



STUDY TO EVALUATE ASSOCIATION OF RIGHT VENTRICULAR DYSFUNCTION WITH PORTAL HYPERTENSION.

Cardiology

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ABSTRACT

Background: Pulmonary artery hypertension (PAH) is the most common cause of right heart failure and right ventricular dysfunction (RVD). Portopulmonary hypertension (POPH) is a form of pulmonary arterial hypertension (PAH) associated with portal hypertension with or without underlying chronic liver disease leading to right ventricular dysfunction. The aim of this study is to evaluate prevalence of right ventricular dysfunction and its association with pulmonary artery hypertension, body mass index (BMI), systemic hypertension and smoking.

Material and methods: This is a cross-sectional observation study, it was conducted on 84 patients with portal hypertension. Trans-thoracic echocardiography was done for calculation of PASP (pulmonary artery systolic pressure) and TAPSE (tricuspid annulus plane systolic excursion), TDI (tissue doppler imaging) S' for RVD.

Observation: Prevalence of RVD was 14.28%, in male it was 15.6% and female it was 20.0%. Sex was insignificant in RVD with p value of 0.74. Mean age of POPH patients were 53.33±8.3 year, age was insignificant with p-value 0.86. BMI, hypertension and PAH was found significant in RVD patients with p-value of 0.01, 0.008 and 0.0001 respectively. Smoking was insignificant (P=0.971).

Conclusion: There is association of right ventricular dysfunction with pulmonary hypertension in portal hypertensive patients.

KEYWORDS

Pulmonary artery hypertension (PAH), Portopulmonary hypertension (POPH), right ventricular dysfunction (RVD).

Introduction:

Pulmonary artery hypertension (PAH) is the most common cause of right heart failure and right ventricular dysfunction. Pulmonary hypertension 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/cm⁵ in the settings of portal hypertension [1]. Portopulmonary hypertension (POPH) is a form of pulmonary arterial hypertension (PAH) associated with portal hypertension with or without underlying chronic liver disease leading to right ventricular dysfunction.

Mantz and Craig reported in 1951 on a woman aged 53 with a history of haematemesis who was admitted for hoarseness and dyspnoea and who died from refractory right heart failure following exploratory laparotomy, since then it has been realised that portal hypertension is an important predisposing factor for primary pulmonary hypertension [2].

Data from epidemiological studies revealed that around 2–6% of patients with portal hypertension develop portopulmonary hypertension and its consequence right ventricular dysfunction. [3,4]

In the French Registry for pulmonary hypertension, patients with POPH accounted for 10% of the PAH population, establishing POPH as the fourth cause of PAH, just below idiopathic PAH, PAH associated to congenital heart disease and PAH associated to connective tissue disease. [5]

POPH shares the common pathological changes described for group 1 of pulmonary hypertension — PAH: alterations at the level of distal pulmonary arteries with intimal proliferation, medial hypertrophy, fibrotic changes, plexiform lesions and in situ thrombosis [6,7].

In addition, the presence of portosystemic shunts allows different vascular mediators to bypass liver metabolism creating an imbalance between vasoconstrictor and vasodilator factors at the level of pulmonary vasculature. Mediators such as endothelin-1, thromboxane A₂, Vasoactive Intestinal Peptide (VIP), and serotonin can have direct vasoactive and mitogenic effects and can cause damage to the pulmonary endothelium [8,9].

Liver transplantation is contraindicated in patients presenting with POPH with mPAP >35 mmHg and a PVR N250 dyn/s/cm⁵ due to an increased postoperative mortality [10,11].

The aim of this study is to evaluate prevalence of right ventricular

dysfunction and its association with pulmonary artery hypertension, body mass index (BMI), systemic hypertension and smoking.

Material and methods:

This is a cross-sectional observation study, it was conducted on 84 patients from November 2016 to September 2017. 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 medusae, 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 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).

Table 1. Staging severity of pulmonary hypertension.

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

HRCT was done in those screened positive for pulmonary artery hypertension (PAH) in echocardiography to rule out lung 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. 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.

Observation:

Table-3. Result summarized below.

variables	RVD present (n=12)	RVD absent (n=72)	p-value
age	53.33± 8.3 year	51.58± 9.4	0.86
male	10(15.6%)	54(84.4%)	0.74
female	2(20%)	18(80.%)	0.74
Systemic hypertension	2(40%)	3(60%)	0.008
Smoking	2(8%)	23(92%)	0.971
Pulmonary hypertension	10(83.3%)	2(16.7%)	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	

(RVD- right ventricular dysfunction)

Overall prevalence of right ventricular dysfunction(RVD) was 14.28%%, in male it was 15.6% and female it was 20.0%. Sex was insignificant in RVD with p value of 0.74. Mean age of RVD 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 RVD 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 RVD patients with p- value of 0.01.

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

Smoking prevalence in RVD patients were 8% as compared to 92% in non- in non-portopulmonary hypertensive patients with P-value of 0.971.

Right ventricular dysfunction(RVD) prevalence in pulmonary hypertension and non- pulmonary hypertension group were 83.3% and 16.7% respectively with p-value of 0.0001.

Discussion : In this study overall prevalence of right ventricular dysfunction is 14.28%.

Study by John J Ryan *et al.* in 2015 said that that increased understanding of adrenergic, angiogenic, fibrotic and metabolic derangements in the RV in PAH will offer new therapeutic targets to enhance RV function.[12]

The prevalence of portopulmonary hypertension 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%.[13]

Study by Ramsay M *et al.* in 2010 concluded that in patients with portal hypertension a pathological state exists in which changes in the pulmonary vasculature cause an increase in pulmonary vascular resistance[14]. The resultant increased work of the right ventricle may cause right heart failure and liver congestion.

Pulmonary arterial hypertension (PAH) is a right heart failure syndrome. In early-stage PAH, the right ventricle tends to remain

adapted to afterload with increased contractility and little or no increase in right heart chamber dimensions. In more advanced stages, RV systolic function cannot remain matched to afterload and dilatation of the right heart chamber progressively develops.

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 leading to right ventricular dysfunction occurs in up to 16%.[16,17]

Prevalence of right ventricular dysfunction in male and female is 15.6% and 20.0% respectively. Sex was insignificant in POPH with p value of 0.974. Female sex is more affected in pulmonary hypertension so the right ventricular dysfunction.

BMI was found statistically significant in right ventricular dysfunction 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/m² 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 and right ventricular dysfunction.[19]

Hypertension was significant in right ventricular dysfunction with p-value of 0.008.

Analysis of REVEAL registry 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 and right ventricular dysfunction[21], but in our study smoking was statistically insignificant with p value of 0.971.

Pulmonary artery hypertension was strongly associated with right ventricular dysfunction with p value of 0.0001.

Conclusion:

This study points towards increasing trends of prevalence of right ventricular dysfunction associated with pulmonary hypertension in portal hypertensive patients. As severe pulmonary hypertension associated with portal hypertension is a contraindication to liver transplantation, early diagnosis and treatment may help patients in liver transplantation.

REFERENCES

- Rodriguez-Roisin R, Krowka MJ, Herve P, Fallon MB. Pulmonary-hepatic vascular disorders (PHD). *Eur Respir J* 2004;24:861–80.
- Mantz FA, Craige E. Portal axis thrombosis with spontaneous porto-caval shunt and resultant cor pulmonale. *Arch Pathol* 1951;52:91–7.
- Castro M, Krowka MJ, Schroeder DR, Beck KC, Plevak DJ, Rettke SR, *et al.* *Mayo Clin Proc* 1996;71:543–51.
- Budhiraja R, Hassoun PM. *Chest* 2003;123:562–7.
- Humbert M, Sitbon O, Chaouat A, Bertocchi M, Habib G, Gressin V, *et al.* Pulmonary arterial hypertension in France: results from a national registry. *Am J Respir Crit Care Med* 2006;173:1023–30.
- Pietra GG, Capron F, Stewart S *et al.* *J Am Coll Cardiol* 2004;43:25S–32S.
- Tuder RM, Abman SH, Braun T, Capron F, Stevens T, *et al.* *J Am Coll Cardiol* 2009;54:S3–9.
- Potres-Aguilar M, Zuckerman MJ, Figueroa-Casas JB, Krowka MJ. *Ann Hepatol* 2008;7:321–30.
- Bernardi M, Gulberg V, Colantoni A, Trevisani F, Gasbarrini A, Gerbes AL. *J Hepatol* 1996;24:161–8.
- Krowka MJ, Mandell MS, Ramsay MA *et al.* *Liver Transplant* 2004;10:174–82.
- Krowka MJ, Plevak DJ, Findlay JY, Rosen CB. *Liver Transplant* 2000;6:443–50.
- John J. Ryan, MD, Jessica Huston, MD. *Can J Cardiol.* 2015 Apr; 31(4): 391–406. 2015 Jan 29. doi: 10.1016/j.cjca.2015.01.023
- Hadengue A, Benhayoun MK, Lebre D, Benhamou JP. *Gastroenterology.* 1991;100:520–8.

14. Ramsay MA, Simpson BR, Nguyen AT, Ramsay KJ, Klintmalm GB. Liver Transplant Surg 1997;3:494-500.
15. National Institutes of Health (NIH) registry : [https:// biolincc.nhlbi.nih.gov/studies/pphreg/](https://biolincc.nhlbi.nih.gov/studies/pphreg/)
16. Plevak D, Krowka M, Rettke S, Dunn W, Southorn P. 1993; 25: 1840.
17. Benjaminov FS, Prentice M, Sniderman KW. Gut 2003; 52: 1355-62
18. B. M. McQuillan, M. H. Picard, M. Leavitt: Circulation, vol. 104, no. 23, pp. 2797-2802, 2001
19. Benza RL, Miller DP, Gomberg-Maitland M et al. REVEAL. Circulation. 2010;122:164-72. [PubMed].
20. Bersohn MM, Turner MP, Chest. 2013 Sep;144(3):959-965. doi: 10.1378/chest.12-2572.
21. Schiess R, Senn O, Chest. 2010 Nov;138(5):1086-92. doi: 10.1378/chest.09-2962. Epub 2010 May 14.