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A Study of Etiological Profile Of Non Cardiogenic Pulmonary Hypertension At A Teritiary Care Hospital

Nikhil Kumar DG[1*], Yeshavanth G[2], Aarthik Shetty[3]

[1*,3]Junior Resident, Department of General Medicine, SSIMS&RC, Davanagere, Karnataka, India
[2]Professor and Head, Department of General Medicine, SSIMS&RC, Davanagere, Karnataka, India

Abstract

Background:
Pulmonary Hypertension is characterized by increased pulmonary artery pressure carries an increased mortality. The Etiological profile and prevalence of Pulmonary Hypertension in various non-cardiac disorders has not been given adequate attention.

Aims and Objectives:
This study was carried out with the objective to describe the etiological profile of non-cardiac Pulmonary Hypertension and severity of these cases in a tertiary Care Hospital

Materials and Methods:
This was a hospital-based observational study conducted at a tertiary care teaching health-care facility from January 2023 to June 2023. All 35 patients with Diagnosed with echocardiographic/ Right Heart Catheterisation(RHC) evidence of Pulmonary Hypertension were included. Patients with Echocardiographic evidence of Pulmonary Hypertension due to underlying Heart diseases were excluded with the help of non-probability purposive sampling after their written and informed consent. A pre-designed and pre-tested structured pro forma was used to collect detailed history, clinical findings, routine blood investigations, Chest x ray Transthoracic echo cardiography, selected patients underwent high resolution computed tomography and spirometry.

Results:
The prevalence of Pulmonary Hypertension was maximum in the age group of 51-60 years (28.57%) and increases after the age of 50 years (77.14%). Males outnumbered females with a ratio of 2.1. The most common etiology was COPD (51.43%) followed by idiopathic Pulmonary Artery Hypertension (iPAH) and Interstitial Lung Disease (ILD).In our study Echocardiographic measured RVSP showed most of the patient had mild Pulmonary Hypertension (46%) and were in WHO functional class II (54.29%).

Conclusion:
Non-cardiac causes of Pulmonary Hypertension are prevalent in day to day practices and institution of therapy is known to improve quality of life and decreases morbidity & mortality associated with the disease.

Keywords: Pulmonary Hypertension; Non Cardiac; COPD

INTRODUCTION

Pulmonary hypertension (PH) is a heterogeneous and highly morbid disease encountered commonly in general medicine, cardiology, and pulmonary medicine clinical practices.(1). Pulmonary Hypertension (PH) is defined as a mean pulmonary artery pressure (mPAP) ≥ 20 mmHg with a pulmonary capillary wedge pressure ≤ 15 mmHg, as measured by cardiac catheterization.(2) Pulmonary hypertension (PH) can be classified as idiopathic/primary when the cause is unknown.

Secondary pulmonary hypertension occurs due to underlying diseases or known risk factors, underlying heart and lung disease being the most common.[3][4]
With most of the public health attention being focused on atherosclerotic cardiovascular disease, the problem of pulmonary hypertension is largely overlooked. The aetiology of pulmonary hypertension is diverse and most of the underlying causes of Pulmonary Hypertension are prevalent in the developing world in a much larger magnitude as compared to the western world.[5].
Among them underlying cardiac diseases constitute the major group and other etiologic entities such as drugs, connective tissue diseases and respiratory diseases being less common in practice. In all these diseases, the development of Pulmonary Hypertension has adverse prognostic effects on the disease progression and outcomes.
The Etiological profile and prevalence of Pulmonary Hypertension in various Non-cardiac disorders has not been given adequate attention and there is paucity of data from our country on this aspect. This study was undertaken to find out the etiological and clinical profile of Pulmonary Hypertension due to non-cardiac causes at a Tertiary Care Hospital.

Aims and Objective
1) To describe the etiological profile of non-cardiac Pulmonary Hypertension in a Tertiary Care Hospital.
2) To describe the severity of disease in these cases of non-cardiac Pulmonary Hypertension with parameters including measured RVSP on Echocardiography, WHO functional class, spirometry, and partial pressure of oxygen in arterial blood.

METHODOLOGY
Study Design: The study was a cross sectional observational study.
Sample size: A total of 35 Patients diagnosed with non-cardiac Pulmonary Hypertension were studied.
Period of study: The study was conducted over a period of 6 months, between January 2023 to June 2023.
Inclusion criteria
- Subject age> 18 years
- Diagnosed with echocardiographic/ RHC evidence of Pulmonary Hypertension
- Willingness to participate in the study

Exclusion Criteria:
- Patients with Echocardiographic evidence of Pulmonary Hypertension due to underlying Heart diseases were excluded

MATERIALS AND METHODS
This was a hospital-based cross-sectional study conducted in a tertiary care teaching facility located in the southern region of India from January 2023 to June 2023. The study was carried out after getting approval from the institutional ethics committee and adhered to the principles enumerated in the Helsinki Declaration of 1975, as revised in the year 2013. The study comprised a total of 35 individuals who presented to S.S. Institute of medical science and research centre as outpatient department or as inpatient who were diagnosed to have Pulmonary Hypertension with Echocardiographic right ventricular systolic pressure (RVSP) or pulmonary artery systolic pressure (PASP) measured by right heart catheterisation >35 mmHg or mean Pulmonary Artery Pressure (mPAP) > 25 mm of Hg on right heart catheterisation (RHC) with normal cardiac structure and functions were included in the study for analysis.
All patients initially underwent complete transthoracic echocardiographic study including two-dimensional, M-Mode, color flow and spectral Doppler echocardiography. The echocardiographic mean pulmonary artery pressure was assessed by Tricuspid Regurgitation jet velocity for confirmation of the diagnosis of Pulmonary Hypertension (PASP was considered equivalent to RVSP in the absence

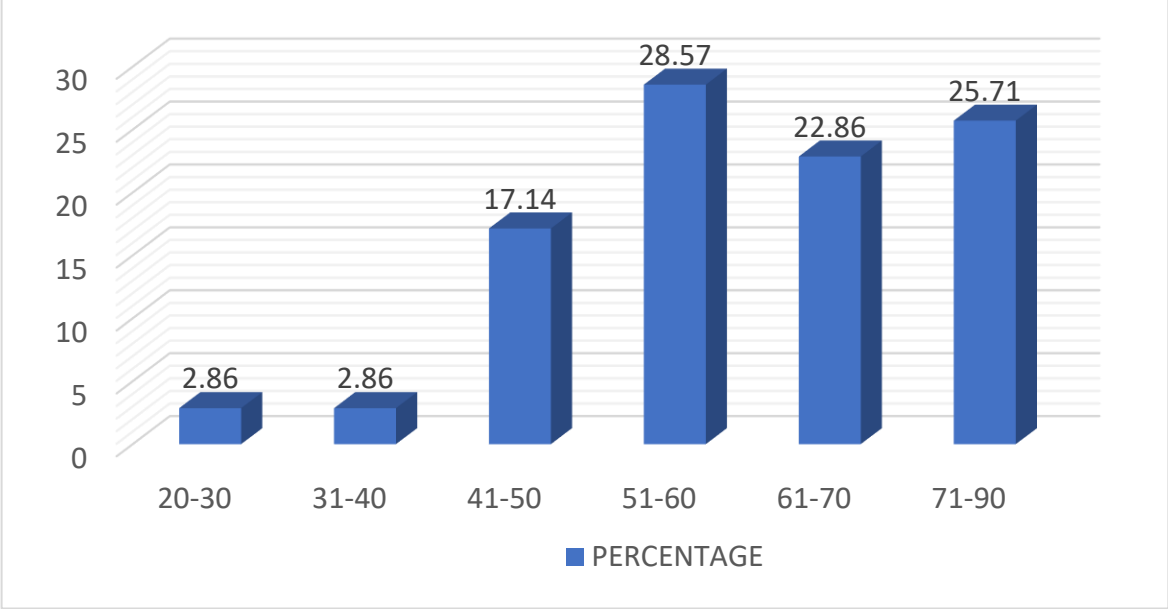
of pulmonary outflow obstruction). The RVSP was approximated by measurement of the systolic regurgitant tricuspid flow velocity v and an estimate of right atrial pressure (RAP) applied in the formula: RVSP = 4v2 + RAP). The patients were classified as suffering from mild, moderate or severe Pulmonary Hypertension as per calculated RVSP.

All patients were subjected to Complete Blood Count (CBC), Renal Function Test (RFT), Liver Function Test (LFT), Thyroid Function Test (TFT), HIV (by ELISA), Anti-Nuclear Antibodies ANA (by ELISA), Chest X Ray, USG Abdomen and Pulmonary Function Testing (PFT), and Arterial Blood Gas (ABG) analysis. They were then classified normal, Restrictive or Obstructive pattern on the basis of the Spirometry. The Obstructive pattern was further sub classified according to GOLD classification. They were also classified as normal, mild, moderate or severe hypoxemia on ABG analysis.

Specialized tests such as High Resolution Computed Tomography of the Chest (HRCT), CT Pulmonary Angiography, Diffusion Capacity for Carbon-Monoxide (DLCO), N Terminal pro- Brain Natriuretic Peptide (NT pro BNP) levels, Polysomnography, and Right Heart Cardiac Catheterization were carried out in selected cases as indicated due to financial burden and ethical issues. Data was diligently recorded and carefully documented on a pre-designed, pre-structured pro forma for the study. The statistical analysis was carried out utilizing IBM's Statistical Package for the Social Sciences version 23 (IBM, USA). The data were initially analyzed and coded using MS Excel Office version 2021. For categorical data, frequency, and proportions were used in the descriptive analysis, whereas mean and standard deviation were used for continuous variables.

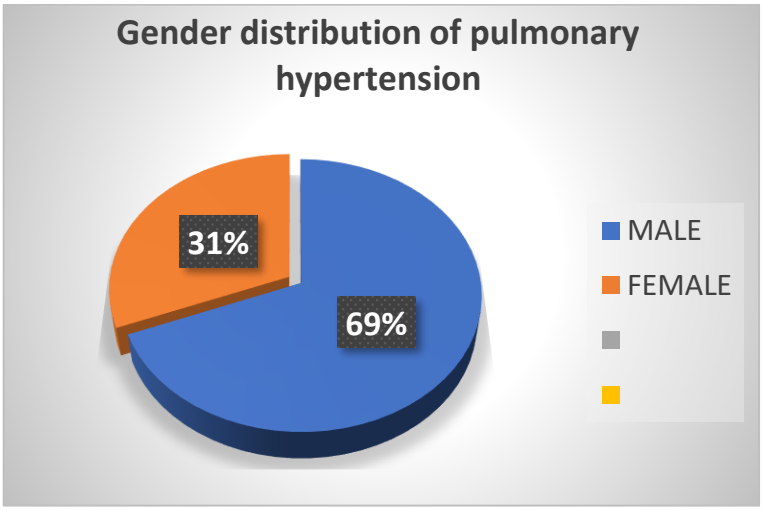
Results

1. Age wise Distribution of Cases with Pulmonary Hypertension



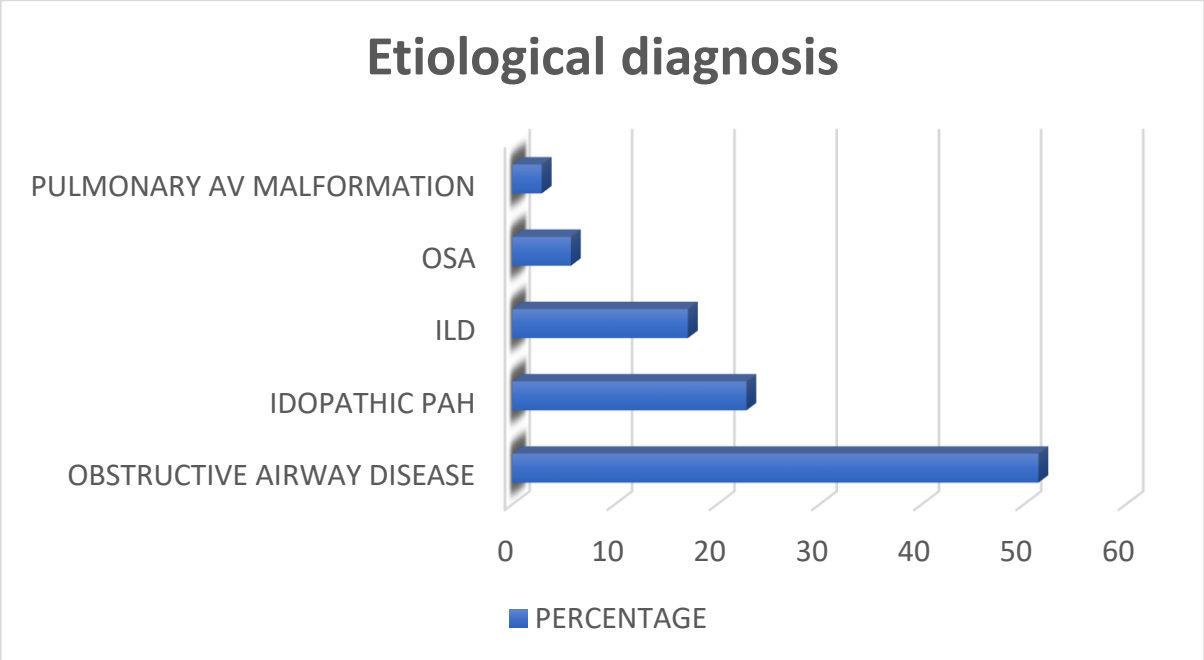
AGE IN YEARS	NO OF CASES	PERCENTAGE %
21-30	1	2.86
31-40	1	2.86
41-50	6	17.14
51-60	10	28.57
61-70	8	22.85
71-90	9	25.71
TOTAL	35	100

2. Gender wise distribution of cases with Pulmonary Hypertension



	NUMBER OF CASES	PERCENTAGE%
MALE	24	69
FEMALE	11	31
TOTAL	35	100

3. Etiological Diagnosis of cases with Pulmonary Hypertension

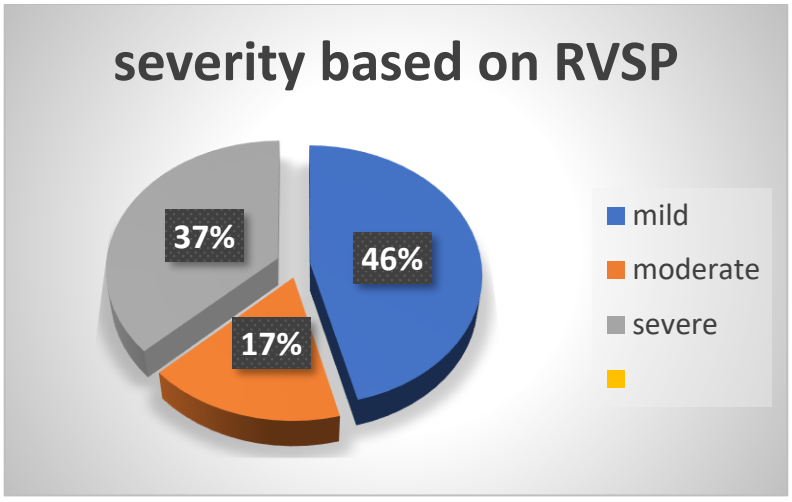


Etiological Diagnosis of cases with Pulmonary Hypertension

Etiology	Number of Cases	Percentage (%)
Obstructive Airway Disease	18	51.43%
Idiopathic PAH (iPAH)	8	22.86%
Interstitial Lung Disease (ILD)	6	17.14%
Obstructive Sleep Apnea (OSA)	2	5.71%
Pulmonary AV Malformation (HHT)	1	2.86%
Total	35	100

4. Distribution of Severity of Pulmonary Hypertension on the basis of Right Ventricular Systolic Pressures

Severity on the basis of RVSP in Echocardiography	Range (in mm of Hg)	Number of Cases	Percentage
Mild (36-50)	36-50	16	46%
Moderate (51-65)	51-65	6	17%
Severe (> 65)	>65	13	37%
Total		35	100



5. Distribution of Severity of Pulmonary Hypertension on the basis of WHO Function Status Classification

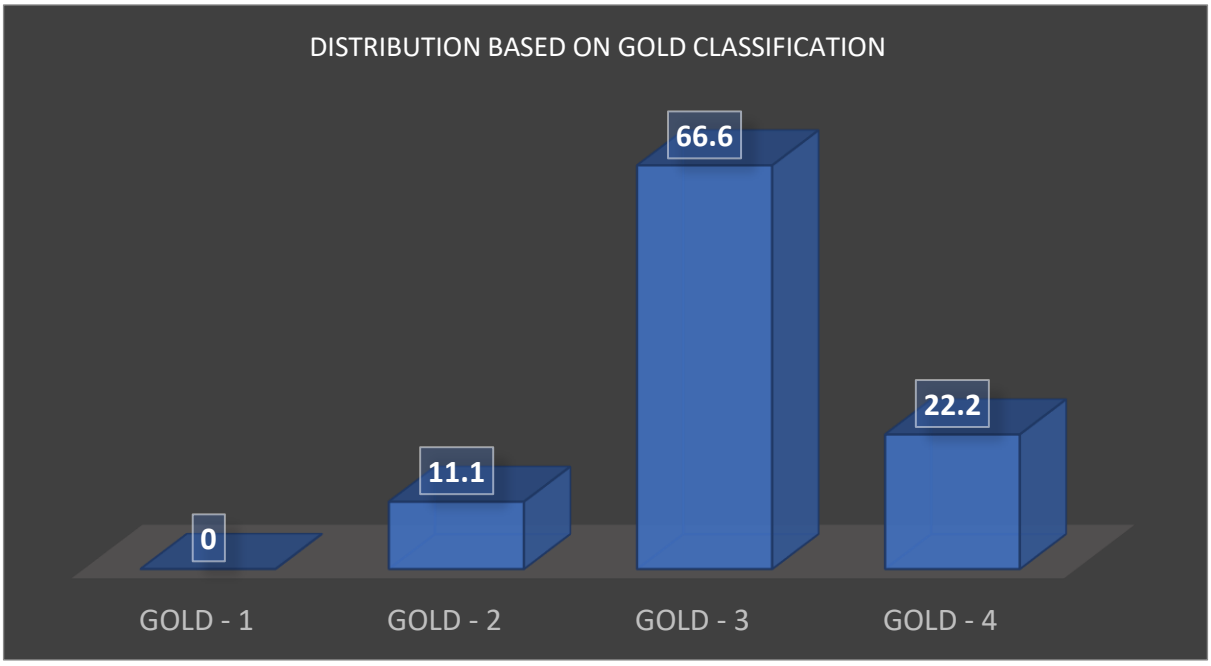
WHO Class	Number of Cases	Percentage (%)
Class I	1	2.86%
Class II	19	54.29%
Class III	10	28.57%
Class IV	5	14.29%
Total	35	100

6. Distribution of Pattern of Spirometry in cases of Pulmonary Hypertension

	Number of Cases	Percentage
Normal	11	31%
Restrictive	6	17%
Obstructive	18	51%
Total	35	100%

7. Distribution of Pulmonary Hypertension cases with Obstructive Airway Disease on the basis of GOLD Classification

GOLD Classification (% Predicted FEV1)	Number of Cases	Percentage
GOLD I (> 70%) (Minimal)	0	0%
GOLD II (50 – 69%) (Mild)	2	11.11%
GOLD III (30 – 49%) (Moderate)	12	66.67%
GOLD IV (< 30%) (Severe)	4	22.22%
Total	18	100%

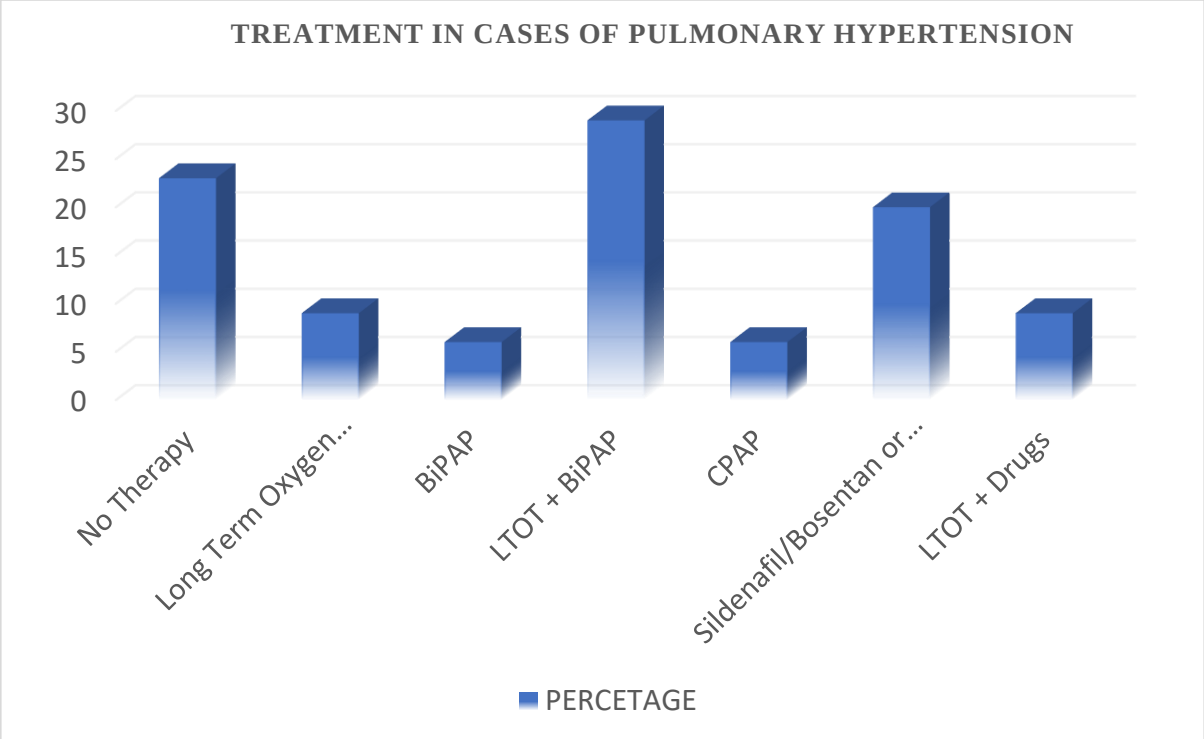


8. Pulmonary Hypertension and level of hypoxemia on ABG analysis

Severity of Hypoxemia (PaO2 in mm of Hg)	Number of Cases	Percentage
Normal (> 80)	4	11%
Mild (60-79)	8	23%
Moderate (40-59)	10	29%
Severe (< 40)	13	37%
Total	35	100%

9. Modalities of Treatment in cases of Pulmonary Hypertension

Therapeutic Modalities	Number of cases	Percentage
No Therapy	8	23%
Long Term Oxygen Therapy (LTOT)	3	9%
BiPAP	2	6%
LTOT + BiPAP	10	29%
CPAP	2	6%
Sildenafil/Bosentan or both (Drugs)	7	20%
LTOT + Drugs	3	9%
Total	35	100%



A total of 35 patients with evidence of Pulmonary Hypertension with no underlying cardiac cause of PH were studied for demographic, clinical, etiological and echocardiographic data. The prevalence of Pulmonary Hypertension was maximum in the age group of 51-60 years (28.57%) and increases after the age of 50 years (77.14%). Males outnumbered females with a ratio of 2.1. The most common etiology was COPD (51.43%) followed by idiopathic Pulmonary Artery Hypertension (iPAH) and Interstitial Lung Disease (ILD).In our study Echocardiographic measured RVSP showed most of the patient had mild Pulmonary Hypertension (46%) and were in WHO functional class II (54.29%).

DISCUSSION

Reviews of pulmonary hypertension (PH) almost invariably begin with a hemodynamic definition accompanied by a reference to the five categories or groups of PH.[6,7]
Updated WHO PH classification.[7]

1. Pulmonary arterial hypertension (PAH)
1.1. Idiopathic PAH
1.2. Heritable
1.2.1. BMPR2
1.2.2. ALK1, endoglin (with or without hereditary haemorrhagic telangiectasia)
1.2.3. Unknown
1.3. Drug- and toxin-induced
1.4. Associated with
1.4.1. Connective tissue diseases
1.4.2. HIV infection
1.4.3. Portal hypertension
1.4.4. Congenital heart diseases
1.4.5. Schistosomiasis
1.4.6. Chronic haemolytic anemia
1.5. Persistent pulmonary hypertension of the newborn
1.6Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)
2. Pulmonary hypertension owing to left heart disease
2.1. Systolic dysfunction
2.2. Diastolic dysfunction
2.3. Valvular disease
3. Chronic obstructive pulmonary disease
3.1. Chronic obstructive pulmonary disease
3.2. Interstitial drug disease
3.3. Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4. Sleep-disordered breathing
3.5. Alveolar hypoventilation disorders
3.6. Chronic exposure to high altitude
3.7. Developmental abnormalities

4. Chronic Thrombo-Embolic pulmonary hypertension (CTEPH)
5. Pulmonary hypertension with unclear thromboembolic multifactorial mechanisms
5.1. Hematologic disorders: Myeloproliferative disorders, splenectomy
5.2. Systemic disorders: Sarcoid, pulmonary Langerhans cell histiocytosis: neurofibromatosis, vasculitis
5.3. Metabolic disorders: Glycogen storage disease, Gaucher disease, thyrold disorders
5.4. Others: Tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis

A total of 35 participants were enrolled in the study. In our study maximum age group affected with Pulmonary Hypertension is 51-60 years, which was similar to study conducted by Eduardo M Moreira et al[8] where incidence is maximum in older age group compared to younger age group and it increases with age which is consistent with our study.

The most common etiology of Non cardiac cause of Pulmonary Hypertension in our study was COPD (51.43%) followed by idiopathic Pulmonary Artery Hypertension (iPAH) and Interstitial Lung Disease (ILD). This is slightly higher compared to study conducted by Limin Zhang et al[9] where incidence of Pulmonary Hypertension in 39.2%.

In meta analysis by Zhang et al[10] they found that as the severity of COPD increased, the prevalence of Pulmonary hypertension gradually elevated, of which most were mild (30.2% incidence) and few were severe (7.2% incidence), consistent with the general understanding of the disease.

In fact, the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) conducted a study on Phase 4 patients, suggesting that up to 90% of them may have an abnormal mPAP (>20 mmHg), most of which may range between 20 and 35 mmHg; only about 1% to 5% of the patients with COPD have a resting mPAP greater than 35 to 40 mmHg.[11] PH in COPD is caused by pulmonary vascular remodeling, which comprise toxic effects of cigarette smoke and is characterized by the following factors that interact either additively or independently: intimal proliferation of poorly differentiated smooth muscle cells, deposition of elastic and collagen fibers, a decrease in pulmonary vascular surface, parenchymal loss, inflammation, and alveolar hypoxia.[12-15] in contrast in our study we found that most of the patients falls in GOLD 3.

CONCLUSION

We conclude that, non-cardiac causes of Pulmonary Hypertension are prevalent in day to day practices and it is important to screen patients for Pulmonary Hypertension in disease like Chronic Obstructive Pulmonary Disease, Interstitial Lung Disease, Obstructive Sleep Apnea hypopnea syndrome and/or Obesity Hypoventilation Syndrome and idiopathic Pulmonary Artery Hypertension as timely diagnosis of Pulmonary Hypertension and institution of therapy is known to improve quality of life and decreases morbidity & mortality associated with the disease.

LIMITATIONS OF THE STUDY

The limitation of the study is that it was conducted at a single centre with a small sample size. A more extensive study involving multiple centres with a larger sample size on the topic would be advisable

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Authors' Contributions:

NK- Definition of intellectual content, literature survey, prepared the first draft of a manuscript, implementation of the study protocol, data collection, and manuscript preparation; **AS, NK and YG-** Concept, design, clinical protocol, and manuscript preparation; **AS and NKDG-** Design of study, literature survey, data analysis, statistical analysis and interpretation, manuscript preparation, editing and manuscript revision, review, and submission of article.

Work attributed to:

Department of General Medicine, SSIMS&RC, Davangere, Karnataka.

Orcid ID: