Frequency of secondary Polycythemia in patients with Chronic Obstructive Pulmonary Disease

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Author Contributions

RU conceived idea, RU ZI SA planned the study, HAN drafted the manuscript, HAN collected data, RU SA did statical analysis and interpretation, RU ZI SA critical reviewed manuscript, ZI approved the final version to be published.

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The Authors declares that there is no conflict of interest.

ABSTRACT

Objective: Secondary polycythemia is an important complication of chronic obstructive pulmonary disease (COPD) but its frequency of occurrence is unknown in our setup. There are many potentially modifiable risk factors to prevent secondary polycythemia. This study was performed to know the frequency of secondary polycythemia in patients with COPD.

Methods and Methodology: This was cross sectional study carried out in the Department of Pulmonology of Khyber Teaching Hospital Peshawar from October 2015 to October 2016. In this study Patients, diagnosed with COPD of aged 40 years and above were included in the study through consecutive, non-probability sampling technique. World Health Organization (WHO) software was used to calculate sample size with the assumptions of 6%[11] proportions of secondary polycythemia in COPD patients, 95% confidence interval and 7% margin of error. Patients with asthma and diagnosed polycythemia were excluded from the study.

Results: 241 patients with Chronic Obstructive Pulmonary Disease were enrolled in this study. 112 (46.5%) patients were male and 129(53.5%) were female. Mean age was 63 years (+ 11.38). All the patients have variable duration of COPD diagnosis; 70 patients had duration of COPD <5 years, 57 patients 6-10 years, 35 patients 11-15years, 36 patients 16-20 years, 30 patients 21-30 years, 12 patients 31-40 years while only one patient had COPD duration of one year, with the mean duration of 13 (±10) years. Secondary Polycythemia was found in 26 (10.8%) patients. Out of these confirmed case females constitute 11 (4.6%) while rest 15 (6.32%) were male. The duration of COPD was found between 15-30 years in patients with Secondary Polycythemia.

Conclusion: COPD Patients had a significant prevalence of secondary polycythemia, and ignoring this may lead to complications.

Key words: COPD; Secondary polycythemia; Peshawar

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Introduction

Chronic obstructive pulmonary disease (COPD) is a respiratory disease associated with persistent airflow obstruction that is progressive in nature and not fully reversible.[1] There is an increased chronic inflammatory response in the airways and the lungs that occurs in response to noxious particles/gases.[2] It is ranked 4th most common cause of death worldwide.[3] In adults aged 40 and above its prevalence is 9-10%.[4] In Pakistan, COPD mortality rate is estimated to be 71 deaths/100,000, which is the world fourth highest rate in the 25 most populous nations.[5] It is diagnosed

through spirometry by demonstrating fixed or partially reversible airflow obstruction (FEV1/FVC ratio <70% post bronchodilator). COPD is treatable a and preventable disease with some important extra pulmonary effects that may contribute to the morbidity and mortality in these patients. The diagnosis of COPD should be suspected in all those patients with chronic cough, dyspnea or sputum production, and/or haveing a history of exposure to risk factors like smoking for the disease. Biggest risk factor is smoking.[6] Other risk factors include exposure to indoor and outdoor pollution, genetic susceptibility etc. In addition to this gastroesophegeal reflux also play an important role in COPD development. The gold standard test for diagnosis of COPD is spirometry.[7] COPD may cause a number of complications like cardiovascular diseases e.g. pulmonary hypertension which may result in cor-pulmonale, arrhythmias, cerebrovascular diseases, depression, osteoporosis, cachexia and skeletal muscle dysfunction which may result in type-II respiratory failure, anemia and increase thrombogenicity. Polycythemia is One of the complications of COPD which occurs secondary to hypoxemia &/or carboxyhemoglobin because smoking is an important causes of COPD.[8]

Secondary polycythemia is defined as an absolute increase in RBC mass which is caused by increased stimulation of RBC production in response to increase in erythropoietin,[9] appropriate or inappropriate. It is suspected when the patient presents with symptoms of headache, vertigo, blurring of vision and signs of plethora and cyanosis. It is diagnosed when Hematocrit (HCT) is >48% in females & >52% in males.[10] Cote C et al. in United States of America found that the prevalence of secondary polycythemia in COPD patients is 6%.[11] It can result in thrombosis, hemorrhage, stroke, myocardial infarction and cardiac failure.[12] In COPD the secondary polycythemia develops when hypoxemia triggers the erythropoietin producing cells in the Kidneys, which results in increased production of Erythropoietin followed by increased level of red cell mass and hematocrit. Secondary Polycythemia is differentiated from Primary Polycythemia by measuring the Erythropoietin level, which is normal in Primary Polycythemia while raised in Secondary Polycythemia.

The main objective of this study is to determine the frequency of secondary polycythemia in patients suffering from chronic obstructive pulmonary disease. This will provide an objective evidence of frequency of secondary polycythemia in COPD patients and will highlight the need for preventive strategies.

Material and Methods

This descriptive cross-sectional study was carried out in the Department of Pulmonology, Khyber Teaching Hospital Peshawar, Pakistan from October 2015 to October2016. Two hundred and forty one patients were included through consecutive, non-probability sampling technique. WHO software for sample size determination was used to calculate sample size with the assumptions of 6%[11] proportions of secondary polycythemia in COPD patients, 95% confidence interval and 7% margin of error. Patients, both males and females, diagnosed with COPD and aged 40 years and above were included in the study. Patients with asthma and diagnosed polycythemia were excluded from the study.

All those Patients fulfilling the diagnostic criteria for Chronic Obstructive Pulmonary Disease as per Pakistan Chest Society Guidelines (post bronchodilator FEV1/FVC ratio <70%) and presenting to pulmonology OPD/ward in Khyber Teaching Hospital, Peshawar, were enrolled in the study after taking a written informed consent. Demographic characteristic was recorded and information regarding duration of COPD was asked. Under aseptic technique 5ml of blood was obtained from the patient and was sent to the hospital laboratory for Hematocrit examination to detect secondary polycythemia. Bias and confounders was controlled by strictly following exclusion criteria. All the tests were done by the same laboratory and under the supervision of an expert hematologist.

Statistical analyses were carried out with SPSS-15. Frequencies and percentages were calculated for nominal variables like gender, COPD and secondary polycythemia. Mean±standard deviations (SD) were calculated for continuous variables like age.

Results

A total of 241 patients, were studied for frequency of secondary polycythemia in COPD. One hundred and twelve (46.5%) patients were male and 129 (53.5%) were female (Table 1).The mean age was 63 (±11.38) years (Table 2). Patients with duration of COPD diagnosed were stratified as; 70 patients had duration of COPD <5 years, 57 patients had duration of 6-10 years, 35 patients had 11-15 years, 36 patients had 16-20 years, 30 patients had 21-30 years, 12 patients had 31-40 years while only one patient had COPD duration of one year, with the mean of 13 (+10) years (Table 3).

Secondary Polycythemia was found in 26 (10.8%) patients. 11 (4.6%) among these confirmed cases were female with hematocrit level of more than 48%

Table 1: Gender distribution of the study cases

Sex Of Patient	Frequency	Percentage
Male	112	46.5
Female	129	53.5
Total	241	100.0

Table 2: Age Distribution of patients

Statistic tests	Age of patient (years)
Mean	63.37
Standard Deviation (±)	11.38

Table 3: Mean and standard deviation of COPD duration

Statistics	Duration Of COPD in Years
Mean	13.23
Standard Deviation (±)	10.04

Table 4: Frequency of secondary polycythemia among study cases

Secondary Polycythemia	Frequency	Percentage
Yes	26	10.8
No	215	89.2
Total	241	100.0

and 15 (6.32%) were male with hematocrit value more than 52% (Table 4). The duration of COPD was found to be 15-30 years in patients with Secondary Polycythemia.

In our study, the risk factors associated with secondary polycythemia in COPD patients were severity of the disease at presentation and duration of disease.

Discussion

Globally COPD, in the coming decades is expected to increase. The main reasons are increased life expectancy, the changing age distribution, and an increasing proportion of the population living above 60 years[13]. In our study the mean age was 63 (+11.38) years, while the mean age was 68 years in study by Chambellan et al.[14] from France.

Worldwide, COPD prevalence is more in males than in females[15]. In our study the predominant gender was female in contrast to the studies from Cote et al.[16] and Tripathy et al.[17] where male are predominantly suffered from COPD. This can be explained by the fact that in our society females are very much exposed to cooking fire smoke from using biomass fuel as wood and animal dung, a type of indoor air pollution. This is supported by a Chinese study which showed that in developing countries and especially in women, cooking fire smoke (indoor air pollution) is a common cause of COPD, in contrast to developed countries where 80-90% cases are associated with cigarette smoking[18]. Similar findings of exposure to indoor air pollution were reported in rural areas of Pakistan.[19]

Secondary polycythemia occurs less frequently in COPD patients in contrast to commonly thinkings.it occurs less frequently nowadays because of more rigorous correction of hypoxemia.[20] 5% increase in hematocrit increases the relative risk of death by 14% and hematocrit is the strongest predictor of mortality after age.[11] Secondary polycythemia is associated with metabolic acidosis, pulmonary hypertension, tissue hypoxia, coronary artery disease, stroke and increased thrombogenicity which may result in fatal pulmonary embolism.[21-25]

Secondary Polycythemia was confirmed in 10.8% patients in our study. Among these confirmed case 4.6% were female and rest 7.1% were male, while it is reported by Cote C et al to be 6% of the COPD patients[11]. In our study the frequency of secondary polycythemia in COPD was higher as compared to the other studies, and this can be explained by two factors. One is the geographical and cultural differences and second is the socioeconomic status of our patients. Most of our patients belong to poor families and work in heavily polluted areas along with exposure to indoor pollution and tobacco smoking and are unable to continue their proper treatment. So the government, and pharmaceutical companies should pay attention to this poor socioeconomic status of our patients by reducing the prices of medications and

the doctors should arrange teaching secessions to educate the patients regarding the disease, its risk factors, proper treatment, proper inhaler techniques and prevention of exacerbations, because all of these play a significant role in the development of COPD complications.

Conclusion

Most complications of COPD are associated with the severity of the COPD. To prevent these complications, all risk factors that accelerate the decline in FEV1 and severity of COPD should be sought and modified, if possible. Not recognizing and addressing these factors may lead to inappropriate escalation of the therapy and avoidable hospitalizations and complications.

Smoking, exposure to indoor air pollution, poor treatment adherence, lack of influenza and pneumococcus vaccination, and improper inhaler technique are common potentially modifiable risk factors that result in accelerated decline in FEV1 and severity of COPD in our set up. Effective smoking cessation counseling needs to be ensured from the very first encounter with COPD patient. Continuous and strict adherence to the COPD medications should be emphasized.

Keeping in mind the impact on health and health care resources, it is essential to develop effective strategies for prevention of COPD complications.

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