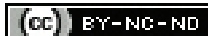


Impact of COPD Phenotype on Disease Specific HR-QoL using CAT and SGRQ-C Score: A Hospital-based Observational Study

NARESH BHAGORA¹, SHER SINGH MEENA², PUSHPENDRA BAIRWA³, HITENDRA JATAV⁴

ABSTRACT

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is the third leading cause of morbidity and mortality worldwide. The chronic and progressive nature of the disease significantly affects patients' Quality of Life (QoL). Tools like the COPD Assessment Test (CAT) and St. George's Respiratory Questionnaire (SGRQ-C) are widely used to assess Health-Related Quality of Life (HR-QoL) in these patients.

Aim: To determine the impact of COPD phenotypes on disease-specific HR-QoL using CAT and SGRQ-C score.

Materials and Methods: This hospital based observational study was conducted at RNT Medical College, Udaipur, Rajasthan, between the period of July 2024 to February 2025. All Diagnosed cases of COPD, as per GOLD guideline, with age above 40 years were included for the study. Patients with significant medical condition and pregnant or lactating women were excluded from the study. The total number of patients included were 160. The modified Medical Research Council (mMRC) Questionnaire was used to quantify the severity of breathlessness along with CAT score. The CAT and SGRQ-C, patient-administered questionnaire was used for HR-QoL assessment. Independent sample t-test and ANOVA test were

used to compare the variables. Statistical analysis was done using MS excel and JAMOWI software version 6.2.

Results: A total of 40 patients in each phenotype were enrolled in the study. Majorities of patients were male (118, 73.75%) and mean age was 62.56 ± 10.71 years. Highest CAT score for cough and phlegm were observed in AE-CB phenotype (2.60 ± 0.96 and 2.93 ± 0.94 , respectively). Highest CAT score for chest tightness and breathlessness were observed in AE Non CB phenotype (1.88 ± 1.18 and 3.03 ± 0.95 , respectively). AE non CB phenotype shows higher physical activity limitation (2.55 ± 0.98) and sleep disturbance (1.85 ± 1.36) while AE-CB phenotype shows poor confidence in leaving home (1.98 ± 1.45) and low energy (1.29 ± 0.20) while performing the routine work. Highest SGRQ-C score were observed in AE-CB (44.53 ± 13.94) and AE Non CB (46.77 ± 9.45), respectively.

Conclusion: The AE non CB and AE-CB phenotypes were found to have the most significant impact on HR-QoL among COPD patients. This suggests that individuals with the AE-CB phenotype notably require a tailored treatment approach that specifically addresses both the frequent exacerbations and the chronic bronchitis component to improve their overall QoL.

INTRODUCTION

The COPD is a one of the leading cause of morbidity and mortality worldwide [1]. As per the WHO in 2020, the prevalence of COPD exceeded 200 million globally, with approximately 3.23 million deaths attributed to COPD. However, the prevalence is likely to be underestimated due to the under-diagnosis of COPD. mMRC Questionnaire is a widely used tool for assessing dyspnoea, with scores ranging from minimal (score of 0) to severe impairment (score of 4) [2].

The concept of phenotyping in COPD has therefore emerged to classify patients into subgroups based on clinical characteristics, disease progression, response to therapy, and prognosis. Type of phenotypes are as follows [3]:

Non-exacerbator (Non AE) is characterised by infrequent or fewer exacerbations with symptoms which not significantly impair their daily activities.

Exacerbator with emphysema (AE Non CB) is characterised by frequent exacerbations with predominant emphysema features like Airflow limitation and reduced lung function, shortness of breath, cough, and reduced exercise tolerance.

Exacerbator with Chronic Bronchitis (AE-CB) is characterised by frequent exacerbations with chronic bronchitis, symptoms like productive cough that lasts for atleast three months per year for two consecutive years, persistent cough and sputum production. Airway inflammation and mucus hypersecretion leads to impaired lung function.

Keywords: Chronic-bronchitis, Emphysema, Non-exacerbator

Asthma-COPD Overlap Syndrome (phenotype ACOS): It has characteristics of both asthma (wheezing, variable airflow limitation, reversible airway obstruction, and allergic triggers) and COPD with presence of exacerbations. ACOS presents significant diagnostic and therapeutic challenges due to the overlap of features from both conditions.

The QoL is significantly impacted due to the chronic and progressive nature of the disease. QoL assessment plays a pivotal role in evaluating the holistic impact of COPD beyond mere physiological parameters. Various tools have been developed to measure QoL in COPD patients, providing valuable insights into their physical, emotional, and social well-being. Two commonly used instruments for assessing QoL in COPD are the CAT and the SGRQ-C score [4].

The COPD significantly affects patients' lives and leads to impairment in HR-QoL across different clinical phenotypes, each of which presents unique challenges and complexities. However, there is a paucity of literature [5,6] from the regional context evaluating the differential impact of various COPD phenotypes on HR-QoL. So this study was planned to study the impact of different COPD clinical phenotypes on patient's disease specific HR-QoL assessed by using CAT and SGRQ-C score [7].

MATERIALS AND METHODS

This hospital based observational study was conducted in RNT Medical College and Hospital, Udaipur, Rajasthan, India during the period of July 2024 to February 2025. Permission was obtained

from the Research review board and ethics committee of the college (No.735/MC/EC/2024).

Sample size: Sample of 37 cases in each group was calculated at confidence interval of 95% and alpha error of 0.05 assuming expected total mean CAT score of 15.8 ± 8.0 and 23.6 ± 8.0 among AE Non CB and AE-CB groups, respectively as per the previous article [5]. Sample was further rounded off to 40 cases in each group.

Inclusion criteria: All diagnosed cases of COPD (as per GOLD guideline [8]) with age above 50 years were included for the study.

Exclusion criteria: Patients unable to perform acceptable spirometry, patients with other severe chronic respiratory diseases and symptoms of respiratory failure, patients with significant medical condition like deranged liver or renal function, DM etc., and pregnant and lactating females were excluded.

Sampling: Allocation concealment for each group was ensured using the opaque sealed envelope method. The allocation process was conducted by a person not directly involved in the research to minimise selection bias. Convenient sampling was employed to achieve the desired sample size.

Study Procedure

Complete history of patient including any known drug allergy was taken. General and systemic examination was done before conducting investigations. The subjects undergo the following: Chest X-ray, complete blood count, liver function test, renal function test, HRCT chest, total eosinophil count and mMRC grade. Spirometry was performed according to American Thoracic society guidelines at each visit before administration of the data collection forms [9].

After performing the necessary investigations, disease- HR-QoL was evaluated using standardised tools such as the CAT [6] and the SGRQ-C [7]. These validated questionnaires are designed to assess various aspects of HR-QoL specific to COPD, including symptoms, functional impairment, and the impact of the disease on daily activities.

Severity of COPD was categorised according to spirometry results, in accordance with GOLD 2022 guidelines [8]. Grade-I COPD with $FEV_1 \geq 80\%$ predicted, Grade-II with FEV_1 50 to 80% predicted, Grade-III at FEV_1 30 to 50% predicted, and Grade-IV with $FEV_1 < 30\%$ predicted. Stable COPD patients were defined as patients having less than 10% change in spirometry values, and no variation in clinical symptoms after two weeks [10].

Assessment of severity of symptoms: The mMRC Questionnaire is a widely used to quantify the severity of breathlessness experienced by individuals during various activities of daily living [11].

CAT score: This is a patient-administered questionnaire designed to evaluate the impact of COPD on QoL and symptom burden. It comprises eight questions, each scored on a scale from 0 to 5, with higher scores indicating greater impairment [6].

Construct validity (including known-group validity and reliability) was evaluated by examining the correlation between SGRQ-C total and subscale scores and clinical measures, as well as other health status measures such as the CAT and mMRC, collected during the baseline assessment [7].

Current smoker is defined as a person currently smoking tobacco (cigarettes, bidis, or other forms) at the time of assessment, either daily or occasionally. Former smoker: A person who has smoked in the past but has quit smoking and has not smoked for a defined period, commonly at least six months prior to assessment. Never smoker: never smoker in his/her life [12].

STATISTICAL ANALYSIS

All collected data were entered in an excel sheet. Quantitative data were expressed as mean $\pm$ Standard Deviation (SD) and qualitative

data were expressed as frequency and percentage. Independent sample t-test of significance was used to compare two means (quantitative data) and ANOVA test was used to compare more than two variables. The confidence interval was set to 95%, and the margin of error was accepted at 5%. The p-value ≤ 0.05 was considered as a significant and p-value > 0.05 would be considered insignificant. Analysis was done using MS Excel and JAMOVI 6.2.

RESULTS

A total of 40 patients (in each group) were enrolled in the study. The age and gender wise distribution are depicted in [Table/Fig-1]. Data related to the smoking history are depicted in [Table/Fig-2].

Phenotype		Male	Female	Age (in years)
		N (%)	N (%)	Mean $\pm$ SD
Non AE	40	27(67.5%)	13 (32.5%)	63.35 $\pm$ 11.55
AE Non CB	40	32 (80%)	8 (20%)	63.78 $\pm$ 11.64
AE-CB	40	30 (75%)	10 (25%)	62.53 $\pm$ 10.67
ACOS	40	29 (72.5%)	11 (27.5%)	60.58 $\pm$ 8.87
Total (overall)	160	118 (73.75%)	42 (26.25%)	62.56 $\pm$ 10.71

[Table/Fig-1]: Distribution of patients as per age and gender.

Phenotype	Smoker	Ex-smoker	Non-smoker
	N (%)	N (%)	N (%)
Non AE	16 (40.0%)	9 (22.5%)	15 (37.5%)
AE Non CB	12 (30.0%)	12 (30.0%)	16 (40.0%)
AE-CB	18 (45.0%)	12 (30.0%)	10 (25.0%)
ACOS	15 (37.5%)	10 (25.0%)	15 (37.5%)
Total (overall)	61 (38.12%)	43 (26.88%)	56 (35.00%)

[Table/Fig-2]: Distribution of patients as per smoking history.

The distribution of different phenotype as per exacerbations and mMRC type are depicted in [Table/Fig-3,4], respectively.

Phenotype	Mild	Moderate	Severe
	N (%)	N (%)	N (%)
Non AE	36 (90.0%)	4 (10.0%)	0
AE Non CB	9 (22.5%)	21 (52.5%)	10 (25.0%)
AE-CB	15 (37.5%)	11 (27.5%)	14 (35.0%)
ACOS	22 (55.0%)	11 (27.5%)	7 (17.5%)
Total (overall)	82 (51.25%)	47 (29.37%)	31 (19.38%)

[Table/Fig-3]: Distribution of patients as per severity of exacerbation.

Phenotype	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
	N (%)	N (%)	N (%)	N (%)	N (%)
Non AE	37 (92.5%)	3 (7.5%)	0	0	0
AE Non CB	20 (50.0%)	4 (10.0%)	10 (25.0%)	4 (10.0%)	2 (5.0%)
AE-CB	20 (50.0%)	4 (10.0%)	2 (5.0%)	10 (25.0%)	4 (10.0%)
ACOS	19 (47.5%)	10 (25.0%)	6 (15.0%)	3 (7.5%)	2 (5.0%)
Total (overall)	96 (60.0%)	21 (13.12%)	18 (11.25%)	17 (10.63%)	8 (5.0%)

[Table/Fig-4]: Distribution of patients phenotypes as per mMRC grade.

Comparison of individual components of CAT score as per different type of COPD phenotype [Table/Fig-5-7]. Highest CAT score for cough and phlegm were observed in AE-CB phenotype followed by AE non CB and ACOS phenotype. Highest CAT score for Chest tightness and breathlessness were observed in AE Non CB phenotype [Table/Fig-5]. AE non CB phenotype shows higher physical activity limitation and sleep disturbance while AE-CB phenotype shows poor confidence in leaving home and low energy while performing the routine work [Table/Fig-6].

Post-hoc analysis shows the difference of mean CAT score (individual) between different phenotypes of COPD patients [Table/Fig-7,8].

Phenotype	N	Cough	Phlegm	Chest tightness	Breathlessness
		(Mean±SD)	(Mean±SD)	(Mean±SD)	(Mean±SD)
Non AE	40	1.90±0.63	1.65±0.58	0.95±0.75	2.10±0.96
AE Non CB	40	2.48±0.82	2.10±1.01	1.88±1.18	3.03±0.95
AE-CB	40	2.60±0.96	2.93±0.94	1.45±0.93	2.33±1.33
ACOS	40	2.45±0.96	2.03±0.92	1.53±1.01	2.28±0.91
Total(overall)	160	2.36±0.89	2.18±0.99	1.45±1.03	2.43±1.10
F value		5.34	14.9	14.9	6.04
p-value		<0.002	<0.001	<0.001	<0.001

[Table/Fig-5]: Comparison of mean individual components CAT score as per different phenotype of COPD patients.

Note: p<0.05 considered as statistically significant

Phenotype	Activity limitation	Confidence in leaving home	Sleep	Energy	Total CAT
	(Mean±SD)	(Mean±SD)	(Mean±SD)	(Mean±SD)	(Mean±SD)
Non AE	1.65±1.07	1.15±0.73	1.00±0.78	0.92±0.14	11.80±4.07
AE Non CB	2.55±0.98	1.70±1.11	1.85±1.36	1.18±0.18	17.35±6.56
AE-CB	2.15±1.16	1.98±1.45	1.63±1.12	1.29±0.20	17.35±8.64
ACOS	1.50±0.87	1.58±1.10	1.18±1.21	1.17±0.18	13.95±6.46
Overall	1.96±1.10	1.60±1.16	1.41±1.18	1.16±0.09	15.11±6.98
F value	8.66	3.67	14.9	2.07	6.71
p-value	<0.001 (S)	0.014 (S)	0.001 (S)	0.106 (NS)	<0.001 (S)

[Table/Fig-6]: Comparison of mean CAT score as per different phenotype of COPD patients.

Note: Test of significant: ANOVA test was conducted; p<0.05 considered as statistically significant

Phenotype		Cough		Phlegm		Chest tightness		Breathlessness	
P1	P2	P1-P2	Level of sig	P1-P2	Level of sig	P1-P2	Level of sig	P1-P2	Level of sig
Non AE	AE Non CB	-0.575	0.003	-0.450	0.023	-0.925	<0.001	-0.925	<0.001
	AE-CB	-0.700	<0.001	-1.275	<0.001	-0.500	0.024	-0.225	0.338
	ACOS	-0.550	0.004	-0.375	0.058	-0.575	0.010	-0.175	0.456
AE Non CB	AE-CB	-0.125	0.512	-0.825	<0.001	0.425	0.055	0.700	0.003
	ACOS	0.025	0.896	0.075	0.703	0.350	0.113	0.750	0.002
AE-CB	ACOS	0.150	0.432	0.900	<0.001	-0.075	0.733	0.050	0.831

[Table/Fig-7]: Post-hoc analysis for individual CAT score between all phenotypes groups.

Note: p<0.05 considered as statistically significant

Phenotype		Activity limitation		Confidence in leaving home		Sleep		Energy	
P1	P2	P1-P2	Level of sig	P1-P2	Level of sig	P1-P2	Level of sig	P1-P2	Level of sig
Non AE	AE Non CB	-0.90	<0.001	-0.550	0.031	-0.850	<0.001	0.266	0.38
	AE-CB	-0.50	0.032	-0.825	<0.001	-0.625	0.016	0.371	0.19
	ACOS	0.15	0.517	-0.425	0.095	-0.175	0.49	0.249	0.29
AE Non CB	AE-CB	0.40	0.085	-0.275	0.279	0.225	0.38	0.105	0.42
	ACOS	1.05	<0.001	0.125	0.622	0.67	0.01	-0.017	0.49
AE-CB	ACOS	0.65	0.005	0.400	0.116	0.450	0.08	-0.24	0.47

[Table/Fig-8]: Post-hoc analysis for individual CAT score between all phenotypes groups.

Note: p<0.05 considered as statistically significant

When assessing QoL using the SGRQ-C score, the highest symptom severity was observed in AE-CB patients. On the other hand, AE Non CB patients experienced greater limitations in daily physical activities (activity) and a more pronounced impact on their psychological well-being (Impact) [Table/Fig-9]. The difference of different component of CAT and SGRQ-C score different phenotype is depicted in [Table/Fig-10,11].

DISCUSSION

This study observed that the majority of patients were above 50 years of age and also no any significant differences were observed in respect to the age or gender of the patients. The highest proportions of exacerbations was observed in AE Non CB patients (77.5%), followed by AE-CB patients (62.5%) and ACOS patients (45%). Only four patients (10%) show non-AE phenotype.

Phenotype	Symptoms	Activity	Impact	Total
	(Mean±SD)	(Mean±SD)	(Mean±SD)	(Mean±SD)
Non AE	34.26±6.82	39.72±8.92	32.88±5.65	36.14±7.48
AE Non CB	44.24±13.97	54.98±10.18	42.30±13.88	46.77±9.45
AE-CB	48.60±17.02	44.94±14.34	39.61±12.98	44.53±13.94
ACOS	41.40±12.49	42.74±10.68	38.64±9.58	41.31±10.42
Total (overall)	42.12±14.00	45.60±12.50	38.36±11.44	42.19±11.23

F value	12.39	13.89	5.18	7.59
p-value	<0.001	<0.001	0.02	<0.001

[Table/Fig-9]: Comparison of mean SGRQ-C score of different phenotype.

Note: p<0.05 considered as statistically significant

Phenotype		Symptoms		Activity		Impact	
P1	P2	(P1-P2)	Level of sig	(P1-P2)	Level of sig	P1-P2	Level of sig
Non AE	AE Non CB	-9.97	<0.001	-15.256	<0.001	-9.416	<0.001
	AE-CB	-14.34	<0.001	-5.222	0.039	-6.733	0.007
	ACOS	-7.13	0.016	-3.013	0.232	-5.755	0.021
AE Non CB	AE-CB	-4.36	0.139	10.034	<0.001	2.682	0.278
	ACOS	2.84	0.334	12.24	<0.001	3.660	0.139
AE-CB	ACOS	7.20	0.015	2.209	0.380	0.978	0.692

[Table/Fig-10]: Post-hoc analysis of SGRQ-C score (Symptoms) for intergroup comparison.

Note: p<0.05 considered as statistically significant

Phenotype (P1)	Phenotype (P2)	CAT score (Total)		SGRQ score (Total)	
		Mean difference (P1-P2)	Level of significance	Mean difference (P1-P2)	Level of significance
Non AE	AE Non CB	-5.550	<0.001	-10.63	<0.001
	AE-CB	-5.550	<0.001	-8.39	0.001
	ACOS	-2.150	0.149	-5.17	0.031
AE Non CB	AE-CB	0.000	1.000	2.24	0.34
	ACOS	3.400	0.023	5.46	0.022
AE-CB	ACOS	3.400	0.023	3.22	0.17

[Table/Fig-11]: Post-hoc analysis of CAT score (total) and SGRQ-C (total) for intergroup comparison.

Note: p<0.05 considered as statistically significant

Regardless of the clinical phenotype, all variations demonstrated significant impairment in HR-QoL, as assessed using the CAT and SGRQ-C scales. The highest total CAT scores were observed in patients with the AE Non CB and AE-CB phenotypes. Among AE-CB patients, the primary concerns were cough, phlegm, and confidence in leaving home. In contrast, AE-Non-CB patients had the highest CAT scores for chest tightness, activity limitation, and breathlessness. The highest symptom SGRQ-C score was observed in the AE-CB phenotype, whereas the activity and impact SGRQ-C scores were highest in the AE non CB phenotype.

The mean CAT scores observed across different populations vary based on patient characteristics. However, large-scale studies enable comparisons of scores across multiple countries despite these differences. A study conducted in Spain by Cosio BG et al., found significantly higher CAT scores in patients with AE-CB [13]. Additionally, CAT scores were numerically higher in individuals with ACOS, followed by those with AE Non-CB and Non-AE. In Italy, a study involving milder cases with a mean FEV1 of 72% reported a mean CAT score of 16.6 [6]. Similarly, a multicenter study in Latin America, which included 795 COPD patients with a mean FEV1 of 49.4%, observed a mean total CAT score of 15.2 [14].

In the present study, highest CAT score was observed in AE-CB and AE Non CB phenotype. Similar observation was found in the study of Chai CS et al., and Anandan J et al., reported that the patients with the AE-CB phenotypes had significantly poorer QoL [5,15].

We observed, AE Non CB and AE-CB patients had significantly higher SGRQ-C total scores. Similar observation made by Anandan J et al., reported ECB and EEM patients also had the worst scores in all individual CAT items and SGRQ-C components [15], however in the study of Chai CS et al., the total SGRQ-C score of AE-CB patients was only marginally higher than those who had ACOS (p=0.187) [5].

In summary, the majority of the above mentioned studies and existing literature consistently indicate that non-AE patients have the best HR-QoL, whereas those with frequent exacerbations, particularly those with the AE-CB phenotype, experience the worst HR-QoL. Furthermore, the present study reinforces these findings

by demonstrating that the AE-CB phenotype is associated with the poorest scores across all CAT items and SGRQ-C components.

Limitation(s)

Being a single-centric study with a relatively small sample size in each phenotype, the findings may not be generalisable to all COPD populations. The cross-sectional design limits the ability to establish causal relationships between COPD phenotypes and HR-QoL. Additionally, HR-QoL assessment relied on self-reported questionnaires, which may be influenced by subjective perception and recall bias.

CONCLUSION(S)

The present study demonstrates that COPD clinical phenotypes have a significant and differential impact on disease specific HR-QoL as assessed by CAT and SGRQ-C. Exacerbation-predominant phenotypes, particularly AE-CB and AE-Non-CB, were associated with higher symptom burden, greater activity limitation, and worse overall HR-QoL scores compared to the non-AE phenotype. AE-CB patients showed the highest symptom severity, while AE-non-CB patients experienced greater impairment in physical activity and overall impact domains. These findings highlight that HR-QoL impairment in COPD is phenotype-specific rather than uniform, underscoring the importance of phenotype-based assessment and individualised management strategies to improve patient-centered outcomes in COPD.

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PARTICULARS OF CONTRIBUTORS:

- Senior Medical Officer, Department of Respiratory Medicine, RNT Medical College and Hospital, Udaipur, Rajasthan, India.
- Senior Medical Officer, Department of Respiratory Medicine, RNT Medical College and Hospital, Udaipur, Rajasthan, India.
- Senior Medical Officer, Department of Preventive and Social Medicine, SMS Medical College, Jaipur, Rajasthan, India.
- Resident, Department of General Medicine, JLN Medical College, Ajmer, Rajasthan, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Hitendra Jatav,
Plot No. 28, HC Bairwa Bhamsthali Colony, Dungarpur-314001, Rajasthan, India.
E-mail: jatav.hitendra001@gmail.com

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