Original Research Article

Study of pulmonary hypertension using 2D echo in thyroid disorders

Mohit Singhal[1*], Pankaj B Palange[2], B D Palange[3]

[1]Junior Resident, [2]Professor & HOD, Department of Medicine, Bharati Vidyapeeth Deemed University, Sangli, INDIA ,[3] Associate professor
Email: mohitpsinghal@yahoo.com

Abstract

Background: Though rare, thyroid dysfunction is known to cause Pulmonary Artery Hypertension (PAH) which is also known to be reversible by restoration of euthyroid state. Hence, timely diagnosis and institution of medications can prevent as well as treat the secondary PAH in these patients. **Aim:** To analyse the prevalence of PAH in newly diagnosed, treatment naïve patients with thyroid dysfunction (hypothyroidism/ hyperthyroidism) and to analyse the association of thyroid dysfunction with occurrence of PAH in treatment naïve patients. Furthermore, to see the improvement of PAH in those diagnosed, with treatment given, after 10 months. **Materials and Methods**: It was an observational prospective study which included 50 newly diagnosed patients with thyroid dysfunction. All were subjected to 2D echocardiography with detailed history and physical examination. Repeat echocardiographic assessment was done after 6 months of treatment for few patients to look for resolution of PAH. The statistical analysis was carried out to determine the association of PAH with thyroid dysfunction using student's t-test and chi-square test of association. **Results:** The study included 37 (74%) females and 13 (26%) males. PAH was present in 11 (22%) patients. Repeat echocardiography after 10 months of treatment (Eltroxin 1.6 microgram/kg for hypothyroid patients and Carbimazole (5/10 mg BD/TDS for hyperthyroid) was performed (those who were diagnosed with PAH at the time of diagnosis of thyroid dysfunction) and reduction in Pulmonary Artery Systolic Pressure (PASP) was observed**. Conclusion:** High prevalence of PAH was observed in patients with thyroid dysfunctions at the time of diagnosis in the treatment naïve patients in the current study and it also reversed with treatment on repeat 2D-echo with treatment. It is, therefore, suggested that every patient of thyroid dysfunction should be screened for PAH, even though further studies are needed to substantiate this, due to an inherent small sample size of the study.

Key Words - Hypothyroidism; Hyperthyroidism; Pulmonary hypertension

***Address for Correspondence:**
Dr Mohit Singhal, JR III, Department of Medicine, Bharati Vidyapeeth Deemed University, Sangli, INDIA.
Email: mohitpsinghal@yahoo.com

Received Date: 08/12/2019 Revised Date: 14/01/2020 Accepted Date: 04/02/2020
DOI: https://doi.org/10.26611/10211413

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 02 April 2020

INTRODUCTION

Pulmonary Artery Hypertension (PAH) is a hemodynamic and pathophysiological condition defined as an increase in mean Pulmonary Artery Pressure (mPAP) > 25 mm Hg at rest and > 30 mm Hg during exercise, as assessed by right heart catheterization[1].It can be primary or secondary. In contrast to primary PAH which is a diagnosis of exclusion, secondary PAH is caused by various conditions most common being cardiac diseases, respiratory diseases or both co-existing. Among the less common causes are connective tissue diseases, haemoglobinopathies like sickle cell anemia, infections like HIV, metabolic disorders like glycogen storage diseases, drugs, toxins, thyroid dysfunction etc.[2] A study suggested that, there was an increased incidence of PAH in patients with thyroid dysfunctions (hypothyroidism and hyperthyroidism) and has been kept under WHO Group V of Dana Point, 2008 Classification of PAH[3] .PAH secondary to thyroid dysfunction is found to be reversible by restoration of euthyroid state i.e., they have a good prognosis if diagnosed and treated timely [1]. There are a lot of patients of thyroid dysfunction who have unexplained dyspnea and the underlying cause maybe PAH. Hence, the purpose of our study was to observe the prevalence of PAH in newly diagnosed, treatment naïve patients of thyroid dysfunction (both

How to cite this article: Mohit Singhal, Pankaj B Palange, B D Palange. Study of pulmonary hypertension using 2D echo in thyroid disorders. *MedPulse International Journal of Medicine.* April 2020; 14(1): 13-17. https://www.medpulse.in/Medicine/

hypo and hyperthyroidism) using 2D-echocardiographic assessment and to assess the reversibility of PAH with treatment, documented by 2D-echocardiography.

AIMS AND OBJECTIVES

1. To study the occurrence of pulmonary hypertension in hypothyroid and hyperthyroidism.
2. Reversibility of pulmonary hypertension after treatment of hypothyroidism and hyperthyroidism.

MATERIALS AND METHODS

Duration of Study - November 2018 to October 2019
Sample Size: 50 cases
Sampling Method: Simple random sampling

All cases taken for the study are evaluated as follows:

1. Cases coming to Bharati Vidyapeeth Sangli either on OPD / IPD basis were screened for clinical evidence of hypothyroidism or hyperthyroidism as per the pre-structured proforma.
2. Thyroid function tests were done in all cases using Enzyme immunoassay to confirm the presence of hypo or hyperthyroidism.
3. Electrocardiography was recorded in all the patients. Chest X-rays were done and examined for roentgenographic signs of pulmonary hypertension, i.e. right descending pulmonary artery diameter of >1.5 cm.
4. 2D-Echocardiography was done in all cases and screened for the presence and severity of pulmonary hypertension.

Right ventricular systolic pressure was calculated from the pressure gradient between the right ventricle and atrium measured by continuous wave Doppler echocardiography according to standard techniques. CVP was not elevated on clinical examination and therefore assumed to be 5 mmHg. Mean right atrial pressure is equivalent to CVP. PASP was calculated by adding up RAP and RVSP.

Patients with PASP of >30 mmHg were treated for the underlying hypothyroidism (thyroxine) and hyperthyroidism (Carbimazole) and reassessed after a period of 10 months with 2D-Echocardiography for the reduction in PASP.

INCLUSION CRITERIA

1. Patients with hypo/hyperthyroidism.
2. Patients more than 18 years of age, both male and female
3. Patients willing to participate in the study

EXCLUSION CRITERIA: Patients with/who are

1. Clinical features of chronic pulmonary diseases like COAD, interstitial lung disease
2. Known cases of connective tissue diseases.
3. Underlying cardiac diseases like VSD, cardiomyopathies, myocarditis etc.
4. Chronic liver disease or cirrhosis.
5. Chronic hypoxemia.
6. Patients on treatment for thyroid disorders for more than 6 months.

RESULTS

Table 1: Distribution of cases in hypothyroidism and hyperthyroidism

	Hypothyroidism	Hyperthyroidism	Total
Number of cases	37	13	50

In our study out of the 50 cases, 37 (74%) cases were of Hypothyroidism and 13 (26%) cases were of Hyperthyroidism.

Table 2: Distribution of mean PASP using 2D-ECHO

	Mean± Sd		P value
Variable	Hypothyroidism	Hyperthyroidism	
2D-ECHO PASP(RVSP+RA)	26.97±5.16	30.62±9.57	0.09

Unpaired t test is applied. P value is significant if < 0.05 PASP value in patients with hyperthyroidism was 30.62mm Hg while that in the patients with hypothyroidism was 26.97mm Hg. Difference between them was comparable.

Table 3: Comparison of PASP in Hypothyroidism and Hyperthyroidism

PASP Group	Thyroid status				Grand total
	Hypothyroidism		Hyperthyroidism		
	N	%	N	%	
Normal (PASP≤ 30 mm Hg)	30	81.08	9	69.23	39
Mild (PASP 31 to 45 mm Hg)	7	18.92	2	15.38	9
Moderate (PASP 46 to 60 mm Hg)	0	-	2	15.38	2
Severe (PASP>60 mm Hg)	0	-	0	0	0
Grand Total	**37**	**74**	**13**	**26**	**50**

81.08% patients with hypothyroidism and 69.23% patients with hyperthyroidism had normal PASP level. While 15.38% patients with hyperthyroidism had mild and moderate PASP each, only 18.92% with hypothyroidism had mild PASP.

Table 4: Comparison of PASP in the follow up group: pre treatment and post treatment

Variable	Mean± Sd		P value
	Before	After follow up	
2D-ECHO PASP mm Hg	38.82±5.51	30±5.14	0.001

Paired t test is applied. P value is significant if < 0.05

The mean PASP by Doppler Echocardiography was 38.82 mm of Hg in the pre-treatment group. And the mean PASP during the follow up (after 10 months) was 30 mm of Hg.

Table 5: Comparison of TSH, T3, T4 and PASP among patients of Hypothyroidism in the follow up group, pre and post treatment

Variable	Hypothyroidism (Mean± Sd)		P value
	Before	After follow up	
TSH (uIU/ml)	16.62±10.36	3.52±1.57	0.01
T3 (ng/ml)	0.67±0.19	1.14±0.42	0.05
T4 (ug/dl)	5.14±2.83	8.66±1.55	0.004
2D-ECHO PASP mm Hg	36.14±3.29	29.71±5.5	0.006

Paired 't' test applied. 'P' value is significant if < 0.05

Among the patients in the Hypothyroidism group with PAH, the pre-treatment values of TSH and PASP were high and reduced in the follow-up (after 10 months of treatment)

Table 6: Comparison of TSH, T3, T4 and PASP among patients of Hyperthyroidism in the follow up group, pre and post treatment

Variable	Hyperthyroidism (Mean± Sd)		P value
	Before	After follow up	
TSH (uIU/ml)	0.1±0.04	2.54±1.84	0.07
T3 (ng/ml)	2.9±0.72	1.16±0.20	0.018
T4 (ug/dl)	16.83±2.88	9.53±1.34	0.013
2D-ECHO PASP mm Hg	43.5±5.80	30.5±5.2	0.023

Paired 't' test applied. 'P' value is significant if < 0.05

Among the patients in the Hyperthyroidism group with PAH, the mean pre-treatment value of TSH was 0.1 and increased to 2.54 in the follow up. Mean PASP value was 43.5 and reduced in the follow-up (after 10 months of treatment) to 30.5.

DISCUSSION

Several studies have shown associations between thyroid disease and pulmonary hypertension. In PAH there is a sustained increase in pulmonary artery pressure and a progressive increase in pulmonary vascular resistance, which leads to right ventricular insufficiency and often premature death. Mean pulmonary artery pressure (MPAP), under physiological conditions and at sea level, is < 20 mmHg, and pulmonary artery systolic pressure (PASP) is < 30 mmHg.

In a study by *Marvisi M et al.,* prevalence of PAH in recently diagnosed hyperthyroids was found to be 35% [6] while in his other study, involving 114 patients with hyperthyroidism (47 with Graves' disease and 67 with multinodular goiter), the prevalence of PAH was 43% [7]. Here PASP, as estimated by echocardiography, was > 30 mmHg.

In a study by *Mercé J et al.* of 39 patients recently diagnosed with hyperthyroidism, the prevalence of PAH (PASP> 35mm Hg) was found to be 41% [8].

In a retrospective study by *Curnock AL et al.*, the prevalence of hypothyroidism in 41 patients with PAH was found to be 22.5% which was higher than the incidence that we found in our study[4]. In a study by *Li JH et al.*, 356 patients having PAH and 698 controls not having PAH were retrospectively evaluated. Of the patients with PAH, thyroid disease was present in 85 patients(24%), and 107 (15%) in controls.[9] In our study PASP in hyperthyroidism was 30.62 while hypothyroidism was 26.97. Difference between them was comparable. 30.76% patients with hyperthyroidism had mild PASP and whereas 18.92% with hypothyroidism had mild to moderate PASP. Our finding on PASP is on the line with published studies.

Reversibility of pulmonary hypertension after treatment of hypothyroidism and hyperthyroidism

Mean PASP values among patients in the follow up group (11 patients: 7 hypothyroids and 4 hyperthyroids) were 38.82 and 30, pre-treatment and post-treatment respectively. This shows a decrease in the overall PASP values following treatment.

Mean TSH, T3, T4 and PASP (pre-treatment) values among the follow up patients were 16.62, 0.67, 5.14, and 36.14 respectively in the hypothyroidism group. Post-treatment values of Mean TSH, T3, T4 and PASP were 3.52, 1.14, 8.66, and 29.71.

Mean TSH value was decreased after 10 months of follow up while values of T3 and T4 had increased after 10 months of follow up. Mean PASP value also decreased in the follow up after 10 months following treatment.

Mean TSH, T3, T4 and PASP (pre-treatment) values among the follow up patients were 0.1, 2.9, 16.83, and 43.5 respectively in the hyperthyroidism group. Post-treatment values of Mean TSH, T3, T4 and PASP were 2.54, 1.16, 9.53, and 30.5.

Mean TSH value was increased after 10 months of follow up while values of T3 and T4 had decreased after 10 months of follow up. Mean PASP values also decreased in the follow up after 10 months following treatment. The change in PASP after the treatment was comparable with the findings of other studies. In a study by *Thurnheer R et al.* in 1997 [10], in 4 hyperthyroid cases mean pre-treatment PASP was 40 ± 11 mmHg. which decreased to 25 ± 6 mmHg after treatment with radioactive iodine or ethionamides.

In an observational study by *Marvisi M et al.,*[6] in 34 hyperthyroid patients (17 without treatment; 17 treated with methimazole; control group 17), mild pulmonary hypertension was present in 35% of the patients in the untreated hyperthyroid group (mean PASP of 28.88 ± 6.41 mmHg) and in none of the patients of the other groups.

In other study by *Marvisi M et al.*[7], the role of methimazole in the regulation of pulmonary vascular resistance in hyperthyroid patients with PAH was studied. After treatment for a period of 15 days, PASP values in the methimazole group decreased from a value of 34.3 ± 3.2 mmHg to 29.2 ± 3.3 mmHg , compared to the partial thyroidectomy group, where decrease was from 34.3 ± 3.0 mmHg to 34.1 ± 2.9 mmHg($p < 0.001$).

Methimazole's role in regulating production of N(G)-nitro-L-arginine methyl ester (L-NAME), an arginine analogue, producing acute NO synthesis inhibition has been shown in some studies.

In literature, the etiology of strong relationship between thyroid disease and pulmonary hypertension remains unclear. One possible explanation is that increased total blood volume contributes to increased pulmonary blood flow and pulmonary vascular resistance. Another possibility is the direct effect of thyroid hormones on the pulmonary vasculature. This theory is supported by ,the reversible change of pulmonary hypertension seen after successful treatment of hyperthyroidism. The mechanisms include an increase in metabolism of intrinsic pulmonary vasodilating substances and a decrease in vasoconstrictor metabolism. Besides the effect of an excess of thyroid hormones, systemic auto antibodies may also play a role in pulmonary vascular endothelium injury and lead to pulmonary hypertension.

CONCLUSION

My study was a prospective study and patients of hypothyroidism/hyperthyroidism with PAH were treated for hypo/hyperthyroidism and were reassessed after 10 months.

To summarize,

1. We found that amongst the 50 pts, hypothyroidism is more common. Majority of the patients had hypothyroidism (74%) and few had hyperthyroidism (26%).
2. PAH was detected in both hypothyroidism (18.92%) and the hyperthyroidism group (30.77%) .
3. We found that hypo/hyperthyroidism may cause PAH and should be excluded in patients with unexplained pulmonary hypertension.
4. Also we found that PAH secondary to thyroid dysfunctions may be reversed by restoration of euthyroid state, and hence patients have a good prognosis if diagnosed and treated timely.
5. So every patient of thyroid dysfunction should be screened for PAH, even though further studies are needed to substantiate this.

LIMITATIONS

1. The sample size of our study was very small and from only one centre. Therefore, study population is not representative of entire Indian population
2. Most of the patients did not give consent for right heart catherization, which is the most precise method for calculation of PASP.
3. Since we have evaluated and enrolled hypo/ hyperthyroidism patients, we could not calculate the actual prevalence of PAH because of lack of denominator.

REFERENCES

1. Farber HW, Loscalzo J. Pulmonary arterial hypertension. N Engl J Med. 2004;351(16):1655-65.
2. Simonneau G, Robbins IM, Beghetti M, Channick RN, Delcroix M, Denton CP, Elliott CG, Gaine SP, Gladwin MT, Jing ZC, Krowka MJ. Updated clinical classification of pulmonary hypertension. Journal of the American College of Cardiology. 2009 Jun 30;54(1 Supplement):S43-54.

3. Rubin LJ. Executive summary: diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. Chest. 2004 Jul 1;126(1):4S-6S.
4. Curnock AL, Dweik RA, Higgins BH, Saadi HF, Arroliga AC. High prevalence of hypothyroidism in patients with primary pulmonary hypertension. Am J Med Sci 1999;318(5):289-92.
5. Badesch DB, Wynne KM, Bonvallet S, Voelkel NF, Ridgway C, Groves BM. Hypothyroidism and primary pulmonary hypertension: an autoimmune pathogenetic link? Ann Intern Med 1993;119(1):44-6.
6. Marvisi M, Brianti M, Marani G, Del Borello R, Bortesi ML, Guariglia A. Hyperthyroidism and pulmonary hypertension. Respir Med 2002;96(4):215- 20.
7. Marvisi M, Zambrelli P, Brianti M, Civardi G, Lampugnani R, Delsignore R. Pulmonary hypertension is frequent in hyperthyroidism and normalizes after therapy. Eur J Intern Med 2006;17(4):267-271.
8. Mercé J, Ferrás S, Oltra C, Sanz E, Vendrell J, Simón I, *et al.*. Cardiovascular abnormalities in hyperthyroidism:a prospective Doppler echocardiographic study. Am J Med 2005;118(2):126-31.
9. Li JH, Safford RE, Aduen JF, Heckman MG, Crook JE, Burger CD. Pulmonary hypertension and thyroid disease. Chest 2007;132(3):793-7.
10. Thurnheer R, Jenni R, Russi EW, Greminger P, Speich R. Hyperthyroidism and pulmonary hypertension. J Intern Med 1997;242(2):185-8.

Source of Support: None Declared
Conflict of Interest: None Declared