ORIGINAL ARTICLE

FREQUENCY OF TYPE-II RESPIRATORY FAILURE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: In chronic obstructive pulmonary disease (COPD) patients the alveoli do not ventilate fully due to bronchial obstruction. This leads to the incomplete ventilation, incomplete clearance of carbon dioxide causing hypercapnia. There are some muscular abnormalities also in COPD patients. All these pathogeneses lead to type 2 (hypercapnic) respiratory failure. The aim of this study was to determine the frequency of type II respiratory failure in patients with COPD. **Methods:** This descriptive cross-sectional study was conducted at Department of Medicine, Hayatabad Medical Complex, Peshawar from 21st Aug 2021 to 20th Feb 2022. A total of 129 patients with COPD were enrolled. COPD was diagnosed based on clinical findings and confirmation with spirometry showing FEV_1/FVC less than 70% of predicted. Confirmation of type II respiratory failure was done by Arterial-blood gas (ABG) test on heparinized arterial blood sample analysis showing hypercapnia (Pa_{CO_2} ≥45 mmHg). **Results:** Type II respiratory failure was observed in 31 patients (24%); 19 (22.9%) patients with type respiratory failure had age more than 55 years. Eight (36.4%) patients with type II respiratory failure had GOLD stage 4 COPD. Age of the patients ranged from 40 to 65 years with mean age 53.410±9.362 years. Male to female ratio was 2.4:1. **Conclusion:** Type 2 respiratory failure is more prevalent in elder patients above 55 years of age, and is more common among males. The severity of COPD does not appear to have a direct relationship with the occurrence of type 2 respiratory failure.

Keywords: COPD, Type II Respiratory Failure, Arterial Blood Gases, Hypercapnia

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INTRODUCTION

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) was created in 2001 and defines COPD as 'a disease state characterized by airflow limitation that is not fully reversible.[1] The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases'. COPD comprises a diverse group of clinical syndromes that share the common feature of limitation of expiratory airflow.[2] The American Thoracic Society defines COPD in terms of chronic bronchitis and emphysema. COPD can also be classified with respect to both phenotype and disease severity. It is a heterogeneous disease process that varies greatly from person to person with respect to lung pathology, natural history of disease, and co-morbidity. The result of this heterogeneity is that different researchers have championed alternative hypotheses about COPD development over the past four decades: The British hypothesis stated that the presence of cough and sputum was the key factor in COPD, and the Dutch hypothesis pointed to the presence of increased airways responsiveness.[3,4] Less widely known hypotheses stressed the part of genetic factors (the Swedish hypothesis) and the role of impaired repair processes in the development of emphysema (the American hypothesis). All these hypotheses probably have elements of truth since COPD is a classic gene-by-environment disease with various manifestations that include increased airways reactivity, a characteristic response to infections, abnormal cellular repair, and development of complications or co-morbid disorders.[5] An interesting genetic area for COPD susceptibility is chromosomal band *15q25*.[1] The cholinergic receptor, nicotinic, alpha 3 (neuronal) gene, *CHRNA3*, the cholinergic receptor, nicotinic, alpha 5 (neuronal) gene, *CHRNA5*, and the iron-responsive element binding protein 2 gene, *IREB2*, are among the genes in this region that have been linked to a probable role in COPD. Both *CHRNA3/5* and *IREB2* have been recognized as viable candidates for a role in COPD susceptibility and progression by GWAS and integrative genomics techniques. It's interesting to note that these genes appear to play very diverse roles in the pathophysiology of COPD, despite being adjacent to each other genomically.[6]

Patients of COPD have been estimated to be 174.5 million only in 2015 which include both moderate to severe chronic obstructive pulmonary disease which have increased by 44.2% from the value in 1990.[7] It is estimated that up to 2040 COPD is expected to rise from 9th to 4th leading cause of life-years lost. Only in 2015 about 3.2 million people died of COPD globally (an increase of 11.6% compared with 1990).[8] The COPD patients frequently present with acute exacerbation. In COPD patients the alveoli do not ventilate fully due to bronchial obstruction. This leads to the incomplete

ventilation, incomplete clearance of CO_2 causing hypercapnia. There are some muscular abnormalities also in COPD patients. All these pathogeneses lead to type 2 (hypercapnic) respiratory failure.[9] In addition to other treatments home base management like home oxygen therapy are also indicated for management of COPD.[10] In a study 231 COPD patients were enrolled in which hypercapnic respiratory failure (Pa_{CO_2} ≥45 mmHg) was present in 58 (25%) patients of which, 20 (9%) had Pa_{CO_2} ≥50 mmHg. That study further evaluated that hypercapnia was more in the higher GOLD stage. In that study 26 (15%) patients of hypercapnic respiratory failure (Pa_{CO_2} >45 mmHg) were in need of day and night oxygen therapy.[11] Another study showed that hypercapnic respiratory failure (Pa_{CO_2} ≥45 mmHg) was present in 65 (28.1%) patients and 23 (10%) had Pa_{CO_2} ≥50 mmHg. Increased BMI, decreased forced vital capacity, and increased HCO_3^- level were significant independent predictors of hypercapnia. The overall mortality was 19.5% in patients with COPD and hypercapnia.[11]

The aim of current study was to determine the frequency of type 2 respiratory failure (hypercapnic) in patient presenting with chronic obstructive pulmonary disease at tertiary care hospital in Peshawar.

MATERIAL AND METHODS

This descriptive cross-sectional study was conducted from 21st Aug 2021 to 20th Feb 2022 at the Department of Medicine, Hayatabad Medical Complex, Peshawar, after approval from Ethical Committee of the Hospital. Patients admitted from the Out-patients Department were evaluated. Sample size was calculated using WHO sample size formula using the proportion (expected frequency of type 2 respiratory failure, p=25%[5], margin of error of 7.5% and with confidence interval of 95%. Non-probability consecutive sampling technique was applied. All known COPD patients aged 40–65 years with symptoms of shortness of breath (respiratory rate >22 breaths/minutes) referred to Medical Department were included. Patients with a documented history of physical abnormality of chest, Glasgow comma scale (GCS) lower than 5 and patients having lung pathology other than COPD were excluded from the study.

Written informed consent was taken from all participants of the study. All patients were managed as per hospital's protocol. Age, sex, duration of COPD, weight, height, and BMI were recorded. Spirometry was done using Contec® SP100 machine and the patient were classified as per GOLD stage. Patients' arterial blood samples were taken in a heparinized syringe under aseptic conditions and were sent for Arterial Blood Gases (ABGs) analysis and Pa_{CO_2} was recorded. Type 2 respiratory failure was labelled when Pa_{CO_2} was ≥45 mmHg.

Data was collected on a designated proforma, and analysed on SPSS-22. Mean±SD was calculated for continuous variables like age, weight, height, BMI, duration of COPD, predicted FEV_1, and Pa_{CO_2} level. Categorical variables like gender, type 2 respiratory failure and Gold stages were presented with frequency and percentages. Effect modifiers like age, sex, duration of COPD, GOLD stage, BMI were stratified against the type 2 respiratory failure. Post stratification Chi-square test was applied and p<0.05 was taken significant.

RESULTS

A total of 129 patients were recruited comprising of 90 (70.5%) male and 38 (29.5%) female patients. The age of the patients ranged from 40 to 65 years. Patients' demographics are shown in Table-1. The classification of the patients according to GOLD severity is shown in Table-2. Majority of the patients had stage-2 (moderate) COPD. It was found that 31 (24%) patients had type-II respiratory failure. Stratification of type 2 respiratory failure with respect to gender, BMI and GOLD stage are shown in Table-3.

Table-1: Patients demographics (Mean±SD) (n=129)

Demographics	Mean±SD
Age (Years)	53.41±9.362
Weight (Kg)	75.54±11.342
Height (Cm)	171.44±9.270
BMI (Kg/m^2)	25.78±4.08789
Disease Duration (months)	18.89±10.006
FEV_1 Predicted (%)	59.42±11.66

Table-2: Frequency and percentage of patients according to GOLD standards (n=129)

GOLD Stage	Frequency	Percent
Stage 1 (mild)	17	13.2
Stage 2 (moderate)	59	45.7
Stage 3 (severe)	31	24.0
Stage 4 (very severe)	22	17.1

Table-3: Stratification of COPD [n (%)]

Parameter	Yes	No	Total	p
Gender				
Male	25 (27.5)	66 (72.5)	91	0.031
Female	6 (4.6)	32 (95.4)	38	
BMI				
Healthy (BMI=18.5–5 Kg/m^2)	6 (9.2)	59 (90.8)	65	0.752
Overweight (BMI=25.1–30 Kg/m^2)	17 (41.5)	24 (58.5)	41	
Obese (BMI= >30 Kg/m^2)	8 (34.8)	15 (65.2)	23	
GOLD Severity				
Mild	2 (11.8)	15 (88.2)	17	0.817
Moderate	13(22.0)	46 (78.0)	59	
Severe	8 (25.8)	23 (74.2)	31	
Very Severe	8 (36.4)	14 (63.6)	22	

DISCUSSION

This study aimed to explore the frequency of type II respiratory failure in COPD. By analyzing the collected data and findings, we strive to gain insights into the impact of COPD on respiratory function. Type II respiratory failure was seen in 24% of the study

participants. This result aligns well with previous research, showing a prevalence of around 25% for type II respiratory failure in COPD patients.[12] The previous results were based on the fact that a number of key factors contribute to type II respiratory failure in COPD including airway obstruction, reduced lung elasticity, and alveolar damage causing elevated levels of carbon dioxide and reduced oxygen in the blood stream. However, the small differences observed between this study and others can be attributed to the variability in contributing factors across different regions and populations. One notable factor is smoking behaviour. Smoking rates can differ significantly between countries, and regions with higher smoking prevalence are likely to experience a greater burden of COPD and its complications, including type II respiratory failure.[13] Environmental factors also play a crucial role in COPD development. Differences in exposure to indoor and outdoor pollutants, occupational hazards, and biomass fuels can influence COPD prevalence and its severity.

Genetic predisposition is another important factor influencing COPD prevalence and severity. Populations with different genetic backgrounds may have varying rates of respiratory failure in COPD patients. For example, Alpha-1 antitrypsin deficiency (A1ATD) is caused by a mutation in the *SERPINA1* gene, leading to deregulation of neutrophil elastase –a protease enzyme. This causes lung tissue degradation and emphysema. Cigarette smoke can hasten lung harm in individuals with A1ATD. Overall, that study emphasizes the importance of understanding the multiple factors contributing to type II respiratory failure in COPD patients.[14]

The higher prevalence of type II respiratory failure in male COPD patients observed in this study is aligned with findings from international studies.[15] This data supports previous findings that COPD is more prevalent among males, primarily due to higher smoking rates, a leading risk factor for the disease in men. While the prevalence in our study is slightly higher than international results, this may be attributed to high smoking rates among males in our country. Other factors such as socioeconomic disparities and lifestyle choices impacting COPD outcomes might also have contributed these findings. It is worth mentioning that male-dominated occupations in Pakistan may expose men to various pollutants, dust, and fumes, increasing the risk of developing COPD and thus type II respiratory failure.[16]

Another study demonstrated a correlation between age of patient and type II respiratory failure in COPD which is consistent with previous research.[17] The natural aging process contributes to hyper-inflated alveoli and reduced elastic recoil, leading to CO_2 retention and respiratory failure. Reduced physical activity and a sedentary lifestyle with age may further exacerbate this condition.[18] Interestingly, the proportion of patients over 55 years was lower than in international studies, potentially influenced by quality of life, life expectancy factors, early smoking practices, and an increased frequency of respiratory infections during childhood and adolescence in our country. These factors collectively contribute to the observed differences in age-related prevalence of type II respiratory failure in COPD patients.[19]

Regarding the COPD severity staging based on the GOLD classification, the study did not find a statistically significant association with the prevalence of type II respiratory failure. These results support previous research findings, showing considerable inter-individual variation and overlap between different stages of COPD for various health outcomes.[20]

The results also indicate lack of association between BMI and Type II respiratory failure in COPD, which is not consistent with a previous study[21] on effects of BMI on type II respiratory failure in COPD. This may be attributed to the small sample size, which limited the power of analysis to detect significant associations. Factors like smoking history, physical activity levels, medication usage, and other health conditions could have acted as confounding variables, influencing the relationship between BMI and COPD outcomes.[22] The participants' diverse characteristics, including varying disease severities, co-morbidities, and lifestyle, might have further masked any potential association between BMI and Type II respiratory failure. To better understand the link between BMI and COPD outcomes, larger and more comprehensive studies controlling for confounders and exploring different patient subgroups are needed, along with meta-analyses to strengthen the overall evidence base.

CONCLUSION

This study highlights the significant frequency of type 2 respiratory failure in COPD patients. Type 2 respiratory failure is more prevalent in elder patients above 55 years of age, and is more common among males. The severity of COPD as determined by GOLD staging does not appear to have a direct relationship with the occurrence of type 2 respiratory failure.

LIMITATIONS OF THE STUDY

This study did not address the underlying causes of COPD. Patients were labelled under the umbrella term COPD and not further classified as chronic bronchitis and emphysema. Addition of these would have made it more comprehensive.

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REFERENCES

1. Han MK, Agusti A, Celli BR, Criner GJ, Halpin DMG, Roche N, *et al*. From GOLD 0 to Pre-COPD. Am J Respir Crit Care Med 2021;203(4):414–23.
2. Batta A. Diagnosis of chronic obstructive airway disease —made easy. Cross Current Int J Med Biosci 2020;2(1):1–5.
3. Nici L, Mammen MJ, Charbek E, Alexander PE, Au DH, Boyd CM, *et al*. Pharmacologic management of chronic obstructive pulmonary disease. An official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med 2020;201(9):e56–69.
4. Gruffydd-Jones K, Keeley D, Knowles V, Recabarren X, Woodward A, Sullivan AL, *et al*. Primary care implications of the British Thoracic Society Guidelines for bronchiectasis in adults 2019. NPJ Prim Care Respir Med 2019;29(1):24.
5. Weiss A, Porter S, Rozenberg D, O'Connor E, Lee T, Balter M, *et al*. Chronic obstructive pulmonary disease: a palliative medicine review of the disease, its therapies, and drug interactions. J Pain Symptom Manag 2020;60(1):135–50.
6. Hardin M, Silverman EK. Chronic obstructive pulmonary disease genetics: A review of the past and a look into the future. Chronic Obstr Pulm Dis 2014 May 6;1(1):33–46.
7. GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990–2015: a systematic analysis for the global burden of disease study 2015. Lancet Respir Med 2017;5(9):691–706.
8. Foreman KJ, Marquez N, Dolgert A, Fukutaki K, Fullman N, McGaughey M, *et al*. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016–40 for 195 countries and territories. Lancet 2018;392(10159):2052–90.
9. Adler D, Janssens JP. The pathophysiology of respiratory failure: control of breathing, respiratory load, and muscle capacity. Respiration 2019;97(2):93–104.
10. Wedzicha JA, Miravitlles M, Hurst JR, Calverley PM, Albert RK, Anzueto A, *et al*. Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society Guideline. Eur Respir J 2017;49(3):1600791.
11. Dreher M, Neuzeret PC, Windisch W, Martens D, Hoheisel G, Gröschel A, *et al*. Prevalence of chronic hypercapnia in severe chronic obstructive pulmonary disease: data from the HOmeVent registry. Int J Chronic Obstruct Pulmon Dis 2019:2377–84.
12. Calverley PM. Respiratory failure in chronic obstructive pulmonary disease. Eur Respir J Suppl 2003;47:26s–30.
13. Alqahtani JS, Oyelade T, Aldhahir AM, Alghamdi SM, Almehmadi M, Alqahtani AS, *et al*. Prevalence, severity and mortality associated with COPD and smoking in patients with COVID-19: A rapid systematic review and meta-analysis. PLoS One 2020;15(5):e0233147.
14. Hurst JR, Siddharthan T. Global Burden of COPD. In: Kickbusch I, Ganten D, Moeti M. (Eds) Handbook of Global Health. Springer, Cham;2021.p. 439–58.
15. Grabicki M, Kuźnar-Kamińska B, Rubinsztajn R, Brajer-Luftmann B, Kosacka M, Nowicka A, *et al*. COPD course and comorbidities: are there gender differences? Adv Exp Med Biol 2019;1113:43–51.
16. Alam SE. Prevalence and pattern of smoking in Pakistan. J Pak Med Assoc 1998;48(3):64–6.
17. Hosseini M, Almasi-Hashiani A, Sepidarkish M, Maroufizadeh S. Global prevalence of Asthma-COPD Overlap (ACO) in the general population: a systematic review and meta-analysis. Respir Res 2019;20(1):229.
18. Tudorache E, Fildan AP, Frandes M, Dantes E, Tofolean DE. Aging and extrapulmonary effects of chronic obstructive pulmonary disease. Clin Interv Aging 2017;12:1281–7.
19. Rehman A, Shafiq H, Jawed S, Behram F. Chronic obstructive pulmonary disease (COPD) screening is still a challenge in Pakistan: COPD in Pakistan. J Aziz Fatimah Med Dent Coll 2019;1(1):18–23.
20. Vitacca M, Paneroni M, Spanevello A, Maniscalco M, Diasparra A, Aliani M, *et al*. Effect of pulmonary rehabilitation on COPD assessment test items in individuals classified as GOLD Group E. Respiration 2023;102(7):469–78.
21. Sangroula P, Ghimire S, Srivastava B, Adhikari D, Dhonju K, Shrestha A, *et al*. Correlation of body mass index and oxygen saturation in chronic obstructive pulmonary disease patients at a tertiary care center in Nepal: A cross-sectional study. Int J Chron Obstruct Pulmon Dis 2023;18:1413–8.
22. Svartengren M, Cai G-H, Malinovschi A, Theorell-Haglöw J, Janson C, Elmståhl S, *et al*. The impact of body mass index, central obesity and physical activity on lung function: results of the EpiHealth study. ERJ Open Res 2020;6(4):00214–2020.

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