

Descriptive Cross-Sectional Study on Blood Disorder and Lung Disease

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Abstract: Background: Chronic Obstructive Pulmonary Disease (COPD) is a chronic inflammatory disease due to smoking. It is avertable as well as treatable. COPD is a one of the main cause of morbidity and mortality affecting developed and developing countries. We aim to estimate burden of anemia at a tertiary care public sector hospital. **Methods:** This is a descriptive cross sectional study, done at JPMC Karachi in 2014. All COPD patients admitted in medicine and pulmonology departments were enrolled in this study. After informed consent, data of complete blood count was accessed from medical record and anemia was labeled as per operational definition. Data analyzed by SPSS version 16.0. Frequency and percentage proportion of qualitative variables, mean and standard deviation of numerical values were calculated with P value <0.05 was taken as significant. **Results:** Of 137 cases, 118(86.13%) were males and 19(13.87%) were females while male to female ratio was 6.2: 1. The average age and weight of the patients was 58.31±12.17 years and 59.36±10.56kg, similarly average duration of disease and hemoglobin of the patients was 5.69±4.42 years and 12.34±1.58 mg/dl respectively. 37.96% (52/137) patients were anemic in our study. Rate of anemia in COPD patients was not significant among age groups (p=0.076) and with duration of disease (p=0.22). **Conclusion:** Anemia seems to be a common feature in COPD (37.96%), mechanisms involved in the genesis of anemia in COPD are poorly studied. Low hemoglobin level can have adverse effects on certain respiratory parameters in COPD, increasing morbidity and mortality.

Keywords: Chronic Obstructive Pulmonary Disease (COPD), Anemia, Hemoglobin.

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INTRODUCTION

Chronic obstructive airway disease (COAD) or chronic obstructive pulmonary disease (COPD) is progressive inflammatory airway disease that is associated with poor quality of life. COPD is one of the leading illness causing mortality worldwide. It includes previously two disease processes that are emphysema and chronic bronchitis. It manifests as a chronic breathing problem and poor airflow with air trapping in lungs. According to recommendation of the Global Initiative for chronic obstructive lung Disease (GOLD), that the chronic obstructive airway disease (COAD) or chronic obstructive pulmonary disease (COPD) will be

diagnosed on the basis of clinical features (signs and symptoms) i-e productive cough (cough with sputum) for at least 3 months/year for at least two years are characteristic of chronic bronchitis and shortness of breathing or dyspnea and cough are characteristic of emphysema. These diseases processes are measured by Spirometry.

On the basis of Spirometry COPD patients were staged on the basis of severity of symptoms into four stages [stage I (FEV1≥80%), stage II (50%≤FEV1<80%), stage III (30%≤FEV1<50 %) and stage IV (FEV1<30 %)] [1]. These symptoms are

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chronic [2], and with passage of time these symptoms worsens and patients deteriorate [3]. It is an emerging burden on the global health system as it is quickly up trending to become one of the leading cause of morbidity and mortality [4]. It is not only considered as a cause of healthcare burden but causing enormous economic and social menace throughout the world [1]. COPD (emphysema and chronic bronchitis) had affected about 174.5 million people or 2.4% of population of the world in 2015 [5] and it occurred mostly in people of having age more than 40 years equally in both genders [6]. In 2015, 3.2 million deaths were reported and it was increased from 2.4 million deaths in 1990 [7,8]. It was estimated that more than 90% deaths were occurred in developing countries [6].

Smoking is considered as one of the leading risk factor for development of Chronic obstructive airway disease (COAD) or chronic obstructive pulmonary disease (COPD) and the duration of smoking were having linear relationship with it [4]. The number of deaths will rise in developing countries because of higher rates of smoking especially in old age people [9]. Smoking is a common risk factor in development of many chronic diseases like coronary heart disease (CHD), congestive cardiac failure (CCF) and bronchogenic carcinoma or carcinoma of lung. COPD (emphysema and chronic bronchitis) often coexists with other co-morbid in patients like ischemic heart disease (IHD), Osteoporosis, Skeletal muscle dysfunction (wasting), Depression and blood disorders (anemia) causing a significant impact on prognosis [10,11]. These co-morbidities had an effects on potentiating the overall morbidities in patients of COPD, so it leads to increased rate of hospitalizations, poor life style, increased expenses of medical care, and eventually death. It is associated with extra-pulmonary manifestations like anemia.

Anemia is caused by chronicity of disease or chronicity of illness, systemic inflammatory or oxidative process [12]. although it is “traditionally” associated with secondary polycythemia but practically many patients are found to be anemic. This anemia is known as anemia of chronic disease (ACD). The systemic effects or systemic inflammation had direct effects of the disease with having a relationship with cause-and-effect output. Screening and treatment of these co-morbid conditions i-e Ischemic heart disease (IHD), Osteoporosis, Skeletal muscle dysfunction (wasting), Depression, nutritional disorders (malnutrition) and blood disorders (anemia) had a role in management of COPD. Chronic systemic inflammation had a vital role in the development of extra-pulmonary manifestations of COPD. Anemia worsens dyspnea or shortness of breathing and limit exercise tolerance [13]. The Hemoglobin (Hb%) levels correlated with reduced functional capacity, increased shortness of breathing, reduced exercise tolerance or capacity, reduced or impaired quality of life (QOL),

increased stay in hospital, early morbidity and mortality with severe inflammation in COPD patients [14].

There are many cofounders in chronic obstructive pulmonary disease patients like old age, nutritional disorders (malnutrition) and cardiovascular disease (IHD, CCF), and leads to development of anemia. Nutritional disorders or Malnutrition had association development of anemia due to with iron, folate or vitamin B12 deficiency [11]. The objective of this study is to assess the burden of anemia in chronic obstructive pulmonary disease patients at a tertiary care hospital Karachi.

Operational definition

Anemia is defined as a decrease in the total number of erythrocytes or decreased concentration of hemoglobin in the blood, in our study hemoglobin levels <13.5 mg/dl in males and <12.0 mg/dl in females were labeled as anemia [15, 16].

METHODOLOGY

This study was a descriptive cross-sectional, which included 137 COPD patients. These COPD patients were admitted in departments of medicine and pulmonology. This study was conducted for six months in 2014 in Jinnah Postgraduate Medical center Karachi. Sample size was calculated by formula:

$$\text{Sample Size}^*: n = Nz^2p(1-P)/d^2 (N-1) + z^2 p(1-P)$$

Numbers of participants were calculated i-e 137 subjects. After taking approval of synopsis from college of physicians and surgeons of Pakistan (CPSP), subjects were enrolled from admitted patients. Diagnosed cases of COPD, of both male and female sex and Age >35 years and <70 years were included. Patients with Co-morbid conditions e.g. heart failure, end stage renal disease, autoimmune disorder such as Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), patients taking iron supplements, history of blood transfusion and refusing for consent were excluded from this study. After informed consent, thorough history and physical examination was done. Data was collected on predesigned proforma. Each patient's laboratory data of complete blood count (CBC) was seen from medical record and anemia was labeled as per operational definition.

Collected data is analyzed by using the Statistical Package for Social Sciences (SPSS) version 16 computer software. Descriptive statistics like frequency, percentage proportion were computed for presentation of qualitative variables like gender, smoker, anemia, Diabetes Mellitus (DM), Hypertension (HTN), educational and economic status. Mean and standard deviation (SD) were calculated for presentation of numeric variables like age, weight and hemoglobin (Hb%). Effect modifier like age, gender, duration of disease, smoking status, DM, HTN, weight

were controlled through stratifications and Chi-square (χ^2 test) was applied to detect difference between categorical variables with significant (<0.05) and non-significant (>0.05) P-value.

RESULTS

137 COPD patients were enrolled and included in this study, out of this 118(86.13%) were males (M) and 19(13.87%) females (F) while M to F ratio was 6.2:1. The mean age and weight of the COPD patients was 58.31 ± 12.17 years (median age 60 years) and 59.36 ± 10.56 kg, similarly mean duration of disease and

hemoglobin of the patients was 5.69 ± 4.42 years and 12.34 ± 1.58 mg/dl respectively as shown in table-1. In COPD patients included in our study frequency of anemia, smoking, hypertension and diabetes mellitus was 37.96% (52/137), 100% (137), 6.6% (9/137) and 2.2% (3/137) respectively as shown in Table- no 2.

In this study anemia in COPD patients has no significant association with age ($p > 0.076$), gender ($p > 0.36$), and duration of the disease ($p > 0.22$) respectively as shown in Table 3.

Table 1: Demographic and clinical characteristics of the patients (n=137)

Variables	Mean \pm SD	Median (IQR)	Range
Age (Years)	58.31 \pm 12.17	60(18)	35-90
Weight (kg)	59.36 \pm 10.56	58(17)	39-87
Duration of disease (months)	5.69 \pm 4.42	5(6)	1-28
Hemoglobin (mg/dl)	12.34 \pm 1.58	12.5(2.5)	9-16

Table 2: Categorical variable in COPD patients (n-137)

Variable	COPD		Total (n-137)
	Yes	No	
Anemia	52 (37.96%)	85 (62.04%)	137
Smoking	137 (100%)	0 (0%)	137
History of Diabetes Mellitus	3 (2.2%)	134 (97.8%)	137
History of Hypertension	9 (6.6%)	128 (93.4%)	137

Table 3: Frequency of anemia in patients with respect to gender, age and duration of disease

		COPD			p-value
Variables		Presence of anemia n=52	Absence of anemia n=85	Total n=137	
Age	36 years-40 Years	1(10%)	9(90%)	10	137 $p > 0.076$
	41 years-50 Years	14(45.2%)	17(54.8%)	31	
	51 years-60 Years	18(38.3%)	29(61.7%)	47	
	61 years-70 Years	9(28.1%)	23(71.9%)	32	
	>70 Years	10(58.8%)	7(41.2%)	17	
Gender	Male	43(36.4%)	75(63.6%)	118	137 $p > 0.36$
	Female	9(47.4%)	10(52.6%)	19	
Duration of disease	\leq 10 Years	39(35.5%)	71(64.575%)	110	137 $p > 0.22$
	>10 Years	13(48.1%)	14(51.9%)	27	

Chi-Square, significant (p -value < 0.05) and non-significant (p -value > 0.05)

DISCUSSION

Anemia is one of the extra-pulmonary manifestations in patients having signs and symptoms of chronic obstructive pulmonary disease (COPD). In this study frequency of anemia has been observed in patients was 37.96%, median hemoglobin (Hb%) level was 12.5 gm/ dl and gender based comparison showed frequency of anemia was 36.4% (43/118) in males and 47.4% (9/19) in females which is not statistically significant ($p > 0.36$). Similar results are reported in a study which includes 53 patients with median hemoglobin level (12.8 gm/dl) and gender based comparison showed frequency of anemia was (49.4% [41/83] in males and 52.2% [12/23] in females with P-value ($P=1.00$) [17]. This study supports our results. In 2015, study was published in British Medical Journal

(BMJ), in which anemia prevalence is in range b/w 33%–44% in COPD patients [18]. Perveen *et al.* done a hospital-based cross-sectional study in which she founded 18% anemia in chronic obstructive airway disease (COPD) patients [19].

Shorr *et al.* had done data analysis of chronic obstructive airway disease (COPD) patients retrospectively in which 33% patients were reported anemic [20]. Anemia is directly associated with worsening of clinical features that leads to mortality or death in chronic obstructive airway disease (COPD) patients. It is considered as predictor, which is affecting the prognosis (long term), so that it is causing mortality in exacerbations of admitted patients. During Exacerbation of symptoms in COPD patients, leads to

increase in concentration of oxidative stress, plasma fibrinogen and serum interleukin (IL-6) levels, so comorbidities increases in patients. The secretion of C-reactive protein (CRP) is increased by the liver due to interleukin 6(IL-6). C-reactive protein (CRP) is an acute phase reactant and is sensitive marker of inflammation [11]. The anemia had multiple complex mechanisms in COPD patients like systemic inflammation and anemia of chronic disease (ACD).

Multiple inflammatory cytokines like interleukins (IL-1&IL-6), and tumor necrosis factor (TNF-alpha) are responsible for inhibition or harmful effect in erythropoietic pathway (erythropoiesis) in COPD patients. The patients having lower levels of hemoglobin (Hb%) concentration or anemia will be associated with poor prognosis in COPD sufferers [21]. ACD occurs due to alternation in iron metabolism.

There is increased level of hepcidin, and increased inflammatory cytokines or interleukins (IL-1&IL-6), and tumor necrosis factor (TNF-alpha) in chronic obstructive airway disease (COPD) patients. These are regulating iron homeostasis in human body. Functional iron deficiency is related to decreased oxygen concentration in the blood leads to decreased tolerance of exercise and limitation in response to pulmonary rehabilitation [22,23]. Yuruk *et al.* had observed in his study that decreased hemoglobin (Hb%) concentrations or anemia was showing association with oxygen saturation within capillaries or microcirculation and after treatment of anemia resulted in improvement of transport capacity of oxygen and oxygen saturation in tissue cells [24].

Anemia is associated with shortness of breathing and it worsens the health related quality of life [25]. Anemia or decreased hemoglobin concentration is major risk factor for repeated admissions (25%) and worsening of dyspnea than non-anemic COPD patients. Dyspnea and easy fatigability are main symptoms of COPD patients and it exerts negative effects on health related quality of life (QOL) of these patients. Hemoglobin correction (whether anemia or polycythemia) in COPD patients may improve QOL and decrease co-morbidity and mortality of these patients [26].

CONCLUSIONS

Anemia is quite common in our study (37.96%), as opposed to medical literature which mentions polycythemia in these patients. Mechanisms involved in the genesis of anemia in COPD are poorly studied; moreover low hemoglobin level can have adverse effects on oxygen saturation and functional class of patients in COPD, leading to increased morbidity and mortality. Further studies are needed to look up if treatment of anemia in COPD patients results into better outcomes.

Conflict of interest: None to declare.

Ethics approval: From College of Physicians & Surgeons, Pakistan (CPSP), Acceptance number: REU NO: 8813

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Patient Consent: Informed consent taken from the patients or their guardian, if language barrier via translator.

The Limitations of our study: Single centre study.

Recommendations: Future studies with more number of patients and effect of anemia correction on COPD should be studied.

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