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Original Article

Pulmonary Arterial Hypertension: Clinical and Echocardiographic Correlated Study

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ABSTRACT

Introduction: *Pulmonary arterial hypertension (PAH) is a type of high pressure that occurs in the right side of the heart and in the arteries that supply blood to the lungs (pulmonary arteries). It has an estimated prevalence of 15-50 cases per million. Idiopathic PAH has an annual incidence of 1-2cases per million people in the US and Europe and is 2-4 times more common in women than in men. The mean age at diagnosis is around 45 years. It is unfortunately most frequently diagnosed when patients have reached an advanced stage of the disease (WHO functional class III and IV). A combination of lifestyle changes, medicines and surgeries may alter the progression of the disease but unfortunately, treatment cannot reverse the symptoms and damage caused by PAH.*

Aims and Objectives: *To study the clinical features of PAH and its echocardiographic changes and also to evaluate the relationship between echocardiographic findings and clinical features in patients with PAH.*

Methods: *Prospective observational study of 50 patients conducted at MGM Medical College and Hospital, Navi Mumbai between November 2013 to October 2015 for a period of almost two years.*

Results and Conclusion: *The study conducted to evaluate clinical and echocardiographic correlation in patients of PAH showed that the incidence of PAH is higher in females. It is more common in the higher age group. Dyspnoea is the most common presenting symptom. Maximum patients had TR jet changes followed by RA/RV (Right Atrium/Right Ventricle) changes in echocardiography. Maximum patients had moderate PAH in accordance with echocardiographic changes. Statistically significant co-relation was found between ABG and echocardiographic changes in the study.*

Keywords: *Pulmonary arterial hypertension, Dyspnoea, Elevated JVP, LoudP2, TR jet changes, RA/RV changes, ABG.*

Introduction

Pulmonary arterial hypertension (PAH) is a rare, progressive disorder characterized by high pressure that occurs in the pulmonary arteries that supply blood from the right ventricle to the lungs. PAH occurs when the pulmonary arteries thicken or grow rigid which makes blood flow more difficult. Signs and symptoms of pulmonary arterial hypertension occur when increased pressure cannot fully overcome the elevated resistance. This results in decreased pulmonary venous blood flow with reduced left atrial and ventricular filling and decreased cardiac output.

Shortness of breath (dyspnea) during exertion and fainting spells are the most common symptoms of pulmonary arterial hypertension. Other symptoms include dizziness, swelling (edema) of the ankles or legs, chest pain, and a rapid pulse.A combination of lifestyle changes, medicines, and surgeries may alter the progression of the disease. Unfortunately, treatment cannot reverse the symptoms and damage caused by PAH. It is a severe disease that progresses rapidly and usually causes right heart failure. In many cases, PAH is fatal and leads to death.

Although Pulmonary arterial hypertension (PAH) is a rare disease, with an estimated prevalence of 15-50 cases per million,[1] the prevalence of PAH in certain at-risk groups is substantially higher. Idiopathic PAH (IPAH) has an annual incidence of 1-2 cases per million people in the US and Europe and is 2-4 times more common in women than in men.[2,3] The mean age at diagnosis is around 45 years, although the onset of symptoms can occur at any age.

The true relative prevalence of heritable PAH (HPAH) and associated PAH (APAH) is unknown, thus it is likely that IPAH accounts for at least 40% of cases of PAH, with APAH accounting for the majority of the remaining cases. Due to the non-specific nature of the symptoms, PAH is unfortunately most frequently diagnosed when patients have reached an advanced stage of disease (WHO Functional Class III and IV). The clinical and echocardio-graphic abnormalities are common during this phase of pulmonary arterial hypertension.

WHO functional classification of PAH

Class I: Patients without limitation of physical activity. Ordinary physical activity does not cause undue dyspnoea or fatigue, chest pain or near syncope.

Class II: Patients with slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity causes undue dyspnoea or fatigue, chest pain or near syncope.

Class III: Patients with marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes undue dyspnoea or fatigue, chest pain or near syncope.

Class IV: Patients with inability to carry out any physical activity without symptoms. They manifest signs of right heart failure. Dyspnoea and/or fatigue may even be present at rest. Discomfort is increased by any physical activity.

Aims and Objectives

1. To study the clinical features of PAH
2. To study the echocardiographic changes in PAH.
3. To evaluate the relationship between echocardiographic findings & clinical features in patients with PAH.

Materials and Methods

The present study was a prospective observational study conducted at MGM Medical College and Hospital, Navi Mumbai. 50 patients fulfilling the inclusion criteria were enrolled in the study. It was conducted between November 2013 to October 2015 for a period of two years. **Inclusion Criteria :** 1)Pulmonary artery systolic pressure >30 mm Hg on 2DEcho. 2)Newly diagnosed cases not on treatment. 3)Age >18 years. **Exclusion Criteria :** 1)Old cases of PAH already on treatment.

Methodology

The patient enrolment was done on the basis of the inclusion criteria. After taking their due consent, the patients were evaluated on the basis of history, clinical features, laboratory investiga-tions and echocardiography and the results were interpreted. Echocardiographic changes were evaluated on the basis of parameters like Ejection fraction, TR (Tricuspid Regurgitation) jet velocity changes, RA/ RV changes and PASP (Pulmonary Artery Systolic Pressure).

Results

The age group and sex wise distribution of over all 50 patients of Pulmonary arterial hypertension included in this study, shows that 66% were female patients and remaining 34% male patients .

Maximum number of patients i.e 76% were in the age group above 30 years. The number of patients developing PAH according to NYHA Class showed maximum percentage was seen in class 3 (48%) followed by class 4 (40%) and class 2 (12%), whereas there were no patients belonging to class 1.

Table 1

No of Patients developing PAH according to NYHA CLASS

CLASS	N=50	PERCENTAGE%
1	ZERO	0%
2	6	12%
3	24	48%
4	20	40%

Table – 2 : Co-relation of various clinical features with severity of PASP.

		PASP						
Clinical features	Condition	Mild (%)	Moderate (%)	Severe (%)	Total (%)	Chi square test	P-value	Significant at 5% level
COUGH	Absent	6	14	13	33(66%)			
	Present	4	7	6	17(34%)	0.214	0.898	NOT
SYNCOPE	Absent	7	16	13	36(72%)	0.323	0.851	NOT
	Present	3	5	6	14(28%)			
DYSPNEA	Absent	5	12	11	28(56%)	0.185	0.912	NOT
	Present	5	9	8	22(44%)			
PEDAL EDEMA	Absent	8	17	13	38(76%)	0.968	0.616	NOT
	Present	2	4	6	12(24%)			
ELEVATED JVP	Absent	10	14	11	35(70%)	5.723	0.057	NOT
	Present	0	7	8	15(30%)			
LOUD P2	Absent	9	12	15	36(72%)	4.361	0.113	NOT
	Present	1	9	4	14(28%)			
SPLIT S2	Absent	9	17	12	38(76%)	3.075	0.215	NOT
	Present	1	4	7	12(24%)			
PARASTERNAL HEAVE	Absent	10	15	15	40(80%)	3.477	0.176	NOT
	Present	0	6	4	10(20%)			

NOTE : JVP – Jugular Venous Pressure, P2 – Pulmonary component of second heart sound, S2 – Second heart sound

Table – 3: Co-relation of various investigations with severity of PASP.

		PASP						
Investigation Features	Condition	Mild (%)	Moderate (%)	Severe (%)	Total (%)	Chi square test	P-value	Significant at 5% level
ABG	Abnormal	0	4	4	8(16%)	6.538	0.038	YES
	Normal	10	17	15	42(84%)			
6MWT	Abnormal	2	12	10	24(48%)	4.008	0.135	NOT
	Normal	8	9	9	26(52%)			
CHEST XRAY	Abnormal	2	12	10	24(48%)	4.008	0.135	NOT
	Normal	8	9	9	26(52%)			
ECG	Abnormal	8	13	11	32(64%)	1.459	0.482	NOT
	Normal	2	8	8	18(36%)			

NOTE : ECG – Electrocardiogram, 6MWT – 6 Minute Walking Test, ABG – Arterial Blood Gas analysis

Graph - 1

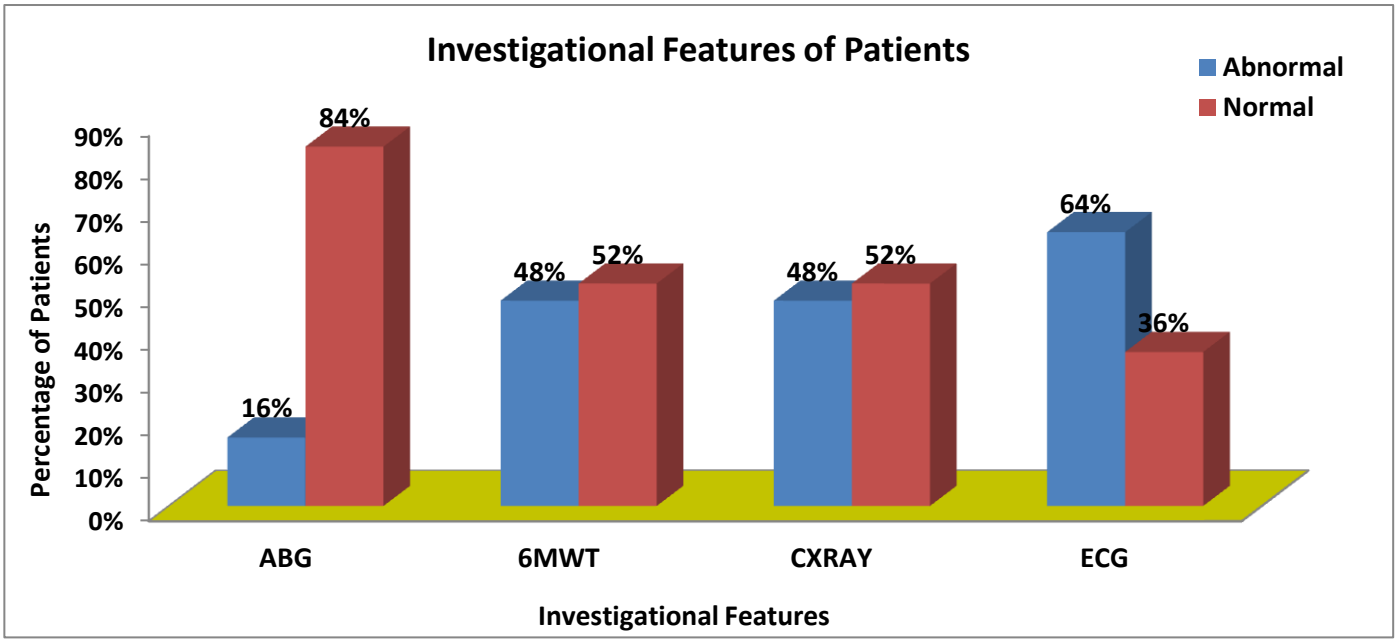

Table - 4 : Co-relation of clinical features with 2DECHO findings and severity of PASP.

Clinical Features			PASP			
		ECHO	Mild	Moderate	Severe	Total
COUGH	Present	E1E2E3E4	1	2	0	3
		Normal or <4 abnormal ECHO parameters	3	5	6	14
SYNCOPE	Present	E1E2E3E4	0	0	2	2
		Normal or <4 abnormal ECHO parameters	3	5	4	12
DYSPNOEA	Present	E1E2E3E4	0	2	2	4
		Normal or <4 abnormal ECHO parameters	5	7	6	18
PEDAL EDEMA	Present	E1E2E3E4	0	3	1	4
		Normal or <4 abnormal ECHO parameters	2	1	5	8

EJVP	Present	E1E2E3E4	0	3	4	7
		Normal or <4 abnormal ECHO parameters	0	4	4	8
Clinical Features				PASP		
		2DECHO	Mild	Moderate	Severe	Total
LOUDP2	Present	E1E2E3E4	0	3	3	6
		Normal or <4 abnormal ECHO parameters	1	6	1	8
SPLITS2	Present	E1E2E3E4	0	1	3	4
		Normal or <4 abnormal ECHO parameters	1	3	4	8
PARA-STERNAL HEAVE	Present	E1E2E3E4	0	3	3	6
		Normal or <4 abnormal ECHO parameters	0	3	1	4

NOTE : ECHO : E1 = RA/RVD , E2= EF , E3 = TR JET and E4 = M.MODE

Table - 4 shows the clinical features co-related with PASP and 2DECHO parameters and which were abnormal in relation to those parameters. So that only 3(6%) patients having cough have all four abnormal echo parameters like RA/RVD, EF, TR JET and M. Mode. Similarly 2(4%), 4 (8%), 4(8%), 7(14%), 6(12%), 4(8%) and 6 (12%) are all abnormal echo parameters of respective clinical features like syncope, dyspnea, pedal edema, elevated jvp, Loudp2, Splits2 and parasternal heave .

Table – 5 : Co-relation of investigations with 2DECHO findings and severity of PASP.

Investigational features			PASP			
		ECHO	Mild	Moderate	Severe	Total
ABG	Abnormal	E1E2E3E4		2	1	3
		Normal or <4 abnormal ECHO parameters		2	3	5
6MWT	Abnormal	E1E2E3E4		3	4	7
		Normal or <4 abnormal ECHO parameters	2	6	9	17
CXRAY	Abnormal	E1E2E3E4		3	4	7
		Normal or <4 abnormal ECHO parameters	2	9	6	17
ECG	Abnormal	E1E2E3E4		3	3	6
		Normal or <4 abnormal ECHO parameters	8	10	8	26

NOTE : ECHO : E1 = RA/RVD , E2= EF , E3 = TR JET and E4 = M.MODE
RA/RVD – Right Atrial/Right Ventricular Diameter ; EF – Ejection Fraction ; TR JET – Tricuspid Regurgitation Jet.

Table - 5 shows the investigations co-related with PASP and 2DEcho parameters and which were abnormal in relation to those parameters. Thus only 3(6%) patients had all echo parameters abnormal for ABG, similarly 7(14%), 7(14%) and 6(12%) respectively for 6MWT, Chest-Xray and ECG investigations had all abnormal echo parameters.

Discussion

Pulmonary hypertension is defined by right-heart catherisation (RHC) as showing a mean pulmonary arterial pressure (mPAP) of >25mmHg and a pulmonary capillary wedge pressure (PCWP) of <15mmHg.

It is classified in a study Simonneau G et al[1] as Group 1 : i)Idiopathic PAH, ii)Heritable PAH, iii)Drug and toxin-induced PAH, iv)Associated PAH secondary to connective tissue diseases, Human immunodeficiency virus(HIV) infection, portal hypertension, congenital heart disease (CHD), schistosomiasis and chronic haemolytic anaemia, v)Persistent pulmonary hypertension of the newborn.

Group 2: Pulmonary hypertension due to left heart disease secondary to valvular lesion, diastolic dysfunction or systolic dysfunction.

Group 3: Pulmonary hypertension due to lung diseases and /or hypoxemia secondary to Chronic obstructive pulmonary disease (COPD), Interstitial lung disease (ILD), other pulmonary diseases with mixed restrictive and obstructive pattern, sleep disordered breathing, alveolar hypoventilation disorders, chronic exposure to high altitudes and developmental abnormalities.

Group 4: Chronic thromboembolic pulmonary hypertension (CTEPH).

Group 5: i) PH with unclear multifactorial mechanisms, ii)Haematological disorders such as myeloproliferative disorders, splenectomy etc, iii)Systemic disorders like sarcoidosis, pulmonary langerhans cell histiocytosis, lymphangioleiomyomatosis etc,

iv) Metabolic disorders like glycogen storage disorders, gaucher's disease etc,

v) Others like tumoral obstruction, chronic renal failure on dialysis, fibrosing mediastenitis etc.

In the present study 50 patients of PAH were included and various parameters were compared with other studies for co-relation. Maximum number of patients were females around 66% against 34% males. Similar findings of female predominance have been reported in various other studies by Shapiro et al[4], David et al and Raymond et al[5,6] and Charles D et.[7] In our study, the mean age was 50±10 which is comparable to other studies by Shapiro et al[4], David et al[5] and Raymond et al.[6]

Maximum patients in the present study belonged to the NYHA grade III (48%) and grade IV (40%), also the most common symptom at presentation was dyspnea on exertion seen in 44% patients, followed by syncope and others. These findings were comparable to findings in a study by Rich S et al.[8]

Our study shows that all the clinical features with regards to pulmonary artery systolic pressure (PASP) are not statistically significant at 5% level i.e P>0.05.These clinical features are cough, syncope, dyspnoea, pedal edema, elevated JVP, loud P2, split S2 and parasternal heave. Maximum patients had moderate severity (50-70mmHg)of pulmonary hypertension in our study population as compared to other studies by David et al[5], Raymond et al[6] and Rich et al.[8]

6MWT was abnormal in 48% patients walking ≤ 332mt as compared to Sitbon et al[11] where it was reported that a 6MWD (6 Minute Walking Distance) of ≤ 250 m was associated with a poor outcome. Miyamoto et al[9] studied 43 patients with IPAH where patients walking < 332 m had a significantly lower survival rate than those walking farther than 332 m.

In co-relation to pulmonary artery systolic pressure (PASP), except ABG which is statistically significant at 5% level i.e., P<0.05 , all other investigations like 6MWT , Chest XRay and ECG were not statistically significant i.e. P>0.05. But investigation reports also show that maximum 64% patients had abnormality in ECG whereas 48%, 48% and 16% were abnormal in 6MWT, Chest-XRay and ABG respectively.

Most of the patients had TR jet velocity changes(62%), followed by RA/RV changes (dilatation), low ejection fraction and M-Mode changes. Recently, Haeck et al[10], in a series of 142 patients with PH of different etiologies (53 [37%] with PAH), observed that RV longitudinal peak systolic strain (19%) was significantly associated

with worse New York Heart Association functional class and all-cause mortality (37 patients died during a median follow-up period of 2.6 years).

In contrast to changes with PASP only 3(6%) patients having cough had all four abnormal 2DEcho parameters like RA/RVD, EF , TR JET and M. Mode. Similarly 2(4%) , 4(8%) , 4(8%), 7(14%) , 6(12%) ,4(8%) and 6(12%) patients were having all four abnormal 2DEcho parameters for the respective clinical features like syncope, dyspnea , pedal edema ,elevated JVP , loud P2, split S2 and parasternal heave. Only 5(10%) patients had abnormal ABG with all abnormal echo parameters , similarly 7(14%) , 7(14%) and 6(12%) respectively for 6MWT, CXRAY and ECG investigations were having all echo parameters abnormal.

As a whole, clinical features in our study were not significant for p value, but investigation in correlation to PASP in patients of PAH had a significant co-relation for ABG. Patients having echocardiographic changes mostly had either moderate or severe pulmonary arterial hypertension. The correlative study on 2DEcho and clinically assessed patients of PAH was lacking as a whole.

Summary and Conclusion

Present study was conducted with aim to evaluate clinical and echocardiographic correlation in patients of PAH. Incidence of PAH was higher in females and it was more common in higher age group. Dyspnoea was the most presenting symptom followed by cough, syncope and pedal edema. ECG changes followed by Chest X-Ray and 6MWT were contributional in diagnosis in our study. Maximum patients had moderate PAH in accordance with echocardiographic changes. Maximum patients had TR jet changes followed by RA /RV changes in echocardiography. Correlation was present in patients' ABG in association with echocardiographic changes in patients with PAH.

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