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STUDY OF PREVALENCE OF PULMONARY HYPERTENSION IN CONNECTIVE TISSUE DISEASE IN A TERTIARY CARE HOSPITAL IN TAMIL NADU.

Cardiology

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ABSTRACT

BACKGROUND: The aim of this study was to assess the overall prevalence of pulmonary hypertension in connective tissue disease patients, few studies in South India have focused on pulmonary arterial hypertension (PAH) associated with connective tissue diseases.

MATERIAL AND METHODS: The present study was conducted between August 2015 and September 2016, among the patient attending cardiology out-Patient in Institute of cardiology, at Rajiv Gandhi Government General Hospital, Chennai, Tamilnadu, India, a total of 105 patients with various connective tissue disease were included in this study.

Results: Patients with connective tissue disease in our study had mean age of 20–60 years. Pulmonary hypertension was seen in 30-50 age group, mostly female gender.

Among 105 patients,Rheumatoid arthritis was on top with more than 50% of the cases, followed by SLE(20%) then systemic sclerosis(14%), remaining were few cases of Sjogren syndrome(1.9%), Ankylosing spondylitis(1.9%),Mixed connective tissue disease(5%) and Psoriatic arthritis(0.9%). Totally 15% of the case had Pulmonary hypertension.

Conclusions: Pulmonary hypertension (PH) is common in connective tissue disease and is associated with high morbidity and mortality, there is paucity of data regarding Pulmonary hypertension from South India.Early Screening echocardiography may be recommended on presentation, during recurrence and in patients with even mild symptoms.

KEYWORDS

Pulmonary Hypertension (PHT); Connective Tissue Disease (CTD)

INTRODUCTION

Pulmonary hypertension is common in patients with connective tissue diseases and it is a fatal complication of connective tissue diseases.The pathogenesis which consists of autoimmunity, inflammation, vascular injury,remodelling ,multi-organ dysfunction and has a high mortality and morbidity[1,2,3]. It eventually leads to right heart failure and death. [4,5] Pulmonary hypertension is seen in almost all forms of Connective tissue disease, including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), mixed connective tissue disorders (MCTDs), Sjogren syndrome(SS) and more serious course in systemic sclerosis .[6,7]

There is significant delay between onset of disease process and Pulmonary hypertension diagnosis in patients with Connective tissue disease. Early diagnosis made and combination treatment shown to improve survival. The treatment approach in pulmonary hypertension associated with Connective tissue disease is different to treatment of other causes of pulmonary hypertension . Therapy is less effective in Connective tissue disease patients than in other forms. Over all comparision of survival in pulmonary hypertension associated patients with connective tissue disease has poor prognosis. Lung transplantation should be considered for patients not responding to routine medical therapy. Research is on focusing the underlying mechanisms of connective tissue disease associated pulmonary hypertension for better targeted therapy.

Definition and classification

Pulmonary hypertension is defined as a mean pulmonary artery pressure of at least 25 mm Hg at rest .[8] It is a progressive and life-threatening disease characterised by elevation of mean pulmonary arterial pressure and pulmonary vascular resistance leading to right heart failure and death.The most recent and widely accepted clinical classification of pulmonary hypertension is that proposed at the Fourth World Symposium on PulmonaryHypertension at Dana Point in 2008.[9]

It classifies pulmonary hypertension into five groups.

Group 1 comprises pulmonary arterial hypertension (PAH) which includes idiopathic PAH, heritable PAH, drug-induced and toxin-induced PAH, PAH associated with various diseases and persistent pulmonary hypertension of the newborn. Group 2 comprises pulmonary hypertension due to left heart disease; Group 3, pulmonaryhypertension owing to lung diseases and/or hypoxia; Group 4, chronic thrombo embolic pulmonary hypertension;and Group 5, pulmonary hypertension of unknowncause.

Connective tissue disease - pulmonary hypertension has been listed as a subgroup within Group 1 PAH. With the multi systemic involvement of CTDs, Connective tissue disease-pulmonary hypertension has features of WHO Groups 1 through 4 and considered multiple pathogenesis involved and has features of several groups.

Methodology

The present study was conducted between August 2015 and September 2016, among 105 patients, attending cardiology out-Patient in Institute of cardiology,in Rajiv Gandhi Government General Hospital, Chennai, Tamilnadu, India. The patients satisfying the American College of Rheumatology criteria for Connective tissue disease were included in this study.

One Hundred and five cases of Connective tissue disease patients attending the cardiology out Patient in our Institute of cardiology, were subjected to detailed clinical history, physical examination,chest X-ray, electrocardiography, echocardiographic examination, study of old medical records and all relevant investigations were done,treatment details were recorded and analysed.

ECHOCARDIOGRAPHIC EVALUATION OF PULMONARY ARTERY SYSTOLIC PRESSURE (PASP)

PASP, also known as systolic pulmonary artery pressure (sPAP) relies on the fact that PASP/sPAP approximates right ventricular systolic pressure (RVSP) in the absence of right ventricular outflow obstruction.[10,11]

PASP/sPAP is calculated from peak Tricuspid Regurgitant Velocity derived by doppler echocardiography using the simplified Bernoulli equation by the formula:

RVSP PASP/sPAP = 4 (TRV)2 + RAP is used to diagnose Pulmonary Hypertension by echocardiography.[12]

Statistical analysis

Statistical analysis was done using SPSS (Statistical Package for Social Sciences) version 15.0 statistical analysis software. Chi-square and Fisher's exact probability test were used and p values of less than 0.05 were considered significant.

Results

A total of 105 patients of Connective tissue disease were studied.

Table 1 gives demographical characteristics of all patients with various connective tissue disease population. Pulmonary hypertension in 105 patients of the study population is reflected in Table 2.

Gender wise distribution of Pulmonary hypertension is mentioned in Table 3.

Table - 1 Demographical Characteristics of 105 patients with Various CTDS

DIAGNOSIS	AGE GROUP (IN YEARS)														
	13-20		21-30		31–40		41–50		51-60		≥60		TOTAL		
	N=1		N=18		N=22		N=38		N=16		N=10		N=105		
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	T
R. A	0	0	1	7	0	10	6	18	2	5	1	5	10	45	55
SLE	0	1	1	5	1	0	1	6	1	3	0	3	4	18	22
MTCD	0	0	0	0	1	3	0	0	0	2	0	0	1	5	6
PA	0	0	0	0	0	1	0	1	0	0	0	0	0	2	2
SYS	0	0	1	2	2	2	2	2	2	1	0	1	7	8	15
AS	0	0	0	0	0	1	0	1	0	0	0	0	0	2	2
SS	0	0	0	1	0	1	0	0	0	0	0	0	0	2	2
PS	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1
TOTAL	0	1	3	15	4	18	9	29	5	11	1	9	22	83	105

RA – **R**heumatoid **A**rthritis**SLE**- **S**ystemic **L**upus **E**rythematous

MCTD- **M**ixed **C**onnective **T**issue **D**isease **PA**- **P**soriatic **A**rthritis **SYS**-**Systemic sclerosis**

AS- **A**nky**L**osing **S**pondylitis**SS**-**S**jogren**S**yndrome **PS**-**P**olymyositis

Table-2 Pulmonary arterial Hypertension in 105 Patients with various connective tissue disorder

Diagnosis	N	Mild	Moderate	Severe	Total	%
R. A	55	4	0	0	4	7.27
SLE	22	2	1	0	3	13.64
MTCD	6	3	0	0	3	50.00
PA	2	0	0	0	0	0.00
SYS	15	1	2	2	5	33.33
AS	2	0	0	0	0	0.00
SS	2	0	0	0	0	0.00
PS	1	0	0	0	0	0.00
TOTAL	105	10	3	2	15	14.29

TABLE-3 Pulmonary arterial Hypertension in 105 Patients with various connective tissue disorder by Gender wise.

Diagnosis	Mild		Moderate		Severe	
	Male	Female	Male	Female	Male	Female
R. A	0	4	0	0	0	0
SLE	0	2	0	1	0	0
MTCD	0	3	0	0	0	0
PA	0	0	0	0	0	0
SYS	0	1	0	2	0	2
AS	0	0	0	0	0	0
SS	0	0	0	0	0	0
PS	0	0	0	0	0	0

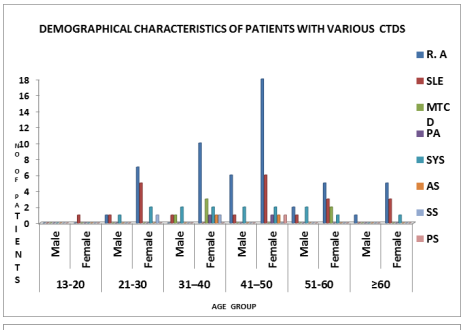
In our study 2 D Echo was done in each of 105 connective tissue disease patients at initial registration and during the course of follow-up.

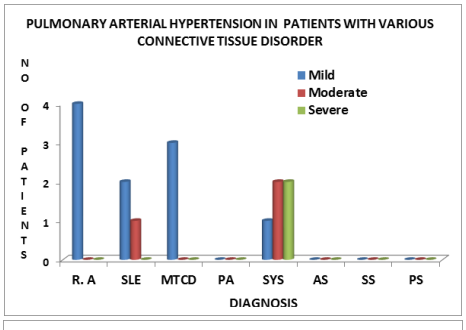
The most common echocardiographic finding was pulmonary hypertension (PH) [cases with Pulmonary arterialsystolic pressure (PASP)>35 mm Hg were considered to have PH] found in 15 (14.29 %) of the patients (table 2)

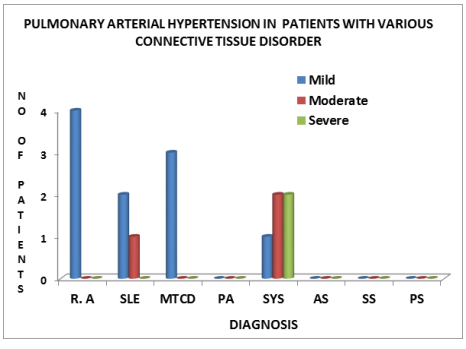
Out of 15 patients with pulmonary hypertension, 10 were found to be mild. They all had mild Pulmonary hypertension (PASP 36-50mmHg). The remaining 5 patients with symptoms had moderate to severe (PASP >50 mmHg) pulmonary hypertension

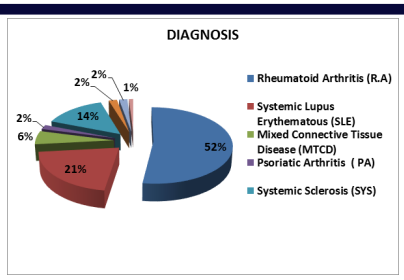
Patients with connective tissue disease in our study had mean age of 20–60 years, Pulmonary hypertension was seen in 30-50 age group, mostly female gender.

Among 105 patients, Rheumatoid arthritis was on top with more than 50% of the cases, followed by SLE(20%), then systemic sclerosis (14%),remaining were few cases of Sjogren syndrome(1.9%), Ankylosing spondylitis(1.9%), Mixed connective tissue disease(5%) and Psoriatic arthritis(0.9%).Totaly 15% of the case had Pulmonary hypertension.









Discussion

This article reports the Study of Prevalence of Pulmonary Hypertension in Connective Tissue Disease in a Tertiary Care Hospital in south india with echocardiography based diagnosis.

A limitation of our study, was that no right heart catheterization data were presented.

Previous studies have revealed assessments based on echocardio graphic measurements have overestimated the true prevalence of pulmonary hypertension and should not be relied upon for establishing the diagnosis and initiating treatment.

Pulmonary hypertension can affect all types of connective tissue disease, seen especially in systemic sclerosis. From various registries, the prevalence of pulmonary hypertension in systemic sclerosis is between 7.85% and 12% [13],the prognosis in scleroderma associated pulmonary hypertension remains poor so early diagnosis is helpful for management.

In our study the incidence of pulmonary hypertension in systemic sclerosis was 33.33%

The prevalence varies widely from 0.5% to 14% in SLE pulmonary hypertension which is typically mild [14],mostly female gender(90%), young (average age of 33 at time of diagnosis), and has Raynaud's phenomenon.

A more accurate estimation of 10.8% of asymptomatic Pulmonary hypertension has been reported in patients with SLE [15].

Presence of Pulmonary hypertension in SLE is not related to the severity or duration of illness[16, 17]. It can also present at any stage of SLE. In our study the incidence was13.64%

Pulmonary hypertension is rare in patients with Rheumatoid arthritis[18] in our study also it was less 7.27%, the prevalence and impact of, pulmonary hypertension in patients with rheumatoid arthritis found to be relatively less in comparison with other connective tissue disease such as systemic sclerosis, SLE and MCTD.

Pulmonary hypertension is the most serious complication of MCTD, reported to be 10 to 50% of patients.[19,20] It was 50% in our study which is similar to other studies[21,22].

The management of connective tissue disease - pulmonary hypertension involves a multidrug regimen. In general, patients with CTD-PHT are less responsive to treatment than other PHT patients.

Combination therapy is favoured in patients with CTD-PHT, with roughly 40% of patients in the REVEAL registry were in combination therapy. Patients with medical therapy failed can be referred for lung transplantation.

Overall ,in patients with systemic sclerosis -pulmonary hypertension face the worst prognosis ; patients with systemic sclerosis are three times likely to die with pulmonary hypertension than counterparts without pulmonary hypertension [23]. Underlying pathology is in pulmonary vasculature involving small vessels and leading to progressive increase in pulmonary vascular resistance, right ventricular over load, and finally right heart failure.

Our study reveals the large number of pulmonary hypertension in connective tissue disease similar to other Indian studies [24,25,26] and the need for early screening with echocardiogram, a simple non-invasive tool available almost in all areas because all cases will not be able to do right heart catheterization because of severe symptoms and non availability.

Conclusion

Pulmonary hypertension is a fatal complication of connective tissue disease especially in patients with systemic sclerosis. Pulmonary hypertension can develop at any time in the course of the disease ,it can be moderate to severe, either respond to immune suppression or not depending upon type and disease severity. In patients with connective tissue disease Pulmonary hypertension, therapy is not beneficial as it is in other forms of pulmonary hypertension.

Further detailed studies with newer echocardiographic parameters and right heart catheterisation need to be undertaken to study the prevalence of pulmonary hypertension [27] and its response to newer immunosuppressive agents.

Hence aggressive immunosuppressive therapy is needed in most patients with CTD-PAH. Systemic sclerosis patients and with other connective tissue disease failed with routine immune drugs may benefit from other PAH-specific therapy[28]. Overall prognosis with CTD-PAH is grave and patients might need lung transplantation and to be evaluated during the terminal course of illness[29,30].

SUMMARY

- Pulmonary hypertension is in increasing trend in connective tissue diseases.
- The presence of Pulmonary hypertension itself confers poor prognosis in connective tissue diseases patients.
- Measurement of tricuspid regurgitant jet velocity is the best non invasive test to detect PAH in patients with connective tissue diseases .
- Other tests like Computed tomography pulmonary angiography and cardiac magnetic resonance imaging also help in screening for Pulmonary hypertension detection
- PAH-specific therapy, in general, is less effective in CTD-PAH patients than with other forms of PAH.
- Early treatment with combined immunosuppression for inflammation and PAH is recommended

In conclusion , pulmonary hypertension are more common in CTD patients , early detection among patients with CTDs is necessary for therapy to reduce high morbidity and mortality. From our study ,we emphasise the fact that further studies involving larger samples are needed to detect PAH earlier in connective tissue disorders. It is also need of hour to consider that early detection using various clinical symptoms and early screening with echocardiogram, a non invasive ,easily available tool for better outcome of suffering patients.

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