

## Dyspepsia in Cirrhotic Hepatitis C Patients

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### Abstract

**Background:** To determine the frequency of patients with dyspepsia, its patterns of presentation and causes along with their associations with gender and age, amongst HCV cirrhotic patients presenting to a tertiary care health facility of Rawalpindi.

**Methods:** In this cross sectional study 207 HCV cirrhotic patients, above 25 years of age irrespective of gender, were included. Patients receiving prolonged treatment of acid suppression prior to hospitalization were excluded. After taking history and performing thorough physical examination, routine laboratory investigations, abdominal ultrasonography and endoscopies were performed to determine the cause of dyspepsia.

**Results:** Amongst 207 HCV cirrhotic patients 146 (70.5%) were presented with dyspepsia. Pain in epigastrium 92 (63.0%), heart burn 81 (55.5%) and water brash 65 (44.5%) were most common patterns of presentation of dyspepsia in HCV cirrhotic patients. Portal hypertensive gastropathy 77 (52.7%) came out as leading etiology of dyspepsia, followed by gastritis 9 (6.2%), ulcer 6 (4.1%) and cholelithiasis 4 (2.7%). Amongst those diagnosed with Dyspepsia, 25 (17.1%) patients were found to have functional dyspepsia i.e. no organic cause was found.

**Conclusion:** Dyspepsia is very frequent phenomenon in HCV cirrhotic patients with most common patterns of presentation as pain in epigastrium and heart burn. The leading cause of dyspepsia was portal hypertensive gastropathy.

**Key Words:** Dyspepsia, Hepatitis C virus, Cirrhosis, Heart burn, Pain epigastrium.

### Introduction

Dyspepsia is a common clinical problem encountered by both primary care physicians and gastroenterologists and a very frequent phenomenon in cirrhotic hepatitis C patients (HCV).<sup>1</sup> The global prevalence of un-investigated dyspepsia is 21% but varies among countries. Prevalence is significantly higher in women, smokers, NSAID users, H.pylori positive individuals and patients with liver cirrhosis.<sup>2</sup>

Indigestion, also known as dyspepsia, is a condition of impaired digestion characterized by upper abdominal fullness, heartburn, nausea, belching, upper abdominal pain, regurgitation, or water brash (bitter tasting liquid coming up into back of throat).<sup>3</sup> About 30-40% of all adults experience symptoms of dyspepsia but organic cause is found in only few cases who seek medical care. The remaining cases are labelled as having functional dyspepsia.<sup>4</sup> Different causes of dyspepsia are gastroesophageal reflux disease (GERD), peptic ulcer, gastrointestinal cancers, gastritis, hiatal hernia, gastroparesis, congestive gastropathy, cholelithiasis, food or drug intolerance and other diseases of gastrointestinal tract, liver, pancreas and other systems.<sup>5-7</sup>

World Health Organization Statistics 2008 lists cirrhosis of the liver as the 18<sup>th</sup> commonest cause of mortality in the world.<sup>8</sup> Worldwide, prevalence of cirrhosis is 4.5% from autopsy studies with 3% diagnosed and 1.5% undiagnosed patients.<sup>9</sup> Pakistan is a cirrhotic state with large number of cirrhosis anywhere in the world. In Pakistan most common cause of cirrhosis is viral hepatitis (hepatitis C more than hepatitis B).<sup>10,11</sup> Hepatitis C is major public health problem with over 180 million people are infected worldwide.<sup>12</sup> Prevalence of hepatitis C is very high in Pakistan. Nearly 60-70% patients of chronic liver disease (CLD) are positive for anti-HCV.<sup>13,14</sup>

Hepatitis C and liver cirrhosis are widely associated with symptoms of dyspepsia, especially patients with chronic hepatitis C and higher score of fibrosis are more likely to have dyspepsia. This is explained by portal flow and volume changes in patients with inflammatory conditions of liver resulting in more congestion and subsequent stretch of glisson's capsule leading to excessive stimulation of hepatic vagal afferent fibers which is responsible for postprandial pain, nausea and fullness.<sup>15,16</sup> Peptic ulcer, gallstones, esophagitis, gastritis, gastroesophageal reflux disease and congestive gastropathy are the most common causes of dyspepsia in HCV cirrhotic patients.<sup>17</sup> In a clinical and epidemiological analysis on prevalence of dyspepsia in cirrhotic patients, 84% (28/33) patients are found to have dyspepsia showing

that the prevalence of dyspepsia is very high in cirrhotics.<sup>17</sup>

### Patients and Methods

This cross sectional study was conducted at Holy Family Hospital, Rawalpindi from April to October 2017 on HCV cirrhotic patients. Diagnosed cases of liver cirrhosis due to HCV infection with age > 25 years, irrespective of gender were included in this study. Patients receiving prolonged treatment (for 3 years) of acid suppression with anti-acids, H2 receptor antagonists or proton pump inhibitors prior to hospitalization and patients undergoing surgery or interventional treatment for any cause of dyspepsia were excluded from the study. Using WHO sample size calculator, minimally required sample size of 207 patients was estimated, keeping expected proportion of dyspepsia as 84%,<sup>17</sup> confidence level as 95% and absolute precision as 5%. Non-probability consecutive sampling technique was adopted till sample size of 207 was attained. After taking history and performing a thorough physical examination, routine laboratory investigations were done. Abdominal ultrasonography and endoscopies were performed to determine the cause of dyspepsia. Data was entered in SPSS version 22. Frequencies along with percentages were calculated for all categorical data whereas mean ± standard deviation was calculated for numerical data. To determine any association of frequencies of dyspepsia and its patterns of presentation with gender and age of HCV cirrhotic patients, Pearson’s Chi square test and Fischer’s exact test was applied at 5% level of significance. Associations were not analyzed for causes of dyspepsia with gender and age as multiple causes in some patients made the sample size inadequate for the statistical tests.

### Results

Majority (58.5%) were males. Mean age of study participants was 52.04±10.69 years. Dyspepsia was found in 70.5% (Table 1)

**Table 1: Gender and age group distributions of patients with or without dyspepsia in HCV cirrhotic patients (n=207)**

Dyspepsia on the basis of history	Gender No (%)			Age No (%)		
	Males	Females	p-value	≤ 45 years	> 45 years	p-value
Dyspepsia present	80 (66.12%)	66 (76.70%)	0.80	43 (69.40%)	103 (71.00%)	0.09
Dyspepsia absent	41 (33.88%)	20 (23.30%)		19 (30.60%)	42 (29.00%)	
Total	121 (100.0%)	86 (100.0%)		62 (100.0%)	145 (100.0%)	

). Pain in epigastrium (63.0%) and heart burn (55.5%) were the most common presentations of dyspepsia (Table 2). Portal hypertensive gastropathy emerged as most common etiology of dyspepsia (Table 3).

**Table 2: Patterns of presentation of dyspepsia in HCV cirrhotic patients**

Patterns of presentation of dyspepsia	Dyspepsia Present No (%) out of 207	Gender No (%)			Age No (%)		
		Males	Females	p-values	≤ 45 years	> 45 years	P-values
Pain in epigastrium	92 (63.0%)	42 (28.8%)	50 (34.2%)	0.00**	26 (17.8%)	66 (45.2%)	0.63
Heart burn	81 (55.5%)	48 (32.9%)	33 (22.6%)	0.85	20 (13.7%)	61 (41.8%)	0.21
Water brash	65 (44.5%)	36 (24.7%)	29 (19.8%)	0.54	18 (12.3%)	47 (32.2%)	0.63
Fullness in upper abdomen	20 (13.7%)	15 (10.3%)	5 (3.4%)	0.11	8 (5.5%)	12 (8.2%)	0.30
Nausea	6 (4.1%)	3 (2.1%)	3 (2.1%)	0.66	1 (0.7%)	5 (3.4%)	0.03*
Anorexia	2 (1.4%)	0 (0.0%)	2 (1.4%)	0.17	1 (0.7%)	1 (0.7%)	0.53
Cough	3 (2.1%)	0 (0.0%)	3 (2.1%)	0.16	1 (0.7%)	2 (1.4%)	0.53
Regurgitation	6 (4.1%)	3 (2.1%)	3 (2.1%)	0.06	2 (1.4%)	4 (2.7%)	0.85

f=frequencies, %=percentages,\*\*Highly statistically significant,\* Statistically significant ; Column percentages may not total to 100% as there is concurrence of symptoms.

### Discussion

Dyspepsia is very frequent phenomenon in HCV cirrhotic patients. In this study the frequency of

**Table 3: Causes of dyspepsia in HCV cirrhotic patients**

Etiology of dyspepsia	Dyspepsia Present No (%) out of 207	Gender No (%)		Age No (%)	
		Males	Females	≤ 45 years	> 45 years
Portal gastropathy	77 (52.7%)	43 (29.5%)	34 (23.3%)	30 (20.5%)	47 (32.2%)
Ulcer (peptic or gastric)	6 (4.1%)	3 (2.1%)	3 (2.1%)	1 (0.7%)	5 (3.4%)
Gastritis	9 (6.2%)	5 (3.4%)	4 (2.7%)	0 (0.0%)	9 (6.2%)
Cholelithiasis	4 (2.7%)	1 (0.7%)	3 (2.1%)	0 (0.0%)	4 (2.7%)
Functional (no organic cause found)	25 (17.1%)	13 (8.9%)	12 (8.2%)	7 (4.8%)	18 (12.3%)
Gastropathy + Hernia	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Gastropathy + Ulcer	10 (6.8%)	4 (2.7%)	6 (4.1%)	4 (2.7%)	6 (4.1%)
Ulcer + Hernia + Gastritis	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Gastropathy + Cholelithiasis	10 (6.8%)	9 (6.2%)	1 (0.7%)	1 (0.7%)	9 (6.2%)
Cholelithiasis + Gastritis	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Gastritis + Hernia	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Gastritis + Ulcer	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Total N (%)	146 (100.0%)	80 (54.7%)	66 (45.3%)	43 (29.5%)	103 (70.5%)

dyspepsia was 146 (70.5%) among 207 HCV cirrhotic patients, which is in accordance to the study conducted in Italy by Grassi M et al that revealed 84% of patients with liver cirrhosis had dyspepsia. Of these 84% patients 24.2% patients were found to have functional dyspepsia which is slightly higher than the frequency of functional dyspepsia 25 (17.1%) in current study.<sup>17</sup> A study conducted by Mohamed HI et al on chronic HCV patients found 65.9 % patients with functional dyspepsia,<sup>18</sup> and a study by Dumitraşcu DL et al revealed functional dyspepsia in 45% of cirrhotic patients.<sup>16</sup> In current study congestive gastropathy emerged as the most common cause of dyspepsia in HCV cirrhotic patients (52.7%), which is in concordance with the findings of Grassi M et al.<sup>17</sup>

A study conducted by Dore MP et al stated that 8% of patients with HCV cirrhosis had active peptic ulcer,<sup>19</sup> which is slightly higher than frequency of ulcer 6 (4.1%) in this study. Studies by Del Olmo JA et al and Conte et al reported 23.3% and 29.5% cirrhotic patients with gall stones respectively which is higher as compared to frequency of gall stones 4 (2.7%) in current study.<sup>20,21</sup>

McCormack TT et al studied patients with portal hypertension of various etiologies and found almost half (51%) of patients with gastritis on endoscopy.<sup>22</sup> Similarly a study by Misra SP et al reported endoscopic evidence of mild gastritis in 42% patients with portal hypertension.<sup>23</sup> The magnitude of gastritis is very high in these studies as compared to our study in which gastritis was found in only 9 (6.2%) HCV cirrhotic patients.

A comparative study conducted by Kalaitzakis E et al concluded that cirrhotic patients had higher gastrointestinal symptoms severity as compared to controls.<sup>24</sup> Whereas Kalaitzakis E et al reported 80% cirrhotic patients with one or more relevant Gastrointestinal (GI) symptoms. The most common GI symptoms reported include abdominal bloating in 49.5% of patients, abdominal pain in 24%, belching in 18.7%, diarrhea in 13.3%, and constipation in 8% of patients<sup>25</sup> while in current study 70.5 % patients were found with Gastrointestinal symptoms or dyspepsia and the symptoms reported include pain in epigastrium in 63%, heart burn in 55.5%, water brash in 44.5%, fullness in upper abdomen in 13.7%, nausea in 4.1%, anorexia in 1.4%, cough in 2.1% and regurgitation in 4.1% HCV cirrhotic patients. Mohamed HI et al observed post prandial distention syndrome (PDS) in 86.1 % of chronic HCV patients.<sup>16</sup> Our study showed no statistically significant association of dyspepsia with either gender or age. A

study conducted by Mahadeva S et al also observed that dyspepsia was not related to any particular age group, worldwide different studies had shown some trends. Despite these trends, age extremities had nothing to do with prevalence of dyspepsia. Even though there was no difference in prevalence of dyspepsia between gender but functional dyspepsia was more prevalent in females as compared to males.<sup>26</sup> Similarly, study by Westbrook JI et al revealed no significant gender differences in number and severity of symptoms of dyspepsia however bloating, nausea, and early satiety were found more frequently among females while regurgitation and heartburn in males.<sup>27</sup> Our study is in congruent with these studies, because no impact of gender and age was found on different patterns of presentation except pain in epigastrium was higher in females than males while nausea was more common in patients above 45 years of age as compared to younger, with highly statistically significant differences in HCV cirrhotic patients.

## Conclusion

1. Dyspepsia is a frequent phenomenon in HCV cirrhotic patients with most common patterns of presentation as pain in epigastrium and heart burn.
2. The leading cause of dyspepsia was observed to be portal hypertensive gastropathy.

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