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Prevalence of Portopulmonary Hypertension in Patients with Hepatic Cirrhosis

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ABSTRACT

Objective: "To determine the frequency of portopulmonary hypertension in patients with hepatic cirrhosis." **Study Place and Duration:** Department of Medicine, Ghurki Trust Teaching Hospital, Lahore for 05 months from 7th Feb 2025 to 8th June 2025. **Methodology:** After meeting the selection criteria, 130 patients were and underwent portal vein Doppler ultrasound and echocardiography. Portopulmonary hypertension was diagnosed if the patient had a tricuspid regurgitation velocity ≥2.8 m/s, an estimated pulmonary artery systolic pressure >35 mmHg on echocardiography, pulmonary arterial pressure >20 mmHg, pulmonary artery wedge pressure ≤15 mmHg, and pulmonary vascular resistance ≥3 Wood units. All findings were documented in a structured proforma and analysed in SPSS. **Results:** The mean age of participants was 55.40 ± 9.76 years. Among them, 71 (54.6%) were male and 59 (45.4%) were female. In this study, porto-pulmonary hypertension was observed in 14 patients (10.77%) with hepatic cirrhosis. Among males, 4 (5.6%) had portopulmonary hypertension, compared to 10 (16.9%) females (p = 0.038*). **Conclusion:** Based on the findings of this study, it can be concluded that portopulmonary hypertension was present in 10.77% of patients with hepatic cirrhosis, with a higher prevalence observed among females.

INTRODUCTION

A gradual, widespread fibrosing nodular disorder that impairs the overall normal liver architecture is known as liver cirrhosis (LC), a consequence of chronic liver disease[1]. In individuals with chronic liver illness, portal hypertension is linked to pulmonary arterial hypertension, which is known as portopulmonary hypertension.[2] This happens when the pulmonary vessel's resistance increases, reducing the amount of blood that can pass through pulmonary vessels.[3] Increased pressure in the pulmonary arteries may force the heart's right ventricle to work harder to pump blood through the lungs, potentially leading to cardiac arrest.[4] Increased mean pulmonary arterial pressure ≥25 mmHg, pulmonary arterial wedge pressure >15 mmHg, and pulmonary vascular resistance 3 Wood units (WU) are hemodynamically classified as portopulmonary hypertension.[5, 6] There are just two methods of treatment: liver transplantation or targeted therapy for pulmonary hypertension. However, despite focused treatment, patient survival is still low.[7, 8]

Porto-pulmonary hypertension is a serious complication of cirrhosis. It can leads to significant morbidity and mortality if left untreated.[9, 10] PPHTN also increases the risk of complications during and after surgery.[11, 12] Some of the globally done researches show following results in portopulmonary hypertension among patients with hepatic cirrhosis. Patients with liver cirrhosis have a steady increase in pulmonary pressure, which raises their chance of passing away[1]. Between 17% and 47% of people have hepatopulmonary syndrome, and after four to five years from the onset of respiratory symptoms, the condition's natural course is marked by severe dyspnea, increasing clinical deterioration, and high mortality[1].

The purpose of this study is to ascertain how common portopulmonary hypertension is in hepatic cirrhosis patients. Literature showed varied frequency of portopulmonary hypertension in liver cirrhotic patients an no local evidence exist in literature that could help us to determine whether the risk of portopulmonary hypertension is high or low in local population. Therefore, we want to conduct this study to get evidence for local population and implement findings in local setting. This condition's modest incidence belies both its ubiquity and a thorough awareness of its clinical aspects, which require additional investigation to gain a deeper understanding. Determining the prevalence of portopulmonary

hypertension in individuals with hepatic cirrhosis was the aim of this investigation.

METHODOLOGY

This cross-sectional study was carried out at the department of Medicine, Ghurki Trust Teaching Hospital, Lahore for about 05 months 7th Feb 2025 to 8th June 2025. WHO sample size calculator was used to calculate the sample size of this study. Sample size of 130 cases is calculated with 95% confidence level, 5% margin of error and percentage of portopulmonary hypertension i.e. 9.3% in cirrhotic patient.[13] For the selection of patients was done on the basis of non-probability consecutive sampling technique, who fulfilled the following criteria.

Inclusion: Patients having age range between 20 to 70 years of both gender and patients diagnosed with liver cirrhosis were included. In this study, cirrhosis was defined as presence of ALT >40 IU, AST>40 IU, with progressive destruction and regeneration of liver parenchyma, leading to fibrosis and coarse liver on Ultrasound abdomen for >6 months.

Exclusion: Similarly patients presented with cardiac disease on echocardiography, patients with chronic pulmonary disease (on chest X-ray) and patients who has other disease with liver malignancy were excluded.

Patients were enrolled from OPD. Informed consent was taken and demographics (name, age, gender, BMI, duration of cirrhosis, presence of hepatitis B or C, diabetes, hypertension, smoking, alcoholism, residence, socioeconomic status, occupation, MELD score and Child-Pugh score were noted. Then patients were underwent portal vein Doppler ultrasound and echocardiography. If patient had TRV is ≥2.8 m/s; ePASP >35 mmHg on echocardiography; mean pulmonary arterial pressure >20 mm Hg with pulmonary artery wedge pressure ≤15 mmHg and pulmonary vascular resistance ≥3 WU, then portopulmonary hypertension was labeled. All the findings were saved in proforma.

Data was entered and analyzed in SPSS version 25. Portopulmonary hypertension was presented as frequency and percentage. Data was stratified for effect modifiers and chi-square test was applied, keeping p-value≤0.05 as significant.

RESULTS

In this study, a total of 130 patients were enrolled. The mean age of the participants was 55.40 ± 9.76 years. Among them, 71 (54.6%) were male and 59 (45.4%) were female. Hepatitis B and C infections were observed in 49 (37.7%) and 60 (46.2%) patients, respectively. Among the enrolled patients, 84 (64.6%) had diabetes mellitus, 96 (73.8%) had hypertension, and 39 (30%) were smokers. Regarding residential status, 54 (41.5%) patients were from rural areas, 25 (19.2%) from semi-urban areas, and 51 (39.2%) from urban areas. Socioeconomic status (SES) analysis revealed that 40 (30.8%) patients belonged to the low SES group, while 90 (69.2%) were from the middle SES group. The most common occupation was housewife, reported by 59 (45.4%) patients, followed by farmers and teachers. According to the Child-Pugh (CP) classification, 54 (41.5%) patients were in Class A, 56 (43.1%) in Class B, and 20 (15.4%) in Class C. The mean body mass index (BMI) of the patients was 25.77 ± 3.93 kg/m^2. The mean duration of cirrhosis was 2.01 ± 0.85 years, with a range from 0.33 to 3.30 years. **(Table 1)**

Table 1

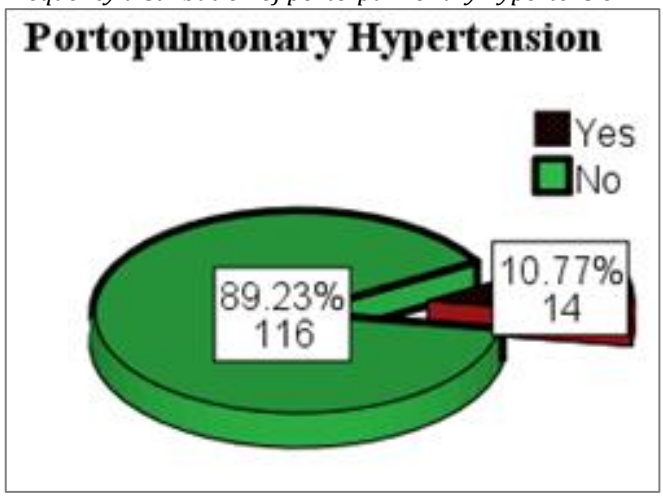
Descriptive and clinical parameters of patients

		Frequency
Age (Years)		55.40 ± 9.76 (35-70)
Gender	Male	71 (54.6%)
	Female	59 (45.4%)
BMI (Kg/m^2)		25.77 ± 3.93 (19-35)
Occupation	Businessman	12 (9.2%)
	Driver	5 (3.8%)
	Farmer	23 (17.7%)
	Govt Employ	5 (3.8%)
	Guard	5 (3.8%)
	HW	59 (45.4%)
	Teacher	21 (16.2%)
Residence	Rural	54 (41.5%)
	Semi Urban	25 (19.2%)
	Urban	51 (39.2%)
Socioeconomic status	Low	40 (30.8%)
	Middle	90 (69.2%)
	High	0 (0%)
Duration of Cirrhosis (years)		2.01 ± 0.85 (0.33-3.30)
Diabetes mellitus		84 (64.6%)
Hypertension		96 (73.8%)
Hepatitis B		49 (37.7%)
Hepatitis C		60 (46.2%)
Smoking		39 (30%)
Child-Pugh class	A	54 (41.5%)
	B	56 (43.1%)
	C	20 (15.4%)

According to this study porto-pulmonary hypertension was found in 14(10.77%) patients. **(Fig 1)**

Figure 1

Frequency distribution of porto-pulmonary hypertension



Among patients aged ≤60 years, portopulmonary hypertension was observed in 4 (4.8%) cases, while it was noted in 10 (21.7%) patients aged >60 years (p = 0.006*). Among males, 4 (5.6%) had portopulmonary hypertension, compared to 10 (16.9%) females (p = 0.038*). In patients with hepatitis B, portopulmonary hypertension was present in 6 (12.2%) cases, whereas 8 (9.9%) cases were observed among those without hepatitis B (p = 0.673 NS). Similarly, in patients with hepatitis C, it was found in 6 (10.0%) cases, compared to 8 (11.4%) in those without hepatitis C (p = 0.793). Among diabetic patients, portopulmonary hypertension was seen in 11 (13.1%) cases, compared to 3 (6.5%) in non-diabetic

patients (p = 0.376 NS). In hypertensive patients, 12 (12.5%) had the condition versus 2 (5.9%) among non-hypertensives (p = 0.376 NS). Portopulmonary hypertension was noted in 2 (5.1%) smokers and 12 (13.2%) non-smokers (p = 0.227 NS). Regarding socioeconomic status, 2 (5.0%) patients from the low SES group had the condition compared to 12 (13.3%) from the middle SES group (p = 0.224 NS). **Table II**

Table II

Comparison of sociodemographic and clinical characteristics of patients based on the presence or absence of portopulmonary hypertension

		Porto-pulmonary Hypertension		P-value
		Yes	No	
Age Groups	≤ 60	4 (4.8%)	80 (95.2%)	0.006
	>60	10 (21.7%)	36 (78.3%)	
Gender	Male	4 (5.6%)	67 (94.4%)	0.038
	Female	10 (16.9%)	49 (83.1%)	
BMI Groups	≤ 25	8 (12.7%)	55 (87.3%)	0.491
	>25	6 (9.0%)	61 (91.0%)	
Duration of cirrhosis	≤ 2	6 (9.7%)	56 (90.3%)	0.701
	>2	8 (11.8%)	60 (88.2%)	
Hepatitis B	Yes	6 (12.2%)	43 (87.8%)	0.673
	No	8 (9.9%)	73 (90.1%)	
Hepatitis C	Yes	6 (10.0%)	54 (90.0%)	0.793
	No	8 (11.4%)	62 (88.6%)	
Diabetes mellitus	Yes	11 (13.1%)	73 (86.9%)	0.376
	No	3 (6.5%)	43 (93.5%)	
Hypertension	Yes	12 (12.5%)	84 (87.5%)	0.354
	No	2 (5.9%)	32 (94.1%)	
Smoking	Yes	2 (5.1%)	37 (94.9%)	0.227
	No	12 (13.2%)	79 (86.8%)	
Socioeconomic status	Low	2 (5.0%)	38 (95.0%)	0.224
	Middle	12 (13.3%)	78 (86.7%)	

***=Significant NS= Not significant**

DISCUSSION

Fibrosis and the breakdown of normal liver architecture are hallmarks of cirrhosis, a degenerative illness that impairs hepatic function and causes portal hypertension. One of the leading causes of death and morbidity is cirrhosis. When portal hypertension and pulmonary hypertension coexist, portopulmonary hypertension results. Although it is common in people with and without hepatic cirrhosis, the former are more likely to have it.[2, 14, 15].

In Pakistan, liver disease-related morbidity and death have steadily declined in recent decades. Vasodilation in the splanchnic vascular bed causes an increase in splanchnic blood flow and an increase in intrahepatic resistance to blood flow in cirrhosis. Patients with CLD have been reported to have a wide range of respiratory conditions that can impact the pleural space and lung parenchyma[16].

In this study, porto-pulmonary hypertension was observed in 14 patients (10.77%) with hepatic cirrhosis. In a Chinese research by Chen et al., the mean age was 73.0+9.0 years, and the prevalence of pulmonary hypertension was 10%, with 5% of the participants being male and 5% being female[17]. In the Gurghean and Tudur research, pulmonary hypertension was detected in 18 out of 23.48% of patients with portal hypertension and 286 patients with liver cirrhosis on echocardiography.[18]

Chiva et al , reported a 1.7% prevalence in a Spanish population of cirrhotic patients.[19] Shao et al., documented 2.8% prevalence in a Chinese population of cirrhotic patients.[9] But Chen et al., observed a 10.0% prevalence in a Chinese population of cirrhotic patients.[20] and Gupta et al., found that the percentage of portopulmonary hypertension was 9.3% in cirrhotic patient.[13] Nonetheless, it is important to consider the differences between the studies with regard to demographic, sample size, research design, diagnostic criteria, and diagnostic process.

According to one study by G Ahmad et al[16] Child-Pugh Class C was observed in 41.4% of cases, whereas Child-Pugh Class B was observed in 58.6%. With a mean body mass index of 28.21+4.21 kg/m2, 27.1% of people were obese. The average length of the illness was 18.89+9.56 months. 22.9% of people smoked. 15.0% of subjects had pulmonary hypertension. 3.6% of patients had severe pulmonary hypertension, whereas 11.4% had mild hypertension[16]. Diabetes was present in 37.1%.

Child-Pugh Class C was observed in 41.4% of cases, whereas Child-Pugh Class B was observed in 58.6%. With a mean body mass index of 28.21+4.21 kg/m, 27.1% of people were obese. The average length of the illness was 18.89+9.56 months. Smokers made up 22.9%[16].

Atsukawa et al.[3] found that, using both earlier and later criteria, the prevalence of portopulmonary hypertension in a Japanese sample of cirrhotic patients was 1.1% and 3.3%, respectively. This suggests that the prevalence of portopulmonary hypertension may be overestimated or underestimated due to differences across studies. More research is still need to determine the revised criteria's clinical relevance in a real-world clinical setting.

According to this study among males, 4 (5.6%) had portopulmonary hypertension, compared to 10 (16.9%) females (p = 0.038*). Similar to our study findings Vergara et al.[10] and Kawut et al.[21] indicated that compared to men, women had a greater risk of portopulmonary hypertension. Previous research has linked the disease's increased prevalence to the involvement of estrogen[22]. Males made up 68% of the sample in the Lahore research by Nadeem et al23. Male gender preponderance was also documented by Farooqi et al. There were 64% more men than women among Alam et al. Our patients were 48.13+7.69 years old on average. The findings of the Nadeem et al. investigation were comparable[23-25].

Considering the discrepancy in portopulmonary hypertension prevalence between cirrhotic individuals, further research with a larger sample size and multicenter design is recommended to validate and expand upon the findings of this study.

CONCLUSION

Based on the findings of this study, it was observed that frequency of portopulmonary hypertension is 10.77% of cirrhotic patients, with a higher prevalence observed among females. Thus we have obtained magnitudes for local population and found risk of portopulmonary hypertension as not ignorable. Therefore, in future, strategies will be made in order to screen cirrhotic patients for presence of portopulmonary hypertension to improve the condition and quality of life of patients with liver cirrhosis.

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