



ORIGINAL ARTICLE

## Impact of anemia on exercise capacity in patients with chronic obstructive pulmonary disease.

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**ABSTRACT... Objective:** To assess the impact of anaemia on exercise capacity in Chronic Obstructive Pulmonary Disease (COPD) patients by comparing the six-minute walk distance (6MWD) between anaemic and non-anaemic individuals. **Study Design:** Cross-sectional study. **Setting:** Department of Pulmonology, Khyber Teaching Hospital, Peshawar. **Period:** November 15, 2019 until May 14, 2020. **Methods:** This study included 162 COPD patients aged 40 to 70 years. Exclusion criteria encompassed any lung pathology other than COPD, malignancy, cardiac pathology, or conditions affecting hemoglobin levels. The 6MWD test was utilized to evaluate exercise capacity. Data analysis utilized SPSS Version 25.0, with descriptive statistics employed to summarize the demographic and clinical characteristics of the study population. A significance level of  $\leq 0.05$  was used to determine statistical significance. **Results:** The mean age of participants was 62.07 years, with a mean hemoglobin level of 12.63 gm/dl. The average 6MWD was 234.78 meters. Among the subjects, 40.74% were male. Anaemic patients had a significantly lower 6MWD ( $190.99 \pm 95.44$  meters) compared to non-anaemic patients ( $278.58 \pm 100.17$  meters;  $p \leq 0.001$ ). There were no significant differences in COPD duration, age, body mass index, or smoking status between the two groups. **Conclusions:** Anaemic COPD patients demonstrated a significantly reduced exercise capacity, covering approximately two-thirds of the distance non-anaemic patients did on the 6MWD test. These findings suggest that early diagnosis and management of anaemia in COPD patients could potentially improve their exercise tolerance and overall quality of life.

**Key words:** Anaemia, Chronic Obstructive Pulmonary Disease, Exercise Capacity, Peshawar, Six-minute Walk Distance.

### INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a condition of the respiratory system that worsens over time, marked by permanent constriction of airflow and posing a substantial impact on worldwide health.<sup>1</sup> The condition primarily arises from contact with harmful particles or gases, typically from sources like tobacco smoke, resulting in a continuous inflammatory reaction within the air passages and lungs.<sup>2,3</sup> COPD not only diminishes pulmonary function but also affects the physical and psychological well-being of individuals, significantly impacting their quality of life.<sup>4</sup>

Exercise intolerance, a hallmark of COPD, is multifactorial in origin, encompassing ventilatory limitation, muscle dysfunction, and cardiovascular

impairments.<sup>5</sup> Among these, the role of systemic factors such as anemia in exacerbating exercise intolerance is gaining increasing recognition.<sup>6</sup> Anemia, defined as a reduced concentration of hemoglobin in the blood, is prevalent in COPD patients and is associated with worse outcomes, including increased dyspnea, reduced exercise capacity, and higher hospitalization rates.<sup>7,8</sup>

The Six-Minute Walk Test (6MWT) has become an invaluable asset in evaluating the functional exercise capacity of individuals with COPD.<sup>9</sup> It simulates daily physical activities and has been correlated with the severity of disease, prognosis, and response to therapy.<sup>10</sup> Despite its simplicity, the 6MWT provides critical insights into the patient's ability to perform daily tasks, thereby serving as a surrogate marker for quality of life.<sup>11</sup>

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Nevertheless, the precise influence of anemia on the exercise capacity of COPD patients, as assessed through the 6MWT, has not been thoroughly investigated in existing literature. This gap underscores the need for comprehensive studies to elucidate the relationship between anemia and exercise intolerance in this patient population. Understanding this relationship is crucial for developing targeted interventions aimed at improving the overall management and prognosis of COPD patients.

This study seeks to fill this gap in knowledge by examining how anemia affects the exercise capacity of COPD patients, measured through the 6MWT. By comparing the exercise capacity between anaemic and non-anaemic COPD patients, this research highlights the significance of screening for and managing anemia as part of a holistic approach to COPD care. These valuable insights are positioned to significantly aid in refining clinical management approaches, with the goal of improving the quality of life for those suffering from this challenging condition.

## METHODS

### Study Design and Setting

This cross-sectional study took place at the Department of Pulmonology, Khyber Teaching Hospital in Peshawar, spanning from November 15, 2019, to May 14, 2020. Approval for the study protocol was obtained from the Institutional Ethics Committee/Institutional Review Board (535/ADR/KMC) (17-06-2019), ensuring adherence to ethical standards in research involving human participants.

### Participants

The research study comprised 162 individuals diagnosed with Chronic Obstructive Pulmonary Disease (COPD), ranging in age from 40 to 70 years. Participants were sourced from both outpatient and inpatient facilities within the Pulmonology Department.

### Inclusion criteria

The inclusion criteria involved individuals who had a verified diagnosis of COPD according to

the criteria set by the Global Initiative for Chronic Obstructive Lung Disease (GOLD), including both those with and without anemia.

### Exclusion criteria

Exclusion criteria were patients with co-existing lung diseases (such as asthma, tuberculosis, or lung cancer), significant cardiovascular disease, uncontrolled hypertension, neurological or musculoskeletal impairments affecting walking ability, and those unable to provide informed consent.

### Data Collection

Prior to data collection, all participants provided informed consent. A structured questionnaire and medical record review were utilized to gather demographic and clinical information, encompassing age, gender, smoking history, duration of COPD, height, weight, and Body Mass Index (BMI).

### Anemia Definition

Anemia was characterized in accordance with the criteria established by the World Health Organization (WHO), where hemoglobin levels were deemed deficient if they were  $\leq 13\text{g/dl}$  in males and  $\leq 12\text{g/dl}$  in non-pregnant females. Hemoglobin levels were assessed using the Sysmex-CA 600 series, administered by a seasoned pathologist with a minimum of five years of expertise.

### Six-Minute Walk Test (6MWT)

The Six-Minute Walk Test (6MWT) was conducted in accordance with the guidelines set forth by the American Thoracic Society (ATS). The test involved measuring the maximum distance (in meters) that a participant could walk along a flat, straight corridor in six minutes. Baseline and post-test measures of systolic and diastolic blood pressures, pulse rate, and oxygen saturation were recorded using a pulse oximeter.

### Statistical Analysis

Data analysis utilized SPSS Version 25.0, with descriptive statistics employed to summarize the demographic and clinical characteristics of the study population. The study compared

the average six-minute walk distance (6MWD) between COPD patients with and without anemia using an independent samples t-test. A significance level of  $\leq 0.05$  was used to determine statistical significance. The influence of factors including age, gender, smoking history, duration of COPD, and BMI on the 6MWD was examined through stratified analysis.

### Ethical Considerations

The research was carried out following the principles outlined in the Declaration of Helsinki. Approval for ethical considerations was acquired from the Institutional Ethics Committee/Institutional Review Board. All participants provided informed consent, guaranteeing confidentiality and the freedom to withdraw from the study at any stage.

### RESULTS

This cross-sectional study was conducted to examine how anemia affects the exercise capacity of patients with Chronic Obstructive Pulmonary Disease (COPD), as measured by the Six-Minute Walk Distance (6MWD). The study took place at the Pulmonology Department of Khyber Teaching Hospital in Peshawar, spanning from November 15, 2019, to May 14, 2020. A cohort of 162 patients diagnosed with COPD, ranging in age from 40 to 70 years, were included in the research.

### Demographic and Clinical Characteristics

The demographic and clinical attributes of the participants are summarized in the Table-I below. The average age of the participants was 62.07 years, with a standard deviation of 7.156 years, reflecting a predominantly senior cohort. The gender distribution showed a higher percentage of females (59.26%) compared to males (40.74%). The mean body weight was observed at 63.70 kg ( $\pm 16.154$  kg), and the average height was 1.6008 meters ( $\pm 0.08785$  meters), resulting in a mean Body Mass Index (BMI) of 24.7814 kg/m<sup>2</sup> ( $\pm 5.84046$  kg/m<sup>2</sup>). The duration of COPD among the participants averaged 13.17 years ( $\pm 7.284$  years), indicating a long-term management scenario for most patients. The hemoglobin (Hb) levels averaged 12.6363 gm/dl ( $\pm 1.88186$  gm/dl), with an equal distribution of anemic and non-anemic patients, each

group representing 50% of the total population. Smoking status revealed that the majority were non-smokers (65.43%), followed by ex-smokers (29.63%) and a minor percentage of current smokers (4.94%).

Variable	Group/Subgroup	N	Mean $\pm$ SD or %
Age (Years)	-	162	62.07 $\pm$ 7.156
Weight (Kg)	-	162	63.70 $\pm$ 16.154
Height (m)	-	162	1.6008 $\pm$ .08785
BMI (Kg/m <sup>2</sup> )	-	162	24.7814 $\pm$ 5.84046
Duration of COPD (Years)	-	162	13.17 $\pm$ 7.284
Hb level (gm/dl)	-	162	12.6363 $\pm$ 1.88186
6MWD (meters)	-	162	234.78 $\pm$ 106.972
Gender	Male	66	40.74%
	Female	96	59.26%
Smoking Status	Current Smoker	8	4.94%
	Non-Smoker	106	65.43%
	Ex-Smoker	48	29.63%
Anemia Status	Anaemic	81	50.00%
	Non-anaemic	81	50.00%

**Table-I. Demographic and clinical characteristics of study participants**

### Six-Minute Walk Test (6MWT) Findings

The central measure of this study, the 6MWD, yielded an average distance of 234.78 meters ( $\pm 106.972$  meters) across all participants. This performance metric served as a pivotal indicator of the exercise capacity among COPD patients within the study.

### 6MWD Performance by Anemia Status

A significant finding of this study was the marked difference in 6MWD performance between anemic and non-anemic COPD patients. Anemic patients covered a significantly shorter distance, averaging 190.99 meters ( $\pm 95.44$  meters), compared to non-anemic patients, who walked an average of 278.58 meters ( $\pm 100.17$  meters). The statistical analysis underscored the significance of this disparity, with a p-value of  $\leq 0.001$ , firmly establishing anemia as a critical determinant of

reduced exercise capacity in COPD patients.

### 6MWD Performance by Demographic and Clinical Variables

The study further explored the impact of various demographic and clinical variables on 6MWD performance. Gender analysis revealed that males, on average, walked farther (260 meters  $\pm$  121.23 meters) than females (217 meters  $\pm$  92.58 meters), with statistical significance marked by a p-value of 0.011. Age was also considered, dividing the cohort into those 60 years and younger versus those older than 60. The younger group demonstrated slightly better performance (249 meters  $\pm$  107.24 meters) compared to the older group (223 meters  $\pm$  105.98 meters), although this difference was not statistically significant ( $p=0.134$ ).

Smoking history presented an interesting insight; current smokers averaged a longer distance (303 meters  $\pm$  133.86 meters) compared to non-smokers (220 meters  $\pm$  97.10 meters) and ex-smokers (256 meters  $\pm$  117.24 meters), with the difference between current smokers and non-smokers being statistically significant ( $p=0.025$ ). The duration of COPD and BMI categories did not significantly affect the 6MWD, with p-values of 0.171 and 0.442, respectively, indicating a lack of statistical significance in these variables' impact on exercise capacity. (See Table-II)

## DISCUSSION

Our study provides compelling evidence of

the significant impact anemia has on exercise capacity in patients with Chronic Obstructive Pulmonary Disease (COPD), as measured by the Six-Minute Walk Distance (6MWD). Our findings support the previous research, showing that systemic conditions like anemia can substantially worsen the physical limitations experienced by individuals with COPD.<sup>12-14</sup>

The reduction in 6MWD observed among anemic COPD patients underscores the essential role of adequate hemoglobin concentration in sustaining exercise capacity. Anemia, by reducing oxygen transport capacity, likely worsens the already impaired oxygen utilization in COPD, resulting in increased dyspnea and diminished physical endurance.<sup>12,15,16</sup> These findings align with a previous study, who also noted a significant decrease in exercise capacity among anemic COPD patients, indicating that anemia management could be crucial in enhancing patient outcomes.<sup>17</sup>

Our analysis identified gender differences in 6MWD performance, with males showing higher exercise capacity than females. This difference could be due to variations in muscle mass, hemoglobin levels, and possibly COPD severity, as noted in other studies.<sup>18,19</sup> The observed gender differences highlights the need for gender-specific approaches in COPD management, including anemia assessment and treatment.

Variable	Group/Subgroup	N	Mean 6MWD (meters) $\pm$ SD	P- Value
Gender	Male	66	260 $\pm$ 121.23	0.011
	Female	96	217 $\pm$ 92.58	
Age Groups	$\leq$ 60 years		249 $\pm$ 107.24	0.134
	$>$ 60 years		223 $\pm$ 105.98	
Smoking History	Current Smoker	8	303 $\pm$ 133.86	0.025
	Non-Smoker	106	220 $\pm$ 97.10	
	Ex-Smoker	48	256 $\pm$ 117.24	
Duration of COPD	$\leq$ 12 years		246 $\pm$ 105.74	0.171
	$>$ 12 years		223 $\pm$ 107.70	
BMI Categories	$\leq$ 25 kg/m <sup>2</sup>		230 $\pm$ 112.29	0.442
	$>$ 25 kg/m <sup>2</sup>		243 $\pm$ 97.05	
6MWD by Anemia Status	Anaemic	81	190.99 $\pm$ 95.44	$\leq$ 0.001
	Non-anaemic	81	278.58 $\pm$ 100.17	

**Table-II. Impact of Demographic and clinical variables on 6MWD performance**



Interestingly, current smokers had longer 6MWDs compared to non-smokers and ex-smokers. While this may seem counterintuitive, it could reflect a selection bias where individuals with milder COPD symptoms continue smoking or the short-term bronchodilatory effects of smoking.<sup>20</sup> However, it is crucial to remember the well-documented long-term adverse effects of smoking on lung function and overall health.<sup>21,22</sup>

The significant impact of anemia on exercise capacity among COPD patients emphasizes the need for routine screening and management of anemia as part of comprehensive COPD care. Moreover, our findings suggest that addressing anemia in COPD patients could enhance their exercise tolerance, potentially improving their quality of life and reducing healthcare utilization. Future research should focus on longitudinal studies to explore the causal relationships between anemia management and exercise capacity in COPD patients, as well as randomized controlled trials to assess the effectiveness of interventions aimed at correcting anemia.

### LIMITATIONS

The cross-sectional nature of this study restricts our ability to deduce causal relationships between anemia and diminished exercise capacity in patients with COPD. Furthermore, the demographic studied, originating from a solitary center, might not accurately reflect the wider COPD population, potentially constraining the applicability of the results. There is a need for future research employing a longitudinal framework, a multicenter strategy, and increased sample sizes to verify and expand upon these conclusions.

### CONCLUSION

In conclusion, our study highlights anemia as a significant factor influencing exercise capacity in COPD patients. Addressing anemia through appropriate diagnostic and therapeutic strategies could potentially enhance physical activity levels, improve quality of life, and reduce the overall burden of COPD. Our findings underscore the importance of incorporating anemia screening and management into the multidisciplinary care

of COPD patients.

### CONFLICT OF INTEREST

The authors declare no conflict of interest.

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This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

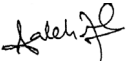
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#### AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Saleh Saadat Afridi	Conceived & designed the analysis collection the data performed analysis wrote the manuscript.	
2	Sara Riaz	Data acquisition, Data intrpretation, Proof reading of manuscript.	