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CIRRHOTIC PATIENTS;
FREQUENCY AND PATTERN OF GASTRIC VASCULAR CHANGES

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ABSTRACT: At present time portal hypertension is perceived as one of the complications of advanced liver disease. It results in various vascular changes in gastrointestinal tract (GI), including esophageal varices, gastric varices and portal hypertensive gastropathy (PHG). PHG and gastric varices are a common cause of acute as well as chronic bleeding from GI tract which resulted in significant mortality among patients. **Objectives:** To determine the frequency of gastric vascular changes in various causes of cirrhosis. **Study Design:** Cross sectional study. **Setting:** Department of Gastroenterology, Pakistan Institute of Medical Sciences, Islamabad. **Period:** 1st August 2007 to 31st July 2008. **Materials and Methods:** Patients of age ≥30 years, with clinical evidence of cirrhosis and without prior treatment of esophagiogastric varices were included in the study. **Results:** A total of 100 patients were enrolled in the study out of which 47 were male and 53 were females with mean age of 53.6 years. The most common type of cirrhosis was turned out to be Hepatitis C affecting 50% of patients and most of the patients were in Child class C. Portal hypertensive gastropathy was present in 74% of patients. Among them 24.3% have mild changes while severe changes were present in75.7% of patients. Gastric varices were found in 40% of the patients and the most common type was IGV type I which was present in 29(72.5%) of the patients. Correlation of severity of PHG was seen with grading of esophageal varices, grading of gastric varices and Child class. **Conclusion:** Frequency of severe gastropathy is higher than the mild gastropathy. It is also concluded that gastric vascular changes are associated with cause of cirrhosis, child class and degree of portal hypertension.

Key words: Liver cirrhosis, Portal hypertension, Gastropathy, varices

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INTRODUCTION

Cirrhosis is an end-stage liver disease in which liver function is compromised due to various long-term injuries. Pakistan is recognized as a state of cirrhosis with the highest number of liver cirrhosis on the planet.[1,2] Amongst several causes of mortality liver cirrhosis is one of the common cause of death and hospital admissions in Pakistan.[3] Viral hepatitis and alcohol are the most common causes of liver cirrhosis worldwide.[1,3] Studies showed Hep C as the most common cause of cirrhosis in Pakistan.[1,3,4]

Portal hypertension is a typical condition that is presently perceived as a complication of advance liver disease. This vascular disorder has been appeared to be a huge reason for upper gastrointestinal (G1) bleeds[5] and its natural course is fundamentally connected with progression of liver disease.[6] Cirrhotic patients are at higher risk of gastrointestinal hemorrhage, with the most well-known source being gastroesophageal varices.[7] Vascular changes caused by portal hypertension in upper gastrointestinal tract includes esophageal varices, gastric varices and portal hypertensive gastropathy (PHG).[8] About 65% of cirrhotic patients with portal hypertension develop PHG. Up to 65-90% of these patients have mild PHG and 10-25% of them develop severe PHG. It has been proposed that PHG is the indicator of variceal drain. Some data recommend that PHG is responsible of 8% of non variceal drain in patients with liver disease.[8]

The exact pathogenesis of PHG is not known but some believe that there is alteration in

the distribution of total gastric blood flow. It is postulated that there is increased blood flow to the mucosa and decreased blood flow to submucosa and decreased blood flow to submucosa and serosal layer which is responsible for the change. Furthermore it is suggested that there are changes in inflammatory mediators which bring about the change. Among them increased NO production. TNF alpha synthesis and sensitivity to prostaglandin inhibition are responsible for the change.[8]

According to the National Italian Endoscopic club (NIEC) PHG can be in the form of Mosaic pattern which may be mild, moderate and severe. Red mark lesion which may be discrete or confluent and black brown spots.[9] The classification of McCormack et al is used in this study which classified PHG as mild when a mosaic pattern, fine pink speckling or superficial reddening is present. Severe when a discrete red spots and diffuse hemorrhagic lesions are present.[9]

There are various ways of classifying gastric varices. One way of classifying them is according to their anatomical location. They can be classified as gastrooesophageal varices (GOV) type I (gastric varices continuing as an extension of esophageal varices and present on the lesser curve). GOV type II (gastric varices as a continuation of esophageal varices and present on the greater curve). They can be isolated gastric varices (IGV) type 1 present in the funds of stomach and IGV type II present on the ectopic sites in the stomach and upper duodenum.[10]

There is very limited data addressing these issues in Pakistani population. So this study will help in identifying the distribution and severity of these vascular changes with regard to different causes of cirrhosis in Pakistan population. This will help us in modifying the therapeutic strategies for gastric varices and PHG.

MATERIAL AND METHODS

This was a cross sectional study conducted in Pakistan Institute of Medical Sciences, Department of Gastroenterology, Islamabad from 20th August, 2007 to 20th August, 2008. Patients of age range ≥30 years, either gender, ultrasound proven cirrhosis of liver (shrunken liver < 9 cm, portal vein diameter >10 mm, and splenomegaly of >12cm) and with and without the presence of esophageal varices were included in the study. Patient with previous treatment for esophageogastric varices, previously surgery on the stomach and non-cirrhotic portal hypertension were excluded from the study.

Informed written consent was taken from all patients participating in the study. Hospital Ethical Committee approval was also obtained. Each participant was interviewed and data on demographics and relevant history was taken from patient's valid medical record. Each and every patient underwent ultrasonography (USG) of abdomen that was carried out by consultant radiologist working in the same hospital. Upper oesophagastroduodenscopy (OGD) was done by consultant endoscopist and was assisted by researcher. Staging and grading of varices was decided by the endoscopist based on international practice guidelines, Endoscopy medicine model EVS 240 series of OLYMPUS was used during the study. All this information was recorded on a pre-designed pro forma.

STATISTICAL ANALYSIS

All the data were entered and analyzed using SPSS version 21.0. All the qualitative variables were presented as frequency and percentage. Mean ± SD was computed for all the quantitative variables. The outcome of investigations was classified into different causes of cirrhosis and child class, grading of esophageal varices of gastric mucosa and grading of gastric varices. Chi-square test/ Fisher exact test/Likelihood ratio Chi-square test was applied as appropriate to assess significant association between various categorical variables. P-value <0.05 was considered significant.

RESULTS

A total of 100 patients were enrolled in the study, out of which 53% were males and 47% were females. Mean (SD) age, height and weight of

the patients was 53.7 (11.1) years, 167.6 (6.2) cm and 68.6 (8.5) kg respectively (Table not shown). Forty eight percent of the patients were in child pugh class C, followed by class B 45% and class A 11% (Table not shown). Esophageal varices were present in 94% patients, out which 45 (47.9%) had F2 varices, 28 (29.8%) had F3 varices and 21 (22.3%) had F1 varices. Portal hypertensive gastropathy (endoscopic changes in gastric mucosa) were observed in 74% patients, out of which 56 (75.7%) were severe changes and 18 (24.3%) were mild changes (Table not shown). Gastric varices were seen in 40% patients, out of which 29 (72.5%) had IGV-I, 5 (12.5%) had GOV-1, 4 (10%) had IGV-11 and 2 (5%) had GOV-II (Table not shown).

Most common cause of cirrhosis was hepatitis C (50%), followed by crypto (16%) and both hepatitis B and C co infections (10%) (Table 1). Hep C and Hep B was reported more in females as compared to males (61.7% vs 39.6% and 10.6% vs 5.7%; respectively, Table-I), whereas, higher proportion of crypto, both Hep B and C co infections and use of alcohol was seen in males as compared to females (17% vs 14.9%, 13.2% vs 6.4% and 15.1% vs 2.1%; respectively Table-I). These results were found to be statistically significant (P-value=0.014, Table-I).

Causes of cirrhosis	Gender		Total	P-value
	Male	Female		
	n (%)	n (%)	n (%)	
Hep "B"	3 (5.7)	5 (10.6)	8 (8)	0.014*†
HepC+ Alc	2 (3.8)	0 (0)	2 (2)	
Hep "C"	21 (39.6)	29 (61.7)	50 (50)	
Hep B+C	7 (13.2)	3 (6.4)	10 (10)	
Alcoholic	8 (15.1)	1 (2.1)	9 (9)	
A Immune	0 (0)	2 (4.3)	2 (2)	
Hemo	2 (3.8)	0 (0)	2 (2)	
Crypto	9 (17)	7 (14.9)	16 (16)	
HepB + Alc	1 (1.9)	0 (0)	1 (1)	
Total	53 (100)	47 (100)	100 (100)	

Table-I. Gender wise distribution of causes of cirrhosis
*P-value<0.05, **P-value<0.0001; † Likelihood ratio Chi-square test

Hep C and Hep B were reported more in patients with child pugh class A as compared to other classes, however higher proportion of crypto and both Hep B and C co infections were reported in Class B and C respectively and the results were found to be statistically significant (P-value=0.047, Table-II). No significant association was observed between causes of cirrhosis and endoscopic changes in gastric mucosa, esophageal varices and gastric varices (Table not shown). Grading of esophagael varices and gastric varices was found to be significantly associated with child pugh classification with F2 esophagael varices being more common in class C and IGV-I gastric varices being more common in Class B (P-value=0.012, Table-II).

There was no significant association between gender and endoscopic changes in gastric mucosa (P-value=0.868, Table-III). Higher proportion of severe endoscopic changes in gastric mucosa was seen in child pugh class C, F3 esophagael varices, and patients with no gastric varices (66.7%, 78.6% and 75% respectively, Table-II). All these results were found to be statistical significant (Table-II).

DISCUSSION

Portal hypertensive gastropathy (PHG) and gastric varices are an important complication of portal hypertension. Through this study authors aimed at the clinical importance of PHG and gastric varices as a significant source of bleeding in cirrhotic patients. Presence of gastric varices and PHG are considered to be predictors of future variceal bleeding. PHG accounts for 8% of non variceal bleeding in cirrhotic patients and both these conditions are considered as a cause of chronic blood loss which can be transfusion dependant. Overall mortality due to bleeding from PHG is 12.5%.[4]

The natural history and risk factors for bleeding from GV and PHG are not extensively studied so further advances are still needed regarding natural history, risk factors, bleeding and mechanism of GV rupture.

Causes of cirrhosis	Child Pugh Classification			Total	P-value
	Class A	Class B	Class C		
Hep "B"	3 (27.3)	3 (7.3)	2 (4.2)	8 (8)	0.047*†
HepC+ Alc	0 (0)	0 (0)	2 (4.2)	2 (2)	
Hep "C"	7 (63.6)	20 (48.8)	23 (47.9)	50 (50)	
Hep B+C	0 (0)	3 (7.3)	7 (14.6)	10 (10)	
Alcoholic	0 (0)	3 (7.3)	6 (12.5)	9 (9)	
A Immune	1 (9.1)	1 (2.4)	0 (0)	2 (2)	
Hemo	0 (0)	2 (4.9)	0 (0)	2 (2)	
Crypto	0 (0)	9 (22)	7 (14.6)	16 (16)	
HepB + Alc	0 (0)	0 (0)	1 (2.1)	1 (1)	
Total	11 (100)	41 (100)	48 (100)	100 (100)	
Grading of esophagael varices					
F1 Varices	5 (45.5)	11 (26.8)	5 (10.4)	21 (21)	0.012*†
F2 Varices	5 (45.5)	17 (41.5)	23 (47.9)	45 (45)	
F3 Varices	1 (9.1)	8 (19.5)	19 (39.6)	28 (28)	
None	0 (0)	5 (12.2)	1 (2.1)	6 (6)	
Total	11 (100)	41 (100)	48 (100)	100 (100)	
Grading of gastric varices					
GOV-1	1 (9.1)	0 (0.0)	4 (8.3)	5 (5)	0.020*†
GOV-11	0 (0.0)	2 (4.9)	0 (0.0)	2 (2)	
IGV-1	1 (9.1)	14 (34.1)	14 (29.2)	29 (29)	
IGV-11	0 (0.0)	0 (0.0)	4 (8.3)	4 (4)	
None	9 (81.8)	25 (61.0)	26 (54.2)	60 (60)	
Total	11 (100)	41 (100)	48 (100)	100 (100)	

Table-II. Association of child pugh classification with causes of cirrhosis and grading of esophageal varices
*P-value<0.05, **P-value<0.0001; † Likelihood ratio Chi-square test

	Endoscopic changes in Gastric mucosa			Total	P-value
	Mild	Severe	None		
	n (%)	n (%)	n (%)	n (%)	
Gender					
Male	9 (17)	31 (58.5)	13 (24.5)	53 (100)	0.868‡
Female	9 (19.1)	25 (53.2)	13 (27.7)	47 (100)	
Total	18 (18)	56 (56)	26 (26)	100 (100)	
Child Pugh Classification					
Class A	5 (45.5)	5 (45.5)	1 (9.1)	11 (100)	0.031*†
Class B	9 (22)	19 (46.3)	13 (31.7)	41 (100)	
Class C	4 (8.3)	32 (66.7)	12 (25)	48 (100)	
Total	18 (18)	56 (56)	26 (26)	100 (100)	
Grading of esophageal varices					
F1 Varices	7 (33.3)	7 (33.3)	7 (33.3)	21 (100)	0.002*†
F2 Varices	11 (24.4)	23 (51.1)	11 (24.4)	45 (100)	
F3 Varices	0 (0)	22 (78.6)	6 (21.4)	28 (100)	
None	0 (0)	4 (66.7)	2 (33.3)	6 (100)	
Total	18 (18)	56 (56)	26 (26)	100 (100)	
Grading of gastric varices					
GOV I	1 (20)	2 (40)	2 (40)	5 (100)	0.000**†
GOV II	0 (0)	0 (0)	2 (100)	2 (100)	
IGV I	2 (6.9)	7 (24.1)	20 (69)	29 (100)	
IGV II	0 (0)	2 (50)	2 (50)	4 (100)	
None	15 (25)	45 (75)	0 (0)	60 (100)	
Total	18 (18)	56 (56)	26 (26)	100 (100)	

Table-III. Distribution of endoscopic changes in gastric mucosa among various variables
*P-value<0.05, **P-value<0.0001; † Likelihood ratio Chi-square test; ‡ Chi-square test

A better understanding of the natural history and pathogenesis will guide to the specific therapeutic modalities for these condition in future.

In this study Hep C was turned out to be the most common cause of cirrhosis affecting 50% of patients. Previous studies done in Pakistan also reported Hep C as the major of source of cirrohsis in Pakistan.[1,3,4]

Portal hypertensive gastropathy was present in 74% of patients which is comparable to studies done by Gupta et al (61%)[11], by Primignani et al (80%)[12] and by Bellis et al (76%).[13] Among them 24.3% have mild changes while 75.7% have severe changes. Grading of esophageal varices and gastric varices was found to be significantly associated with child class of cirrhosis, F2 esophagael varices and IGV-I gastric varices varices being more common in Class C and B respectively. Severity of PHG was found to be significantly associated with child class, grading of esophageal varices and grading of gastric varices.

In a study done by Gupta et al, mild PHG was present in 85% and severe in 15%. There was no relationship of PHG to: (i) a history of upper gastrointestinal bleed; (ii) size of oesophageal varices; (iii) aetiology of liver cirrhosis; or (iv) liver function status as assessed by Child Pugh's scores. The prevalence of PHG was higher in those patients with oesophagogastric varices (69%) compared with patients with oesophageal varices alone (55%).[11]

Primignani et al[12] suggested a correlation exists between PHG and the severity of portal hypertension, as the prevalence of gastropathy was higher in patients with large EV than in those with small varices. However in a study done by Bellis et al[13] this association is weak as also reflected by the results of my study.

The relationship of PHG with severity of liver disease is controversial. In this study there seems to be no relationship between PHG and severity of liver disease, similar to the finding in a study done by Claudio et al. Controversially, others found that the degree of liver dysfunction is correlated with the severity of PHG in patients with cirrhosis.[14,15]

It has also been previously shown that the overall prevalence of PHG was higher in patients in Child Pugh class B than in patients in class A and C, and that the prevalence of severe gastropathy was lowest in patients in class C . In one study during 18+/-8 months of follow-up, gastropathy was stable in 29% of patients, deteriorated in 23%, improved in 23%, and fluctuated with time in 25%. This shows that gastropathy is a dynamic condition which may progress from mild to severe but can be improved with time and even disappear.[12]

No correlation of PHG with etiology of cirrhosis was noted as shown in previous studies. Frequency of PHG was independent of the age and sex of the patient but significant association of PHG has been reported with older age group.[13]

Prevalence of gastric varices has been reported to vary between 2% and 70%. This high variability is probably related to difference in patient population, stage of cirrhosis the techniques used for diagnosis and classification. Gastric vartices are significantly more common in bleeders than in non bleeders probably indicating that they develop at advanced stage of portal hypertension.[16.17]

Gastric varices were found in 40% of patients and the most common type found out to be isolated gastric varices type I (IGV I) which was present in 29% of patients. Significant association of PHG with the grade of gastric varices was observed, being more common with IGV type I which is similar to some studies. This is in contrast to some studies where this association is weak.[16]

In a national study done in Karachi prevalence of gastric varices in patients with portal hypertension was 15%. IGV I was the most common type with frequency of 44%. GOV I, 32% and GOV II 30%.[18]

The present study evaluates the relationship

between PHG with portal hypertension by demonstrating the frequency of PHG and gastric varices in cirrhotic patients and their significance. Existing data about this association is scarce and conflicting. The reported prevalence of PHG has wide variation in results which may be related to patient selection absence of uniform classification and inter and intraobserver variation.[19] The relationship of PHG with severity of liver disease, presence and size of gastroesophageal varices and cause of cirrhosis is controversial some studies support this association and others may not. This suggests that there are some unidentified factors in the pathogenesis of PHG which play a role. Hence, more studies are required to evaluate the pathogenesis and natural history of PHG and its relation with portal hypertension to improve the therapeutic modalities for this condition and better patient care.

CONCLUSION

In this relatively small and hospital based study it is observed that frequency of severe gastropathy is higher than the mild gastropathy. It is also concluded that gastric vascular changes are associated with cause of cirrhosis, child class and degree of portal hypertension.

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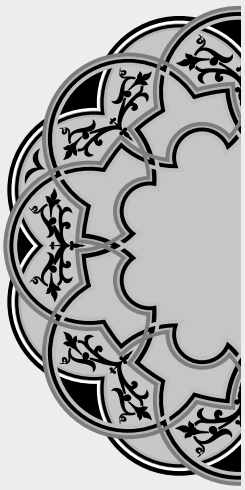
PREVIOUS RELATED STUDY

Abdul Aziz Sahto, Amir Shahzad, Mahnaaz Faiz Sahito. Cirrhotic patients; Prevalence of portal hypertensive gastropathy undergoing upper gastrointestinal endoscopy at a tertiary care hospital ini shaheed benazeerabad (Original) Professional Med J 2016;23(9): 1099-1103.



"It is not happy people who are thankful,
It is thankful people who are happy."

Unknown

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Ammarah Saeed	First author of paper, who planned search on said topic, Collected literature, Analysis of data, Final complited results, other help	
2	Dr. Tehzeeb zehra	Second author, Collected literature, Final work	
3	Dr. Ayaz Ahmad	Contributed through collection of data and its analysis part.	
4	Dr. Umbreen Idrees	Contributed in literature collection, helped in compilation of result.	
5	Dr. Sajjad Sabir	Contributed in collection of results and data before formed submission	