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Studying Pulmonary Arterial Hypertension in Patients With Patterns of Interstitial Lung Disease Using Computerized Tomography (CT) Amongst the Population of Tertiary Care Hospitals in Hyderabad

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Abstract
Pulmonary hypertension (PH) is defined on Right Heart Catheterization (RHC), as a resting mean pulmonary artery pressure (m PAP) greater than or equal to 25 mmHg. Interstitial Lung disease (ILD) is one of the common causes of pulmonary hypertension and the presence of pulmonary hypertension in this setting is an unfavorable prognostic sign. The above study was conducted at Department of Radiology of tertiary care hospital. Total of 133 patients fulfilling the inclusion and exclusion criteria were included in the study. All HRCTs were performed on a 64-slice DUAL source multi-detector CT (MDCT) scanner (GE 750 HD). Sections were obtained with 0.625 or 1.25mm collimation at 1.25mm intervals and reconstructed using a high spatial frequency algorithm. Most of the patients in our study are between 30-70 years of age. Out of 135 patients with ILD, 53 patients were UIP and 33 patients with NSIP patterns, 4 histopathologically proved Sarcoidosis cases. PAH is more prevalent in Fibrotic NSIP than UIP. There is significance between ground glass opacities and emphysema in patients with PAH. It was found that there is increased prevalence of PAH in NSIP (Fibrotic NSIP>Cellular NSIP) more than the most common UIP pattern.

INTRODUCTION

Pulmonary hypertension (PH) is defined by Right Heart Catheterization (RHC), as a resting mean pulmonary artery pressure (m PAP) greater than or equal to 25 mmHg[1,2]. PH commonly complicates lung disease and chronic hypoxia, such as Idiopathic pulmonary fibrosis (IPF). When present in lung disease, PH is associated with a poor outcome[3]. Interstitial Lung disease (ILD) is one of the common causes of pulmonary hypertension and the presence of pulmonary hypertension in this setting is an unfavorable prognostic sign[4-6]. The presence of PH has major implications for a patient with ILD in terms of exercise capacity and mortality[7,8]. Early and accurate detection of PH is therefore important for prognostication, timing of referral for transplantation, and possible entry into clinical trials. Studies investigating the occurrence of PH in ILD have focused on specific population groups, such as lung transplant candidates with idiopathic pulmonary fibrosis (IPF)[9,10] and patients with sarcoidosis (11,12) or scleroderma-related ILD[13,14].

The prevalence of PH in patients with ILD varies greatly according to the underlying disease, the severity of the disease and the diagnostic approach used to identify PH.

The gold standard investigation for confirming PH in this population, as in any patient, remains right heart catheterization (RHC). However, performing RHC in patients with IPF is not without risk in what is an older population, often with serious co-morbidities. Informed referral for RHC, based on clinical signs and non-invasive tests suggestive of PAH, is desirable. Unfortunately, clinical signs of PAH are often unreliable in patients with any chronic respiratory disease and standard tests such as echocardiography can be surprisingly inaccurate[15,16]. There remains the need, therefore, to further interrogate non-invasive methods of detection of PH in patients with ILD. Many studies have done a comparison of the pulmonary artery with IPF and COPD but none have measured the Right and Left pulmonary artery along with dPA and rPA in different patterns of ILD.

The study aims to find out the prevalence of pulmonary arterial hypertension in patients with patterns of interstitial lung disease using Computerized Tomography (CT) amongst the population of tertiary care hospitals in Hyderabad.

MATERIALS AND METHODS

Study Place: The above study was conducted at the Department of Radiology, Continental hospitals, Hyderabad, Telangana for period of 2 years.

Study Design: Prospective cross-sectional study.

Inclusion Criteria: Patients who underwent the high resolution CT scan of lung during the study period in Continental hospitals, Hyderabad and diagnosed with HRCT patterns of Interstitial Lung Disease.

Exclusion Criteria: Patients w already diagnosed with pulmonary hypertension, cardiac disease, having previous infection history like Tuberculosis, patient treated with chemo and radiotherapy, whose HRCT chest is normal and with other serious co-morbidities.

Sample Size: The sample size taken for the study was 133 patients.

Data Analysis: The collected data was analysed with IBM.SPSS statistics software 23.0 Version MS Excel coding. Level of significance was set at $p<0.05$P value <0.05 was considered to be significant. $p<0.0001$ was considered to be highly significant.

Ethical Consideration: The Institutional Ethical Committee permission was obtained before starting the study.

The study proforma was completed for every patient included in the study. The demographic details including name, Age, Sex and other preoperative investigation findings were noted. MDCT was performed for the study population. All HRCTs were performed on a 64-slice DUAL source multi-detector CT (MDCT) scanner (GE 750 HD). Sections were obtained with 0.625 or 1.25mm collimation at 1.25mm intervals and reconstructed using a high spatial frequency algorithm. All patients were scanned from lung apices to lung bases at full suspended inspiration using standard exposure parameters (90 mA and 120kVp) in a single breath hold. Contrast study was done in few cases where indicated, with 80-100 ml (1ml per kg) of non-ionic iodinated contrast material at 2-5 ml / sec. Supine and prone, inspiratory and expiratory scans were done when indicated. All the scans were viewed with appropriate window settings (1400-1500 HU) and window level (-500-700 HU). The results were analyzed, studied and also compared with similar studies of the past with elucidation of the diseases where HRCT gave a specific diagnosis.

RESULTS AND DISCUSSIONS

Out of 135 patients with various types of ILD, the most common pattern found in our study is Usual Interstitial Pneumonia (53) around 40 percent and sarcoidosis is the least prevalent. The above table shows that the fibrotic type of NSIP is more prevalent than the cellular NSIP type.

Out of 135 patients in the study, which includes males (61) and females (74) , the percentage of Interstitial Lung Disease is high among females which is about 54.8% and the percentage of males getting affected are 45.2%.

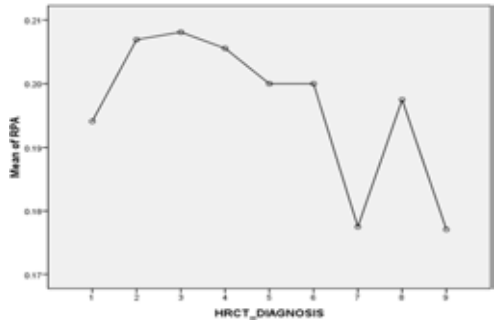

Fig. 1: Comparison between RPAD and HRCT diagnosed ILD

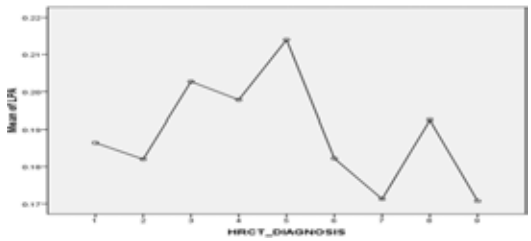

Fig. 2: Comparison between LPAD and HRCT diagnosed ILD

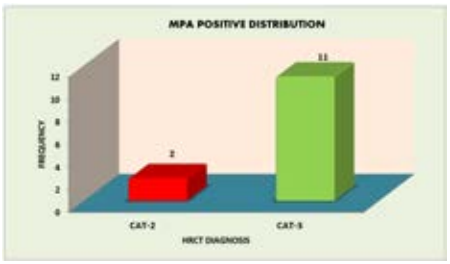

Fig. 3: Bar diagram correlating dPA>22mm with fibrotic and cellular NSIP

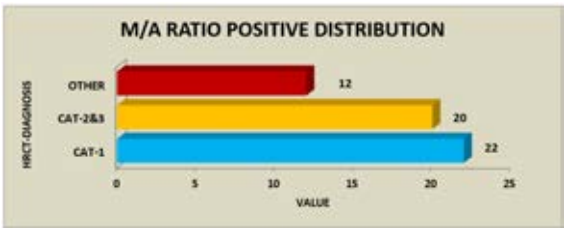

Fig. 4: Positive rPA IN UIP and NSIP

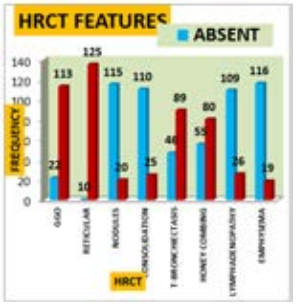

Fig. 5: Honey combing pattern in ILD and main pulmonary arterial diameter.

Of 135 patients who have undergone HRCT diagnosis, the age group includes 24 and 93. Among them, patients of the age group between 54 and 73 had a higher incidence than other age groups.

On comparison with right pulmonary artery diameter with HRCT diagnosed interstitial lung disease in our patient study population of 135 patients, the RPAD is found to be dilated more than 20mm equally in both sexes and mean RPAD is more in Fibrotic NSIP than all Interstitial Lung Disease.

In above study population of 135 patients, based on the above comparison with left pulmonary artery diameter with HRCT diagnosed interstitial lung disease, the LPAD is found to be dilated more in males

53% than females and the mean LPAD is found to be more dilated in Smoking related ILD than the rest of the Interstitial Lung Disease.

In MPA positive distribution, CAT-3 which is fibrotic NSIP is of higher value that ranges 11(84%) when compared with CAT-2 (Cellular NSIP) which is 2. Hence, PAH is more common in Fibrotic type NSIP than the cellular type.

In above study, the rPA Positive distribution that is the ratio >1 is seen more in UIP pattern than NSIP. Indicates that UIP pattern has more incidence 40% of having PAH than the rest of the ILD.

In the above study, made by chi square test between honey combing pattern in ILD and Main pulmonary arterial diameter. It shows p-value 0.353 which is >1 making it there is no significance between PAH and honey combing pattern in ILD in our study.

In above study population of 135 patients with ILD, based on observation the most common pattern of ILD is UIP with mean age group being 5th-7th decade. The average mean of dPA and rPA in our study was 27±4 and 0.953±1.43. The dPA was dilated in more than 40 percent and rPA more than 1 in more than 49 percent of patients in our study. There were 30 percent of patients with ILD who had both parameters (rPA and dPA) increased. The most common pattern was interlobular septal thickening with least common pattern being nodules.

We found in above study the percentage of frequency of patient getting affected with Interstitial Lung Disease is high among females which is about 54.8% and the percentage of males getting affected are 45.2% which is in accordance with result published by Lynch DA[17]. NSIP more commonly affects women and the mean age of presentation is usually about a decade younger than UIP. There is significance found in the p-value found in chi square test between the gender and different HRCT diagnosed interstitial lung disease which is less than 0.05.

Ahmed *et al*. showed that PAH is more common in UIP than in NSIP[18]. In above study population, UIP pattern is most common among all ILDs. We found that dilated dPA is 41% in UIP more than the NSIP which is

Table 1: Disease distribution in ILD

HRCT Diagnosis	Total
UIP	53
NSIP	12
(f)NSIP	21
COP	9
Smoking related ILD	5
HSP	9
CVD	8
sarcoidosis	4
miscellaneous	14
TOTAL	135

Table 2: Gender distribution in ILD

Gender	Frequency	Percent Affected
Male	61	45.2
Female	74	54.8
TOTAL	135	100.0

Table 3: AGE

HRCT-Diagnosis	24-33	34-43	44-63	54-63	64-73	74-84	84-93	HRCT-Total
1	2	1	5	13	13	17	2	53
2	1	0	1	4	6	0	0	12
3	0	0	4	6	3	5	3	21
4	0	0	2	3	3	1	0	9
5	0	0	0	2	2	1	0	5
6	2	1	3	0	3	0	0	9
7	0	1	1	2	3	1	0	8
8	0	2	0	1	1	0	0	4
9	2	0	5	5	1	1	0	14
AGE-Total	7	5	21	36	35	26	5	135

Table 4: Comparison between RPAD and HRCT diagnosed ILD

RPAD	1	2	3	4	5	6	7	8	9	Total
>20	23	7	12	5	2	5	2	2	2	60
<=20	30	5	9	4	3	4	6	2	12	75
Total	53	12	21	9	5	9	8	4	14	135

Table 5: Analysis of variance (ANOVA) table of HRCT honey combing effect on group

HRCT-Honeycom BING	Sum of squares	Df	Mean square	F	Sig.
Between Groups	.212	1	.212	.869	.353
With in groups	32.381	133	.243		
Total	32.593	134			

33% and rPA is more than 1 in 41% of UIP patients which is more than what we found in NSIP (37%). Also RPA and LPA is more dilated in UIP (38% and 46%) than NSIP (31% and 26%). Thus, in our study PAH is more prevalent in UIP than NSIP which is in accordance to Ahmed S study. Webb *et al*. showed that fibrotic type is more common than cellular type, which has good prognosis[19,20]. Based on our study, PAH is more commonly prevalent in Fibrotic type than the Cellular type as the parameters dPA, rPA, RPAD and LPAD is elevated more in fibrotic than cellular type. Thus making fibrotic NSIP type have poorer prognostic outcome than the cellular type.

In above study, honeycombing was seen in 59% of the cases on HRCT. Detection of honeycombing has greater clinical significance as its presence strongly suggests the diagnosis of usual interstitial pneumonia. It also indicates the end stage, whereby the patient will gain little from a lung biopsy[21]. Among the patients with honeycombing patterns in HRCT in our study, 49 percent were found to have more than 29 mm as MPA diameter and 44 percent were found to have rPA more than 1, whereas the p-value found was more than 0.05 in chi square test, making no significance between honey combing pattern and increased dPA and rPA. Traction bronchiectasis or bronchial dilatation resulting from lung fibrosis was visible in 65% of the cases on chest HRCT[22]. They were typically associated with reticular opacities and in some cases with honeycombing. The presence of fibrosis with basal and peripheral distribution was characteristic of idiopathic pulmonary fibrosis. Anand Devaraj *et al*.[23] in American journal of radiology published Pulmonary hypertension, reflected by pulmonary arterial enlargement on CT scans, is a highly significant prognostic indicator in the evaluation of patients with bronchiectasis.

Rajaram *et al*.[24] in 2015 found Ground glass opacities were frequent in PAH (41%).There was statistically significant correlation between HRCT Ground Glass Opacities and pulmonary artery hypertension.

The prevalence of PH in sarcoidosis ranges from 5.7%-74%[12]. Outcome in pulmonary sarcoidosis is largely influenced by two separate pathological processes-interstitial fibrosis and pulmonary arterial hypertension. The latter is being increasingly recognized as relatively frequent in sarcoidosis. Decreased lung volume increases the risk of PH developing in patients with sarcoidosis. In Japanese

population, study conducted by Handa *et al*.[11] found that the frequency of PH in sarcoidosis patients is 5.7% and Simon LF Walsh *et al*.[25] found that in patients with sarcoidosis, independent of HRCT patterns the rPA category was proved to be predictive of mortality, suggesting that the rPA might capture the prognostic effect of an underlying vasculopathy. In our study, there were only3% patients with histopathologically and radiologically proven sarcoidosis. Both males and females are equally affected in the age group between 40-70 years.

Out of all patients founded with Collagen vascular disease (CVD), 87 percent have increased rPA more than 1, whereas the dPA, RPAD and LPAD are increased less than 25% in our study. But PAH is more prevalent (45%) in CVD[26,27]. Hence making rPA a better predictor of PAH in CVD than central pulmonary artery diameter[12,28-30].

CONCLUSION

We can conclude that the pulmonary artery diameters in patients with Interstitial Lung Disease (ILD) and its HRCT patterns and found that there is increased prevalence of PAH in NSIP (Fibrotic NSIP>Cellular NSIP) more than the most common UIP pattern. Also, there was significance between gender in ILD and main pulmonary artery diameter but there was no age significance in developing PAH . Patients with emphysema and ground glass opacities have more dilated central pulmonary artery and ratio with aorta > 1, making it significant in these patients to develop PAH. Hence, Proper Treatment and follow up is required in these patients with ILD having PAH.

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