Original Research Article

Study of laboratory parameters in left ventricular diastolic dysfunction in patients with pulmonary arterial hypertension

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Abstract

Background: Pulmonary arterial hypertension (PAH) is defined by right-heart catheterization (RHC) showing precapillary pulmonary hypertension with a mean pulmonary artery pressure (mPAP) of >25 mmHg and a normal pulmonary artery wedge pressure (PCWP) of <15 mmHg. The prevalence of PH in stable COPD varies from 20 to 91% depending on the definition of PH (mPAP > 20 versus >25mmHg), the severity of COPD (forced expiratory volume in the first second: FEV1), and the method of measuring the pulmonary artery pressure (echocardiography versus right heart catheterization) **Amis and objectives:** To study the laboratory parameters in left ventricular diastolic dysfunction in patients with pulmonary arterial hypertension. **Materials and method:** The present study was conducted in the department of Cardiology at Sher-I-KashmirInstitute of Medical Sciences, Soura, Srinagar for the two year duration. Thirty five consecutive patients of any age with different severity of pulmonary arterial hypertension due to chronic obstructive airway disease (emphysema and chronic bronchitis) constituted the study group (Group-I) and were labeled as "cases". Pulmonary arterial hypertension was diagnosed in them as presence of right ventricular systolic pressure of more than or equal to 40mmHg. Thirty five normal subjects who were matched for age and sex constituted the other group (Group-II or "controls"). **Results:** The laboratory parameters of the study group also revealed that cases had higher values of hemoglobin and hematocrit, as compared to the control group. Urea (mg/dl) and Creatinine (mg/dl) were also raised in case groups as compared to control groups and the difference observed was statistically significant. Similarly Bilirubin (mg/dl), AST and ALT were also raised in case group as compared to control with statistically significant difference. Similarly arterial blood gas analysis of the study group also showed that pco2 values were much higher in the cases as compared to the control population. **Conclusion:** Thus we conclude that the laboratory parameters of the study group had higher values of hemoglobin and hematocrit, as compared to the control group. The renal function and liver function was also deranged. A higher cardiothoracic ratio in the cases, along with enlarged mean right pulmonary artery diameter and prominent bronchovascular markings seen on chest x-ray. Obstructive pattern was seen on the pulmonary function tests among the cases.

Key Word: laboratory parameters, left ventricular diastolic dysfunction, pulmonary arterial hypertension

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INTRODUCTION

Pulmonary arterial hypertension (PAH) is defined by right-heart catheterization (RHC) showing precapillary pulmonary hypertension with a mean pulmonary artery pressure (mPAP) of >25 mmHg and a normal pulmonary artery wedge pressure (PCWP) of <15 mmHg[1,2]. The classification of pulmonary hypertension (PH) has gone through a series of changes since the first classification proposed in 1973 which designated only two categories, primary pulmonary hypertension or secondary PH,

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depending on the presence or absence of identifiable causes or risk factors[3,4]. In 1998, a second World Symposium on PH was held in Evian (France) and this classification attempted to create categories of PH that shared similar pathogenesis, clinical features and therapeutic options[5]. This classification allowed defining homogenous groups of patients to conduct clinical trials and to obtain approval for specific PAH therapies worldwide. In 2003, the third World Symposium on PH (Venice, Italy) did not propose major changes. However, the terms idiopathic PAH, familial PAH, and associated PAH were introduced. The other prominent change was to move pulmonary veno-occlusive disease (PVOD) and pulmonary capillary hemangiomatosis (PCH) from separate categories into a single subcategory of PAH. The prevalence of PH in stable COPD varies from 20 to 91% depending on the definition of PH (mPAP > 20 versus >25mmHg), the severity of COPD (forced expiratory volume in the first second: FEV1), and the method of measuring the pulmonary artery pressure (echocardiography versus right heart catheterization)[6-11]. In severe COPD patients with or without resting PH, steady-state exercise may raise pulmonary artery pressure (PAP) to about twice the level of its resting value[12]. In severe COPD activities of daily living such as climbing stairs or walking can induce transient PH. In patients with severe COPD, oxygen saturation may fall during REM sleep by 20–30%[13,14] and PAP may rise by as much as 20mmHg[15]. During an acute exacerbation of COPD, PAP may rise by as much as 20mmHg and return to its baseline after recovery[16,17]. In hemodynamic terms PAP depends upon cardiac output (CO), pulmonary vascular resistance (PVR), and pulmonary artery wedge pressure (PAWP). Resting PH in COPD results predominantly from an elevated PVR whereas PH during exercise results predominantly from an increase in CO in the face of a relatively “fixed” PVR, that is, there is reduced recruitability and distensibility of pulmonary vessels[18]. Hyperinflation increases PVR[19] as well as PAWP[19,20] and PAP[19], particularly during exercise. Traditionally, elevated PVR in COPD has been considered to be the consequence of hypoxic pulmonary vasoconstriction and vascular remodeling, destruction of the pulmonary vascular bed by emphysema, polycythemia, and hyperinflation. Recently, it has been recognized that endothelial dysfunction and systemic inflammation also play key roles in the pathogenesis of PH. In fact it is believed that the initial event in the natural history of PH in COPD could be endothelial dysfunction caused by cigarette smoke[21].

AMIS AND OBJECTIVES

To study the laboratory parameters in left ventricular diastolic dysfunction in patients with pulmonary arterial hypertension

MATERIALS AND METHOD

The present study was conducted in the department of Cardiology at Sher-I-**Kashmir** Institute of Medical Sciences, Soura, Srinagar for the two year duration. Thirty five consecutive patients of any age with different severity of pulmonary arterial hypertension due to chronic obstructive airway disease (emphysema and chronic bronchitis) constituted the study group (Group-I) and were labeled as **"cases".** Pulmonary arterial hypertension was diagnosed in them as presence of right ventricular systolic pressure of more than or equal to **40** mmHg **[22,23].** Thirty five normal subjects who were matched for age and sex constituted the other group (Group-II or **"controls").** The patients in our study were clinically stable and medications such as inhaled steroids, (3-**2** agonists and the ophylline were continued. Complete hemogram including hemoglobin, total leukocyte count, differential leukocyte count, platelet count, and the hematocrit was performed in all the selected patients in both the groups. Liver function tests and Kidney function test was also performed. X-ray chest (PA view) to determine the cardiothoracic ratio, the size of pulmonary arteries and the lung parenchyma was done. Electrocardiograph including all 1**2**leads and Pulmonary function tests to measure Forced Expiratory Volume in first second (FEV1) and Forced Vital Capacity (FVC). The ratio of FEV1 to FVC was noted down. Arterial blood gas analysis to measure the PaO_2, $PaCO_2$, pH and the oxygen saturation was done. All patients and controls were made to undergo two-dimensional and M-mode echocardiography and Doppler examinations by a cardiologist who was blinded to the group status of the individual subjects. The SPSS (Statistical Package for Social Sciences) for Windows (version 10.0) was used for data analysis. The tests used included the student's t-test, the chi-square test and bivariate (Pearson) correlation analysis. All the data are presented as mean±SD unless indicated otherwise. A P value of <0.05 was taken as the criterion of statistical significance.

RESULTS

Table 1: Laboratory parameter in the study population

Parameter	Cases (n=35)	Controls (n=35)	P value
Hb (gm/dl)	13.91±2.78	11.81 ±2.02	0.001
TLC(xl0^{9}L-')	7211.54±1857.75	6288.97±2881.78	0.117
pit count (xl0^{9}L^{-1})	1.93±24.53	1.08±36.48	0.001
Hct (%)	45.37±9.17	35.78±6.03	0.000
Urea (mg/dl)	43.77±23.94	27.29±7.27	0.000
Creatinine (mg/dl)	1.09±0.29	0.87±0.22	0.000
Bilirubin (mg/dl)	1.09±0.52	0.95±1.08	0.000
ASTIU	45.57±19.99	36.46±17.65	0.047
ALT IU	41.91±21.32	31.69±l7.64	0.032
ALPIU	262.23±62.30	323.37±246.69	0.163

Hb=hemoglobin, **TLC=** total leukocyte count, **Plt=** platelet, Hct= hematocrit, **AST=** aspartate aminotransferase, **IU=** international units, **ALT=** alanine aminotransferase, **ALP=**alkaline phosphatise

The laboratory parameters of the study group also revealed that cases had higher values of hemoglobin and hematocrit, as compared to the control group. Urea (mg/dl) and Creatinine (mg/dl) were also raised in case groups as compared to control groups and the difference observed was statistically significant. Similarly Bilirubin (mg/dl), AST and ALT were also raised in case group as compared to control with statistically significant difference.

Table 2: Arterial blood gas parameters in the study population

	Cases (n=35)	Controls (n=35)	P value
pH	*7.38±9.92*	*7.38±2.25*	*0.792*
$Pa0_2$ (mmHg)	*67.60±12.38*	*70.25±6.75*	*0.271*
$PaC0_2$ (mmllg)	*52.29±9.25*	*39.13±3.10*	*0.000*
$Sa0_2$ (%)	*87.05±8.09*	*92.86±3.31*	*0.000*

$PaCO_2$= partial pressure of carbon dioxide in arterial blood, PaO_2= partial pressure of oxygen in arterial blood, $Sa(J_2$ - saturation of oxygen in arterial blood Similarly arterial blood gas analysis of the study group also showed that pco2 values were much higher in the cases as compared to the control population.

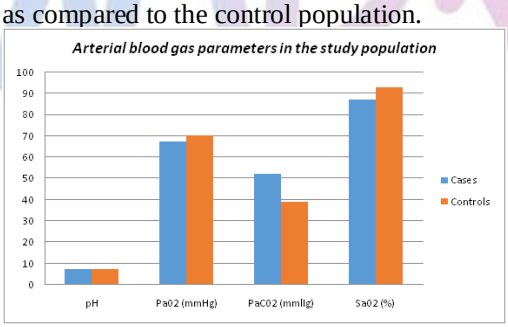

Table3: Chest X-ray findings in the study population.

		Cases (n=35)	Controls (n=35)	P value
	CTR (%)	0.55±6.83	0.49±5.1 5	0.000
	RPA(mm)	I5.57±1.59	12.6±1.10	0.000
Parenchyma	Normal n (%)	14 (40%j	34 (97.14%)	
	Consolidation, n (%)	6(17.1 %)	1 (2.85%)	0.000
	Prominent BVM, n(%)	15 (42.85%)	0	

CTR=cardiothoracic ratio; **RPA=**right pulmonary artery; **BVM=**bronchovascular markings

The chest x-ray findings were showing a higher cardiothoracic ratio in the cases than controls, along with enlarged mean right pulmonary artery diameter and prominent bronchovascular markings.

Table 4: ECG findings in the study population

		Cases (n=35)	Controls (n=35)	P value
Rate (per minute)		82.66±9.64	83.60±8.88	0.672
Axis	Normal, n(%)	0	35 (100%)	-
	Right, n(%)	35 (100%)	0	
P Pulmonale, n(%)		29 (82.85%)	0	0.000
RVH, n(%)		34 (97.14%)	0	0.000

RVH=right ventricular hypertrophy

The electrocardiographic findings in the study group revealed right axis deviation, P pulmonale and right ventricular hypertrophy in almost all the cases while controls (35) had normal axis with no P pulmonale and right ventricular hypertrophy.

Table 5: Pulmonary function tests in the study population

PFT	Cases (n=35)	Controls (n=35)	P value
FEV1	0.554±0.223	0.816±0.169	0.000
FVC (L)	0.874±0.262	1.031±0.192	0.006
FEV1/FVC (%)	62.029±9.392	79.086±5.393	0.000

FEV1=forced expiratory volume in first second; **FVC=**forced vital capacity

The pulmonary function tests were also carried out in the study population which revealed that cases showed an obstructive pattern as compared to the controls. The FEV1/ FVC ratio was lower in cases than controls (62.029±9.397 vs 79.086±5.393, respectively, p 0.000).

DISCUSSION

The present study was conducted to observe the laboratory parameters in left ventricular diastolic dysfunction in patients with pulmonary arterial hypertension due to COPD. A total of 70 subjects (35 patients with chronic obstructive airway disease and 35 apparently healthy persons) were studied by detailed two-dimensional and Doppler examination. The necessary laboratory investigations and tests were performed and were comared with control group. It was observed that the laboratory parameters of the study group had higher values of hemoglobin and hematocrit, as compared to the control group. Urea (mg/dl) and Creatinine (mg/dl) were also raised in case groups as compared to control groups and the difference observed was statistically significant. Similarly Bilirubin (mg/dl), AST and ALT were also raised in case group as compared to control with statistically significant difference. Similarly arterial blood gas analysis of the study group also showed that pco2 values were much higher in the cases as compared to the control population. Arterial oxygen tension is normal or only slightly lower than normal at rest and arterial carbon dioxide tension is decreased because of alveolar hyperventilation. COPD as a cause of hypoxic PH is diagnosed on the evidence of irreversible airflow obstruction together with increased residual volumes and reduced diffusion capacity for carbon monoxide and normal or increased carbon dioxide tension. A decrease in lung volume together with a decrease in diffusion capacity for carbon monoxide may indicate a diagnosis of interstitial lung disease. The chest x-ray findings were showing a higher cardiothoracic ratio in the cases than controls, along with enlarged mean right pulmonary artery diameter and prominent bronchovascular markings. According to Rich S, *et al*[24] in 90% of patients with IPAH the chest radiograph is abnormal at the time of diagnosis. Findings include central pulmonary arterial dilatation, which contrasts with 'pruning' (loss) of the peripheral blood vessels. Right atrium and RV enlargement may be seen in more advanced cases. The chest radiograph allows associated moderate-to-severe lung diseases or pulmonary venous hypertension due to left heart disease to be reasonably excluded. Overall, the degree of PH in any given patient does not correlate with the extent of radiographic abnormalities. The electrocardiographic findings in the study group revealed right axis deviation, P pulmonale and right ventricular hypertrophy in almost all the cases while controls (35) had normal axis with no P pulmonale and right ventricular hypertrophy. The ECG may provide suggestive or supportive evidence of PH by demonstrating RV hypertrophy and strain, and right atrial dilatation. RV hypertrophy on ECG is present in 87% and right axis deviation in 79% of patients with IPAH.[24] The absence of these findings does not exclude the presence of PH nor does it exclude severe haemodynamic abnormalities. The ECG has insufficient sensitivity (55%) and specificity (70%) to be a screening tool for detecting significant PH. Ventricular arrhythmias are rare. Supraventricular arrhythmias may be present in advanced stages, in particular atrial flutter, but also atrial fibrillation, which almost invariably leads to further clinical deterioration.[25] The pulmonary function tests were also carried out in the study population which revealed that cases showed an obstructive pattern as compared to the controls. The FEV1/ FVC ratio was lower in cases than controls (62.029±9.397 vs 79.086±5.393, respectively, p 0.000).Pulmonary function

tests and arterial blood gases will identify the contribution of underlying airway or parenchymal lung disease. Patients with PAH usually have decreased lung diffusion capacity for carbon monoxide (typically in the range of 40–80% predicted) and mild to moderate reduction of lung volumes. Peripheral airway obstruction can also be detected.

CONCLUSION

Thus we conclude that the laboratory parameters of the study group had higher values of hemoglobin and hematocrit, as compared to the control group. The renal function and liver function was also deranged. A higher cardiothoracic ratio in the cases, along with enlarged mean right pulmonary artery diameter and prominent bronchovascular markingsseen on chest x-ray. Obstructive pattern was seen on the pulmonary function tests among the cases.

REFERENCES

1. Rubin LJ: Primary pulmonary hypertension. N Engl J Med 1997, 336(2):111–7.
2. Simonneau G, *et al*: Updated clinical classification of pulmonary hypertension. J Am Coll Cardiol 2009, 54(1 Suppl):S43–54.
3. Wagenvoort CA, Wagenvoort N: Primary pulmonary hypertension: a pathological study of the lung vessels in 156 clinically diagnosed cases. Circulation 1970, 42:1163–84.
4. Hatano S, Strasser T: Primary Pulmonary Hypertension. Report on a WHO meeting. October 15–17, 1973. Geneva: WHO; 1975.
5. Fishman AP: Clinical classification of pulmonary hypertension. Clin Chest Med 2001, 22(3):385–91. vii.
6. B. Burrows, L. J. Kettel, A. H. Niden, M. Rabinowitz, and C. F. Diener, "Patterns of cardiovascular dysfunction in chronic obstructive lung disease," The New England Journal of Medicine, vol. 286, no. 17, pp. 912–918, 1972.
7. E. Weitzenblum, A. Sautegeau, and M. Ehrhart, "Long-term course of pulmonary arterial pressure in chronic obstructive pulmonary disease," The American Review of Respiratory Disease, vol. 130, no. 6, pp. 993–998, 1984.
8. M. Oswald-Mammosser, M. Apprill, P. Bachez, M. Ehrhart, and E.Weitzenblum, "Pulmonary hemodynamics in chronic obstructive pulmonary disease of the emphysematous type," Respiration, vol. 58, no. 5-6, pp. 304–310, 1991.
9. S. M. Scharf, M. Iqbal, C. Keller *et al*., "Hemodynamic characterization of patients with severe emphysema," American Journal of Respiratory and Critical CareMedicine, vol. 166, pp. 314–322, 2002.
10. G. Thabut, G. Dauriat, J. B. Stern *et al*., "Pulmonary hemodynamics in advanced COPD candidates for lung volume reduction surgery or lung transplantation," Chest, vol. 127, no. 5, pp. 1531–1536, 2005.
11. M. J. Cuttica, R. Kalhan, O. A. Shlobin *et al*., "Categorization and impact of pulmonary hypertension in patients with advanced COPD," Respiratory Medicine, vol. 104, no. 12, pp. 1877–1882, 2010.
12. E.Weitzenblum, "Chronic cor pulmonale," Heart, vol. 89, no. 2, pp. 225–230, 2003.
13. J. R. Catterall, N. J. Douglas, and P. M. A. Calverley, "Transient hypoxemia during sleep in chronic obstructive pulmonary disease is not a sleep apnea syndrome," The American Review of Respiratory Disease, vol. 128, no. 1, pp. 24–29, 1983. Pulmonary Medicine 13
14. E. C. Fletcher and D. C. Levin, "Cardiopulmonary hemodynamics during sleep in subjects with chronic obstructive pulmonary disease. The effect of short- and long-term oxygen," Chest, vol. 85, no. 1, pp. 6–14, 1984.
15. G. Coccagna and E. Lugaresi, "Arterial blood gases and pulmonary and systemic arterial pressure during sleep in chronic obstructive pulmonary disease," Sleep, vol. 1, no. 2, pp. 117–124, 1978.
16. A. S. Abraham, R. B. Cole, I. D. Green, R. B. Hedworth-Whitty, S.W. Clarke, and J.M. Bishop, "Factors contributing to the reversible pulmonary hypertension of patients with acute respiratory failure studies by serial observations during recovery," Circulation Research, vol. 24, no. 1, pp. 51–60, 1969.
17. E. Weitzenblum, A. Loiseau, C. Hirth, R. Mirhom, and J. Rasaholinjanahary, "Course of pulmonary hemodynamics in patients with chronic obstructive pulmonary disease," Chest, vol. 75, no. 6, pp. 656–662, 1979.
18. K. Kubo, R. L. Ge, T. Koizumi *et al*., "Pulmonary artery remodelling modifies pulmonary hypertension during exercise in severe emphysema," Respiration Physiology, vol. 120, no. 1, pp. 71–79, 2000.
19. J. L. Wright, L. Lawson, P. D. Pare *et al*., "The structure and function of the pulmonary vasculature in mild chronic obstructive pulmonary disease. The effect of oxygen and exercise," The American Review of Respiratory Disease, vol. 128, no. 4, pp. 702–707, 1983.
20. J. Butler, F. Schrijen, A. Henriquez, J. M. Polu, and R. K. Albert, "Cause of the raised wedge pressure on exercise in chronic obstructive pulmonary disease," The American Review of Respiratory Disease, vol. 138, no. 2, pp. 350–354, 1988.
21. J. A. Barber`a and I. Blanco, "Pulmonary hypertension in patients with chronic obstructive pulmonary disease: advances in pathophysiology and management," Drugs, vol. 69, no. 9, pp. 1153–1171, 2009.
22. Padity E, *et al.* ECHO diagnosis of pulmonary hypertension in chronic lung diseases. Phrenology 1992; 46: 131-140.
23. Schiller NB, Shah P,. *Et al.* Recommendations for quantization of left ventricle by two dimensional echocardiography. American Society of Echocardiography. J Am Soc Echocardiography 1989; 2: 358-367.
24. Rich S, Dantzker DR, Ayres SM, Bergofsky EH, Brundage BH, Detre KM, Fishman AP, Goldring RM, Groves BM, Koerner SK. Primary pulmonary hypertension. A national prospective study. Ann Intern Med 1987; 107: 216–223.
25. Tongers J, Schwerdtfeger B, Klein G, Kempf T, Schaefer A, Knapp JM, Niehaus M, Korte T, Hoeper MM. Incidence and clinical relevance of supraventricular tachyarrhythmias in pulmonary hypertension. Am Heart J 2007; 153: 127–132.

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