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Effect of Smoking on Pulmonary Hypertension: Prospective Observational Study

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Abstract **Original Research Article**

Pulmonary hypertension is a very common disease defined as as a mean pulmonary artery pressure (mPAP) ≥ 25 mm Hg along with a pulmonary artery wedge pressure ≤ 15 mm Hg. This study was conducted to know the role of smoking on pulmonary hypertension. Aims and objective-To study the socidemographic profile of pulmonary hypertension patients taken as study subjects, to study the status of smoking among the study subjects. And to find the correlation between smoking and pulmonary hypertension. Material and method- it is a Prospective Observational study conducted in a tertiary hospital. After obtaining ethical committee clearance patient who are fulfilling the inclusion criteria are selected. The purpose of the study was explained to the patient and informed consent obtained. Data was collected using a pretested study proforma meeting the objectives of the study Pulmonary Hypertension grading was done. Data was analysed using appropriate statistical method. Result- Mean age of patients is 62.9 ± 14.7years and maximum number of patients belongs to age group 61-80 years. Minimum age was 13 year and maximum age was 96 year. Out of 100 patients 51 were Male and 49 were Female.43 % patients were smokers and 57% were nonsmokers. 51% had mild pulmonary hypertension, 23 % had moderate and 26% had severe pulmonary hypertension. It was observed that pulmonary hypertension is common among nonsmokers (57 %), P value is 0.583 which is statistically insignificant. Discussion- Tobacco smoke exposure is common in all PH-classes. Pulmonary diseases are very common in smokers and so is PH. Developement of PH is multifactorial in such patients. However more studies are needed to find the correlation between smoking and pulmonary hypertension.

Keywords: Pulmonary hypertension, smoking, lung diseases.

INTRODUCTION

Precapillary pulmonary hypertension (PH) has been defined as a mean pulmonary artery pressure (mPAP) ≥ 25 mm Hg along with a pulmonary artery wedge pressure ≤ 15 mm Hg (to differentiate from pulmonary venous hypertension due to left heart disease)[1]. The patho- physiology of PH is still incompletely understood. It is thought that excessive vasoconstriction possibly in combination with inflammation may lead to endothelial dysfunction, which impairs the production of vasodilators along with an overexpression of vasoconstrictors [2]. The pathophysiology of PH in CLD is multifactorial and includes hypoxic pulmonary vasoconstriction, pulmonary vascular remodeling, small vessel destruction, and fibrosis. The effects of PH on the right ventricle (RV) range between early RV remodeling, hypertrophy, dilatation, and eventual failure with associated increased mortality. Few studies showed that smoking causes pulmonary remodeling leading to pulmonary hypertension [3-6]. Animal studies have shown that tobacco smoke exposure can lead to pulmonary endothelial dysfunction and plexogenic PH [7, 8]. This finding may even was found in some studies on human [9, 10]. Current study was conducted to know the role of smoking on pulmonary hypertension.

Aims and objective

- To study the socidemographic profile of pulomonary hypertension patients taken as study subjects
- To study the status of smoking among the study subjects.

- To find the correlation between smoking and pulmonary hypertension

MATERIAL AND METHODS

Study site: This study was conducted by Department of Respiratory Medicine in Ruby Hall Clinic, a 550 bedded Hospital, NABH accredited, with well-equipped Emergency and Critical Care Unit. It is one of largest hospital of Maharashtra.

Study population

Patients with lung disease who fulfill the inclusion and exclusion criteria, attending the outpatient department or undergoing inpatient treatment at Ruby Hall Clinic, Pune during the period of September 2014 to December 2015**.**

Study design

Prospective Observational study

Sample size calculation

By considering the prevalence of pulmonary hypertension among patients of lung diseases and /hypoxia as 45% (in our hospital), we have calculated the sample size by using following formula

N = 4* P * Q/ L^ 2

Where P = Prevalence

Q = 100-P

L = experimental error (10%)

Thus N = 99

We have considered the sample size 100.

Time frame to address the study

September 2014 to December 2015

Inclusion Criteria

Clinically diagnosed as lung disease and /or hypoxemia with subsequent confirmation by spirometry, Chest x ray, ABG and CT scan and echo screening showing raised pulmonary artery pressure which includes

- Chronic obstructive pulmonary disease
- Interstitial lung disease
- Other pulmonary diseases with mixed restrictive and obstructive pattern
- Sleep-disordered breathing
- Alveolar hypoventilation
- Chronic exposure to high altitudes
- Developmental abnormalities

Exclusion Criteria

- Valvular heart diseases
- Acute Left Ventricular Failure and Pulmonary edema secondary to other causes (hypertension, ischemic heart disease, cardiomyopathies)
- Primary pulmonary hypertension
- Chronic thromboembolic pulmonary hypertension

Methodology

After obtaining ethical committee clearance patient who are fulfilling the inclusion criteria are selected. The purpose of the study was explained to the patient and informed consent obtained. Data was collected using a pretested study proforma meeting the objectives of the study Pulmonary Hypertension grading was done. Data was analysed using appropriate statistical method.

STATISTICAL ANALYSIS

Descriptive statistics

Analysis was done by calculating proportions and percentages for qualitative data and mean, s.d, range for quantitative data.

Inferential statistics

Z-test (Standard Error of difference between two proportions) will be applied to check whether there is any statistically significant difference in proportions of different parameters.

Unpaired t-test will be applied to check the significant difference in means of different parameters. Statistical analysis was done by using Microsoft Excel and SPSS-22.

And Chi square test was used to find the correlation.

RESULTS

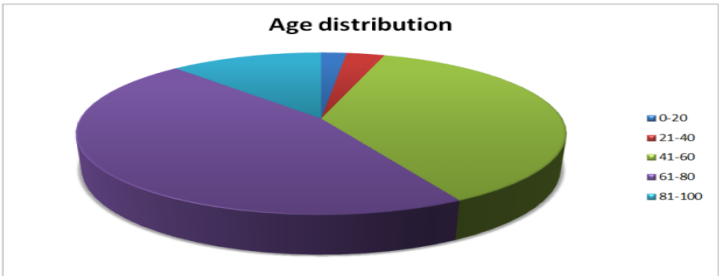

Fig-1: Age distribution of patients

Mean age of patients is 62.9 ± 14.7years and maximum number of patients belongs to age group 61-80 years. Minimum age was 13 year and maximum age was 96 year.

Table-1: Gender distribution of patients

Gender	Number of patients (n)	Percentage
Male	51	51
Female	49	49
Total	100	100

Table above shows the gender distribution of study subjects. Out of 100 patients 51 were Male and 49 were Female.

Table-2: Smoking status of patients

Smoking	Number of patients(n)	Percentage
Yes	43	43
No	57	57
Total	100	100

It has been observed that 43% patients were smokers and 57% were nonsmokers.

Table-3: Mean pulmonary artery pressure (mPAP)

	Number of patients (n)	Percentage (%)
Mild	51	51
Moderate	23	23
Severe	26	26
Total	100	100

It was observed that out of 100 patients 51% had mild pulmonary hypertension, 23 % had moderate and 26% had severe pulmonary hypertension.

Table-4: Association of smoking and severity of pulmonary hypertension

Smoking		Mean pulmonary artery pressure			Total	Chi Sq	P value
		Mild	Moderate	Severe			
	No	30	11	16	57		
		58.8%	47.8%	61.5%	57.0%		
	Yes	21	12	10	43	1.077	0.583
		41.2%	52.2%	38.5%	43.0%		
Total		51	23	26	100		
		100.0%	100.0%	100.0%	100.0%		

It was observed that pulmonary hypertension is common among non-smokers (57 %), P value is 0.583 which is statistically insignificant.

DISCUSSION

In the current study it was found that most of the study subjects were male that is 51% and rest were females. PH in females is almost similar to males. A higher susceptibility could perhaps explain the lower active but higher secondhand smoke exposure in PH women. If predisposed women, for example those who are genetically more susceptible due to alterations in genes responsible for PAH, such as BMPR2 mutations, are exposed to constituents of tobacco smoke, a lower cumulative dose might be sufficient to initiate pulmonary vascular remodeling, ultimately leading to PH.

The mean age of study subjects was around 62 years. Study conducted by Keush S *et al*. also found that the mean age of study subjects was 57 years [11]. In present study it has been observed that the there was not any correlation between the smoking and pulmonary hypertension. Similar finding had been observed in study conducted by Keush S *et al*. in which they observed no overall difference of tobacco smoke exposure between PH-patients and controls [11].

It has been known from animal experiments that tobacco smoke inhalation leads to immediate and temporary elevation of the pulmonary arterial pressure. This has been shown in dogs, frogs, rabbits, cats, rats and guinea pigs [12], and animal models of guinea pigs and rats exposed to tobacco smoke were used to study PH and the vasoproliferative response [13, 14].

Tobacco smoke exposure also induced cell proliferation of smooth muscle cells of the vasculature [14, 15], led to infiltration of inflammatory cells, and gene expression with overproduction of different mediators responsible for cell proliferation and vasomotor regulation, namely inducible nitric oxide synthase [16], endo-thelin, vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF) and others [17]. The alterations lead to endothelial dysfunction of the pulmonary vasculature [18]. In PAH patients, similar inflammatory processes with

disturbances in endothelial and smooth muscle cell function, overexpression of growth factors (PDGF, VEGF, fibroblast growth factor) and an unbalance in vasodilators and vasoconstrictors (endothelin 1, serotonin, thromboxane A2, nitric oxide, prostacyclin) are prominent.

The present study has the following limitations. First, we cannot exclude a selection bias. Although we systematically included consecutive PH patients, we cannot exclude that some PH patients were missing in the present analysis due to logistics or for time reasons. Second, as this survey was based on questions regarding tobacco smoke exposure, patients may not have remembered every detail of the amount and timely sequence of tobacco smoke exposure, resulting in a declaration bias of smoking history or exposure to environmental tobacco smoke.

CONCLUSIONS

Tobacco smoke exposure is common in all PH-classes.Pulmonary diseases are very common in smokers and so is PH. Developement of PH is multifactorial in such patients. However more studies are needed to find the correlation between smoking and pulmonary hypertension.

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