 71 were with medium varices and 40 were having large varices.

Conclusion: Hepatitis C is the most common cause of liver cirrhosis. Male are more affected as compared to females. Most of the patients are in Child pugh class A and the majority of the patients with liver cirrhosis have medium varices.

Key words: Hepatitis C, Liver cirrhosis, Esophageal varices

INTRODUCTION

Liver cirrhosis is a condition defined histopathologically as fibrosis of liver parenchyma, resulting in nodule formation¹. Cirrhosis of the liver is the end stage of a complex process of hepatocyte injury resulting in partial degeneration and fibrosis of the liver. In the past, it was considered that liver cirrhosis is irreversible, but now, it is proven that liver cirrhosis can be reversed by removing the cause leading to cirrhosis, like alcoholic cirrhosis can be reversed after discontinuing alcohol and in the same way reversal of fibrosis can be seen after treating successfully hemochromatosis.

The world wide incidence of liver disease is 5-10%². Incidence of cirrhosis varies from country to country and region to region. In countries where alcohol consumption is more common, alcoholic cirrhosis and where alcohol consumption is low, hepatotropic viruses are the major cause of cirrhosis. cirrhosis is 50.3% and of non alcoholic

cirrhosis is 39.5%³.

The damage to hepatic parenchyma leads to activation of stellate cells called myofibroblasts which in turn secrete transforming growth factor-B1 (TGF-B1) leading to fibrotic response and proliferation of connective tissue. The balance between matrix metalloproteinases and naturally occurring tissue inhibitors of metalloproteinase (TIMP1-2) is disturbed, causing matrix breakdown and replacement of liver parenchyma by connective tissue leading to scar tissue formation⁴. The scar tissue and presence of regenerating nodules of hepatocytes obstruct the portal blood circulation resulting in portal hypertension. Complications of liver cirrhosis are portal hypertension, dilated portosystemic collateral veins commonly esophageal varices, ascites, spontaneous bacterial peritonitis, hepatic encephalopathy, hepatorenal syndrome, hepatopulmonary syndrome.

Esophageal varices are the second leading cause of death in cirrhotic patients. Prevalence of esophageal varices is higher in patients with decompensated cirrhosis i.e. 60% as compared to those with compensated cirrhotic patients which is 30%⁵. In liver cirrhosis patients prognosis of the

Department of Physiology, Lahore Medical & Dental College, Lahore

**Head of Physiology Department, SIMS, Lahore*

***Punjab Institute of Cardiology, Lahore*

Correspondence to Dr. Syeda Zainab, Email: drsyedazainab@hotmail.com Cell: 0331-4336707

disease can be assessed by categorizing patients according to Child Pugh classification⁶. This study was carried out to determine the most common cause of liver cirrhosis and prevalence of different grades of esophageal varices in Pakistan.

SUBJECTS AND METHODS

It was a cross sectional study conducted in the Deptt. of Physiology, UHS, Lahore from March 2010 to October 2010. Two hundred patients with hepatic cirrhosis were recruited from Gastroenterology Department, Sh. Zayed Hospital, Lahore through convenient sampling. Irrespective of the cause of liver cirrhosis, diagnosed patients were selected having an age range of 20-60 years. Detailed history was taken and a clinical examination was performed according to inclusion and exclusion criteria. Patients were categorized according to Child Pugh classification as A, B and C (Table 1). All patients were subjected to endoscopy using upper GI Gastroscope GIF. E₃ Olympus⁷, after an overnight fast of 12hours. On the endoscopic findings, four groups were formed; group I patients with no varices, group II with small varices, group III with medium varices and group IV with large varices (Table 2).

The data was entered and analyzed using SPSS 17.0 Mean±SD was given for normally distributed quantitative variables. Frequencies and percentages were given for qualitative variables.

RESULTS

A total of 200 patients having liver cirrhosis were taken. 79 were females (39.5%) and 121 were males (60.5%). The mean±SD age of the patients was 46.79±7.59 years. The mean± SD duration of disease

of the patients was 31.18±29.72 months. Hepatitis C was present in 182 patients having a percentage of 91%. The patients having combined hepatitis B and hepatitis C were 6 with the percentage of 3%. Hepatitis B patients were 10 having a percentage of 5%. The alcoholic patients were 2 with a percentage of 1%. In Child Pugh class A, there were 89 patients (44.5%), 71 patients were in Child Pugh B (35.5%) and 40 patients were in Child Pugh C (20%). The patients having no varices were 59 but 141 patients were having esophageal varices. Thirty patients were having small varices, 71 were with medium varices and 40 patients were with large varices.

Table 1: Child-Pugh score⁷

Measure	1 point	2 points	3 points	Units
Bilirubin (total)	<34 (<2)	34-50 (2-3)	>50(>3)	µmol/l (mg/dL)
Serum albumin	>35	28-35	<28	mg/L
INR	<1.7	1.71-2.20	> 2.20	no unit
Ascites	None	Suppressed with medication	Refractory	no unit
Hepatic encephalopathy	None	Grade I-II (or suppressed with medication)	Grade III-IV (or refractory)	no unit

Points	Class	Life expectancy	Mortality
5-6	A	15-20	10%
7-9	B	Candidate for transplant	30%
10-15	C	1-3 months	82%

Table.2. Guideline for Diagnosing Esophageal Varices⁸

1. A screening esophagogastroduodenoscopy (EGD) for the diagnosis of esophageal and gastric varices is recommended when a diagnosis of cirrhosis has been made		
2. Surveillance endoscopies are recommended on the basis of the level of cirrhosis, presence and size of the varices:		
<i>Patients with and Repeat EGD</i>		
Compensated cirrhosis	No varices Small varices	Every 2-3 years Every 1-2 years
Decompensated cirrhosis	-	Yearly intervals
3. Progression of gastrointestinal varices can be determined on the basis of the size classification at the time of EGD. In practice, the recommendations for medium-sized varices in the three-size classification are the same as for large varices in the two-size classification:		
<i>Size of varix</i>	<i>Two-size classification</i>	<i>Three-size classification</i>
Small	<5 mm	Minimally elevated veins above the esophageal mucosal surface
Medium		Tortuous veins occupying less than one-third of esophageal lumen
Large	>5 mm	Occupying more than one-third of the esophageal lumen

Table.3. Baseline characteristics of the patients with liver cirrhosis (n=200)

Characteristics of patient	Liver cirrhotic pts
Male	121 (60.5%)
Female	79 (39.5%)
Age (years)	46.79±7.59
Duration of disease (months)	31.18± 29.72
Etiology	
HCV	182(91%)
HBV	10(5%)
HBV,HCV	6 (3%)
Alcoholic	2 (1%)
Child pugh class	
A	89(44.5%)
B	71(35.5%)
C	40(20%)
Esophageal varices	
No varices	59
Varices present	141
Small varices	30
Medium varices	71
Large varices	40

DISCUSSION

In Pakistan, the prevalence of chronic liver cirrhosis is rapidly increasing. It is becoming the most common cause of morbidity and mortality¹⁰. In liver cirrhotic patients, gastrointestinal hemorrhage from varices is the most common complication leading to death¹¹. Hepatitis C is the most common cause of liver cirrhosis in Pakistan¹²⁻¹⁴ that is 14 million people are suffering from hepatitis C virus¹⁵⁻¹⁸. The present study finding is in accordance with these studies that HCV is the most common cause of liver cirrhosis in 182 patients out of 200 patients studied i.e., a percentage of 91%. HBV patients came out to be 10 (5%) and Co-infection HBV and anti HCV is 6(3%)¹⁹ alcoholic patients were only 2(1%)^{20,21}. The prognosis of the disease reported by various studies was on the basis of Child Pugh classification and results were that Child class A patients had significantly longer survival as compared to Class B and C. In the present study, the patients with Child class 'A' was 89(44.5%) Child class 'B' was 71(35.5%)^{20,21} and Child class 'C' was 40 (20%) that is majority of patients were in Child class A which is in accordance with a previous study which reported 37% Child class A patients²². On the basis of endoscopy, patients were evaluated for presence or absence of varices and categorization of esophageal varices was also done to evaluate the progression of esophageal varices.

Cirrhosis is the most advanced form of liver disease. Variceal hemorrhage is one of the most lethal complications of cirrhosis. Once esophageal varices have formed the risk of bleeding is 20% to 35% within 2 years²³. In patients who have first episode of bleeding the mortality rate is 17% to 57% and those who have survived the first episode and do

not get treatment have a risk of recurrent bleeding of 66% within 6 months of the first episode²⁴. The cirrhotic patients with large varices have more chances for bleeding. Preventive efforts would be to identify the patients having large varices¹¹. In 1997, the American Colledge of Gastroenterology recommended screening endoscopy for patients of liver cirrhosis⁹. Also, in 1998, the American Association for the study of liver disease recommended screening endoscopy to identify varices particularly for patients in Class B and C, and in class A when there is evidence of portal hypertension (thrombocytopenia or large portal vein collaterals on abdominal imaging)¹⁴. Prophylactic therapy if started immediately after identifying large varices will decrease the incidence of bleeding leading to reduction in the mortality rate¹⁶. In the present study, most of the patients i.e., 141 patients out of 200 were having varices and only 59 patients were having no varices. On categorization of the varices according to grading, medium sized varices were most common among all varices that is in 71 patients, small varices were in 30 patients and large varices were in 40 patients this was in contrary with some previous studies which may be due to different sample population^{23,18}.

It is concluded that hepatitis C is the most common cause of cirrhosis and most of the patients are in Child Class A. Varices are seen in most of the cirrhotic patients and mostly are medium varices.

Acknowledgements: We wish to thank Vice Chancellor and the Director Administration of the University of Health Sciences, Lahore for providing the opportunity and necessary facilities, to carry out this research. We express our gratitude Dr. Anwar A.

khan, Dean of Shaikh Zayed Hospital, Lahore for his help and support during this research work.

REFERENCES

1. Friedman SL. Hepatic fibrosis. In: Schiff ER, Sorrell MF and Maddrey WC eds. *Schiff's Diseases of the Liver*. 8th ed. Philadelphia, Pa: Lippincott-Raven. 1999; 371-85.
2. Culafic DM, Mirkovic DS, Vukcevic MD, Rudic, JS. Plasma and platelet serotonin levels in patients with liver cirrhosis. *World J Gastroenterol*. 2007; 13(43): 5750-3.
3. Fleming KM, Aithal GP, Dodaran SM, Card TM, West J. Incidence and prevalence of cirrhosis in the United Kingdom, 1992-2001: A general population based study. *J Hepatol*. 2008; 49: 732-8.
4. Iredale JP. "Cirrhosis: new research provides a basis for rational and targeted treatments". *BMJ*. 2003; 327: 143-7.
5. D' Amico G, Luca A. Clinical hemodynamic correlation, Prediction of the risk of bleeding. *Gastroenterol*. 1997; 11: 243-56.
6. Janjua NZ, Nizami MAM. Knowledge and practice of barbers about hepatitis B and C transmission in Rawalpindi and Islamabad. *J. Pak. Med. Assoc*. 2004; 54:116-9.
7. Yan GZ, Duan YY, Ruan LT, Cao TS, Yuan LJ. Non invasive quantitative testing of liver function using ultrasonography in patients with cirrhosis. *Hepatogastroenterol*. 2006; 53: 15-20.
8. World Gastroenterology Organisation .Esophageal varices. *WGO*. 2008; 17.
9. Van-Der-Poel CL, Cuyper HT, Reesint HW. HCV virus six years. *Lancet*. 1994; 346: 1475-9.
10. Chohan, AR, Umar M, Khaar B, Khurram M, Zahid, M. Demographic features of hepatocellular carcinoma. A study of 30 cases. *J Rawal Med Coll*. 2001; 344: 1239-40.
11. Khan AA, Rehman KU, Haider Z, Shafqat F. Seromarkers of hepatitis B and C in patients with cirrhosis. *J Coll Phys Surg Pak*. 2002; 12: 105-7.
12. Qasmi SA, Aqeel S, Ahmed M, Aslam SI, Ahmed M. Detection of hepatitis B virus in normal individuals of karachi. *J Coll Physicians Surg*. 2000; 10(12): 467-9.
13. Walker MP, Appleby TC, Zhong W, Lau JY, Hong Z. Hepatitis C virus therapies: current treatments, targets and future perspectives. *Antivir chem Chemother*. 2003; 14: 1-21.
14. Maddrey WC. Update in hepatology. *Ann Intern Med*. 2001; 13(4): 216-23.
15. Farooqi JA, Khan PM. Viral etiology of liver cirrhosis patients in sawat. *Pak J Gastroenterol*. 2002; 16(2):53-5.
16. D'Amico G, Morabito A, Pagliaro L. Survival and prognostic indicators in compensated and decompensated cirrhosis. *Dig Dis Sci*. 1986; 31: 468-75.
17. Pagliaro L, D'Amico G, Pasta L. Portal hypertension in cirrhosis: natural history. In: Bosch J, Groszmann R, eds. *Portal hypertension: pathophysiology and treatment*. Cambridge, MA: Black well Scientific, 1994:72-92.
18. Ehab H, Nashaat HA Sabry M. Non Endoscopic predictors of esophageal varices and portal hypertensive Gastropathy. *Nature and Science*. 2010; 8(6):43-50.
19. Groszmann R, Bosh J Grace N: Hemodynamic events in a prospective randomized trial of propranolol versus placebo in the prevention of a first variceal hemorrhage. *Gastroenterology*, 1999, 99:1401-1407.
20. Zaman A, Becker T Lapidus J: Risk factors for the presence of varices in cirrhotic patients without a history of variceal hemorrhage. *Arch Intern Med*, 2001, 161: 2564-70.
21. Boyer T. Natural history of portal hypertension. In: LaBrecque D, ed. Vol 1. *Clinics in liver diseases-portal hypertension*. Philadelphia L: WB Saunder; 1997, 31-44.
22. Grace N, Groszmann R Garcia-Taso G: Portal hypertension and variceal bleeding: An AASLD single topic symposium. *Hepatology*; 1998, 28: 868-80.
23. Almani SA, Memon AS, Memon AI, Shah MI, Rahpoto, MQ, Solangi R. Cirrhosis of liver : etiological factors, complications and prognosis. *I LUMHS*. 2008; 2: 61-6.
24. Sarin S, Lamba G, Kumar M: Comparison of endoscopic ligation and propranolol for the primary prevention of variceal bleeding. *N Engl J Med*; 1999, 340:988-93.