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Original Research Article.

Study of Prevalence of Pulmonary Artery Hypertension in Portal Hypertensives Patients in RIMS, Ranchi

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ABSTRACT

Background: The development of pulmonary hypertension i.e. mean pulmonary artery pressure (mPAP) above 25 mmHg with normal capillary wedge pressure and pulmonary vascular resistance(PVR) above 240 dyn/s/cm−5 in association with elevated pressure in portal circulation is known as portopulmonary hypertension (POPH). Comparing with idiopathic PAH, patients with POPH have a worst survival profile, with a 3-year survival of only 38% versus78% for idiopathic PAH. Recent evidence from France shows that POPH is the fourth most common form of PAH reported overall in the population-based French National Registry, after idiopathic PAH and PAH associated with connective tissue diseases and con- genital heart disease. The aim of this study is to evaluate frequency of POPH in portal hypertensive patient.

Materials and Methods: A cross sectional study of patient admitted in RIMS, medicine department was performed fulfilling features of portal hypertension with ultrasound showing splenomegaly, ascites, portal vein diameter more than 13 mm, portal vein velocity less than 15 cm/s and upper gastrointestinal endoscopy showing esophageal varices and patient with connective tissue disease, congenital heart disease, left ventricular systolic or diastolic dysfunction, valvular heart disease, lungs disease, sleep related breathing disorder, chronic hemolytic and myeloproliferative disorder were excluded. All patient underwent screening with echocardiography for measuring pulmonary artery systolic pressure (PASP) and PASP more than 35 mmHg were considered for POPH which was confirmed with right heart catheterisation by measuring mean pulmonary artery pressure (mPAP) of more than 25 mmHg.

Observation: Among forty-two patient in this study, there were thirty-three male patients and nine female patients. POPH was seen three female and two male patients with total of five out of forty- two with prevalence of 11.9% out of which 7.1% were female and 4.8% were male.

Conclusion: Portopulmonary hypertension prevalence is 2–6%. In this study pulmonary hypertension is significantly high in portal hypertensive patient with percentage of 11.9% and more prevalent in female.

Keywords: Portopulmonary Hypertension (POPH); Pulmonary Arterial Hypertension (PAH); Pulmonary Artery Systolic Pressure (PASP); Mean Pulmonary Artery Pressure (mPAP); Pulmonary Vascular Resistance (PVR).

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INTRODUCTION

Portopulmonary hypertension (POPH) is a form of pulmonary arterial hypertension (PAH) associated with portal hypertension with or without underlying chronic liver disease. POPH is increasingly recognized and recent evidence suggests that it is fourth leading causes of PAH, idiopathic POPH leading followed by connective tissue and congenital heart disease.[1] POPH is defined as an increase in mean pulmonary arterial pressure (mPAP) above 25 mmHg associated with normal capillary wedge pressure and a pulmonary vascular resistance (PVR) above 240 dyn/s/cm−5 in the settings of portal hypertension.[2] Epidemiological study has estimated prevalence of pulmonary artery hypertension in portal hypertensive individual to be 2% to 6%, but it may be higher i.e 8.5% in those referred for liver transplant.[3-5]

The pathophysiology of POPH is poorly understood although the pathological changes in pulmonary vasculature in advanced POPH are similar to those seen in idiopathic pulmonary

hypertension.[6-9] The prognosis in patients with liver disease who also suffer from significant POPH is considered to be poor.

Patients with portopulmonary hypertension are clinically similar to those with primary pulmonary hypertension (PPH), except for being 5–10 years older on average, with an equal sex ratio (against a 2:1 female to male ratio in PPH).

Higher degree of pulmonary artery pressure (PAP) may preclude a patient from liver transplant as mortality in these patients is high.[10,11]

According to a recent study from the Mayo Clinic, cardiopulmonary mortality of liver transplantation is 100% if mean pulmonary artery pressure exceeds 50 mm Hg.[12]

No regression of pulmonary hypertension has been reported after liver transplantation. It is not known whether combined liver-lung transplantation may be a reasonable option for some patients.

Enough data is lacking with regard to portopulmonary hypertension patient undergoing successful liver transplantation.

Hence the aim of this study is to evaluate prevalence of POPH, grading severity of POPH and its association with body mass index (BMI), diabetes, systemic hypertension, smoking and right ventricular dysfunction.

MATERIALS AND METHODS

This is a cross-sectional observation study, it was conducted on 147 patients from November 2017 to October 2019 in Department of Medicine, R.I.M.S, Ranchi, Jharkhand, India.

Inclusion criteria for portal hypertension were sign and symptoms like ascites, malena, hematemesis, splenomegaly, icterus, caput medusa, cachexia. Portal hypertension was confirmed by ultrasound abdomen with features of dilated portal vein>13mm, portal vein velocity <15cm/sec, loss of respiratory variation i.e biphasic flow in portal vein, splenomegaly, ascites and supporting features like liver cirrhosis, thrombosis of portal or hepatic vein.

Patient suffering from connective tissue disease, congenital heart disease, left ventricle systolic dysfunction, valvular heart disease, lung disease, sleep related disorder breathing, chronic hemolytic and myeloproliferative disorder, HIV, family history of pulmonary hypertension and with history of intake of anorexic drug were excluded from this study. Those screened positive of portal hypertension underwent trans-thoracic echocardiography for calculation of PASP (pulmonary artery systolic pressure) as described in table-1, below and for right ventricular dysfunction using TAPSE (tricuspid annulus plane systolic excursion) and TDI (tissue doppler imaging) S' was calculated (table-2).

HRCT was done in those screened positive for pulmonary artery hypertension (PAH) in echocardiography to rule out lung's disease as a secondary cause of PAH. Blood pressure was measured frequently during hospital stay and hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg; or use of antihypertensive medications. Patients with elevated serum glucose level or on treatment for diabetes were considered as diabetes. Body mass index (BMI) was calculated by body weight (kg)/height (m2). Smokers were defined by self-report of cigarette smoking during the year prior to study.

SPSS version-20, used for statistical analysis. For categorical variables; Pearson Chi-square was used. Quantitative mean with standard deviation was used.

Table 1: Staging severity of POPH

PAH (pulmonary artery hypertension)	Mean PAP (pulmonary artery pressure)	PASP (pulmonary artery systolic pressure) at rest
Mild	>25mm hg	>35mm hg
Moderate	>40mm hg	>50mm hg
Severe	>50 mm hg	>70mm hg

Table 2: Right ventricular dysfunction

TAPSE (tricuspid annulus plane systolic excursion)	<15mm
TDI (tissue doppler imaging) S'	<10mm/sec

Table 3: Result summarized below.

Variables	POPH present(n=12)	POPH absent(n=135)	p-value
Age	53.33± 8.3 year	51.58± 9.4	0.86
Male	10(8.2%)	112(91.8%)	0.974
Female	2(8%)	23(92%)	0.974
Diabetes	3(21.4%)	11(67.6%)	0.05
Systemic hypertension	2(40%)	3(60%)	0.008
Smoking	2(8%)	23(92%)	0.971
Right ventricular dysfunction	11(84.6%)	2(15.4%)	0.0001
BMI (kg/m^2) Normal-18.5 to 24.99	3(2.9%)	101	
BMI (kg/m^2) Overweight-25to 29.99	8(22.2%)	28	0.01
BMI (kg/m^2) Obese>30	1(14.28%)	6	

Table 4: Grading severity of POPH.

PAH (pulmonary artery hypertension)	Mean PAP (pulmonary artery pressure)	POPH patient number/ percentage
Mild	>25mm hg	5(41.6%)
Moderate	>40mm hg	6(50%)
Severe	>50 mm hg	1(8.4%)

RESULTS

There were 14 patients with PASP > 35 mmhg, who underwent right heart catherization through right femoral approach with swan-ganz catheter in cath-lab under fluoroscopy of which 12 patients found positive for POPH with mean PAP >25mmhg.

Overall prevalence of portopulmonary hypertension was 8.1%, in male it was 8.2% and female it was 8.0%. Sex was insignificant in POPH with p value of 0.974. Mean age of POPH patients were 53.33+ 8.3-year, age was insignificant with p-value 0.86.

Patients with normal BMI range group were less commonly affected with POPH with prevalence of 2.9%. Overweight and obese group were more commonly affected with prevalence of 22.2% and 14.3% respectively. BMI was found significant in POPH patients with p- value of 0.01.

Diabetes prevalence was 21.4% in portopulmonary hypertensive group as compared to 67.6% in non-portopulmonary hypertensive group. Study was statistically significant with p-value of 0.05.

Hypertension prevalence in POPH patients was 40% as compared to 60% in non-portopulmonary hypertensive patients. Hypertension is significant with p-value of 0.008.

Smoking prevalence in POPH patients were 8% as compared to 92% in non-portopulmonary hypertensive patients with P-value of 0.971. Right ventricular dysfunction (RVD) prevalence in POPH and non-POPH group were 84.6% and 15.4% respectively with p-value of 0.0001.

Out of 12 patients with POPH, 41.6% were mildly portopulmonary hypertensive with mean pulmonary artery pressure(mPAP) of 25 to 39mmhg, 50% were moderately portopulmonary hypertensive with mPAP of 40 to 49mmhg and 8.3% were severely portopulmonary hypertensive with mPAP >50mmhg.

DISCUSSION

In this study overall prevalence of portopulmonary hypertension (POPH) is 8.1%.

In a retrospective series of 436 patients with the diagnosis of primary pulmonary hypertension, 13% were also diagnosed with portal hypertension.[13]

The prevalence of POPH in patients undergoing liver transplant (LT) is considered to be higher, with one study by Hadengue A et al. showing a prevalence of 8.5%.[5]

Study by Ramsay MA et al. patients undergoing liver transplantation, the incidence of POPH was found to be between 4% and 6%.[14]

The fraction of patients with portopulmonary hypertension in the National Institutes of Health (NIH) registry was 8%, and it can be seen in up to 10% of patients evaluated for liver transplantation.[15]

Study by Plevak D and Benjaminov FS et al., patients who have advanced liver disease, especially those assessed or referred for liver transplantation, pulmonary hypertension occurs in up to 16%.[16,17]

Prevalence of POPH is similar in male and female i.e 8.2% and 8.0% respectively. Sex was insignificant in POPH with p value of 0. 974. Female sex is more affected in primary pulmonary hypertension but not in portopulmonary hypertension.

Mean age of patients with portopulmonary hypertension were 53.33± 8.3 year, which shows older individual are more at a risk with portal hypertension, as compared to primary pulmonary hypertension in which the mean age at diagnosis is around 45 years, although the onset of symptoms can occur at any age.

BMI was found statistically significant in POPH patients with p-value of 0.01.

A retrospective single center study by Scott E. Friedman and Bruce W. Andrus et al. in 2012 reported 5% of otherwise healthy individuals with a BMI > 30 kg/m^2 had moderate or severe pulmonary hypertension (PASP greater than 50 mm Hg on echocardiogram).[18]

REVEAL registry, the largest pulmonary hypertension database in the United States, indicate a higher prevalence of overweight and obese individuals among those with idiopathic forms of PAH.[19]

Hypertension was significant in POPH with p-value of 0.008. Analysis of REVEAL registery by Bersohn MM et al. in 2013 concluded increased systolic blood pressure and heart rate as high-risk group.[20]

Studies by Schiess R et al. in 2010 concluded that tobacco smoking was significantly more common in PAH and tobacco smoke exposure may be a risk factor for men with pulmonary hypertension[21], but in our study smoking was statistically insignificant with p value of 0.971. RVD was strongly associated with POPH with p value of 0.0001. Maximum patients were in mild to moderate range in the severity of POPH.

This study points towards increasing trends in prevalence of POPH and its association with obesity, hypertension and diabetes. Our region is lacking any study in POPH. We need more study in our different region to get accurate estimation of prevalence of POPH. As severe POPH is a contraindication to liver transplantation, early diagnosis and treatment may help patients in liver transplantation and managing complication of portal hypertension.

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