Nor. Afr. J. Food Nutr. Res. 2023; 7 (16): 85 – 100

https://doi.org/10.51745/najfnr.7.16.85-100

https://www.najfnr.com

ORIGINAL ARTICLE

Determinants of malnutrition and associated parameters in subjects with stable chronic obstructive pulmonary disease: A cross sectional study

Chandan Vinay Srigiripura [1*], Chaya Sindaghatta Krishnarao [2], Jayaraj Biligere Siddaiah [2], Padukudru Mahesh Anand [2], Asna Urooj [3]

1. Department of studies in Food Science & Nutrition, Manasagangothri, University of Mysore, Mysuru, Karnataka, India. chandanvinays.chandanvinays@esic.gov.in
2. Department of Respiratory Medicine, JSS Medical College, JSS Academy of Higher Education & Research, Mysuru, India. chaya.sindaghatta@gmail.com / drjayarajbs@yahoo.com / mahesh1971in@yahoo.com
3. Department of studies in Food Science & Nutrition, Manasagangothri, University of Mysore, Mysuru, Karnataka, India. asnaurooj@foodsci.uni-mysore.ac.in

ABSTRACT

Background: Chronic obstructive pulmonary disease exerts local and systemic manifestations including malnutrition which has deleterious consequences on health, quality of life and survival. Nutritional status is known to impact the prognosis of COPD.**Aims:** An attempt was made to study the nutritional status of subjects with stable COPD using PGSGA, identify malnutrition and analyze the factors contributing to malnutrition. **Patients and Methods:** Using convenient sampling, 110 subjects of both sexes (105 men and 5 women) with stable COPD aged between 40 – 75 years (61 ± 9 years), visiting the Pulmonologist at JSS Hospital, Mysuru were included in the study. The subjects underwent spirometry, anthropometry, evaluation of body composition, calorie intake and health related quality of life using standard methods. Differences in the parameters between groups of subjects with varying nutritional status and association with PGSGA score were statistically evaluated. **Results:** Moderate to severe malnutrition was seen in 59% of the subjects. The presence of GI symptoms [OR=62.217, 95% CI (10.834-357.292)], grade 4 dyspnea [OR=67.302, 95% CI (1.287-3520.295)] and increasing disease years [OR=1.151, 95% CI (1.021-1.299)] were found to significantly increase the odds of risk of malnutrition, with very severe dyspnea showing the highest risk of malnutrition followed by presence of GI symptoms. Total SGRQ scores, activity and impact scores were significantly higher in the malnourished groups ($p < 0.001$). The presence of nutrition impact symptoms, seen in 50% of the subjects was associated with lower calorie intake. Severe dyspnea, severe COPDand increasing disease years increased the risk of malnutrition. However, the small sample size and single-center study may not accurately represent the true proportion of malnutrition among female COPD patients in the community.

Keywords: PGSGA, COPD, Malnutrition, Pulmonary function, Dyspnea.

ARTICLE INFORMATION

* **Corresponding authors:** Chandan Vinay Srigiripura
E-mail: knowdiet@gmail.com Tel. (+91) 7760219901

Received: July 24, 2023
Revised: October 21, 2023
Accepted: October 26, 2023
Published: November 19, 2023

Article edited by:
- Pr. Mustapha Diaf

Article reviewed by:
- Prof. Parvaiz Koul
- Prof. Meghit Boumédiène Khaled

Cite this article as: Srigiripura, C. V., Krishnarao, C. S., Siddaiah, J. B., Anand M. P., & Urooj. A. (2023). Determinants of malnutrition and associated parameters in subjects with stable chronic obstructive pulmonary disease - A cross sectional study. *The North African Journal of Food and Nutrition Research,* 7 (16): 85 – 100. https://doi.org/10.51745/najfnr.7.16. 85 - 100

1 Introduction

Chronic obstructive pulmonary disease (COPD) is a respiratory condition associated primarily with the limitation of airflow which is not fully reversible. The global initiative for obstructive lung disease defines COPD as 'a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and alveolar abnormalities usually caused by significant exposure to noxious particles and gases' [1]. The prominent extrapulmonary effect of COPD are systemic inflammation, oxidative stress, skeletal muscle dysfunction and weight loss. COPD is the third leading cause of death in the world and the second leading cause of death in India second to ischemic heart disease, across all ages and both the sex groups [2, 3].

In 2019, 3.3 million deaths were globally reported due to COPD and 212.3 million individuals with COPD were reported [4]. The WHO defines Disability Adjusted Life Years (DALYs) as a time-based measure for a disease or health condition are the sum of the years of life lost to due to premature mortality (YLLs) and the years lived with a disability (YLDs) due to prevalent cases of the disease or health condition in a population and one DALY represents the loss of the equivalent of one year of full health [5]. COPD is found to be the leading cause of disability among chronic respiratory diseases and is reported as the second leading contributor of DALY in 2016. In India, 75.6% of DALYs due to chronic respiratory diseases is attributed to COPD and among the DALYs reported due to COPD globally, 32% was found in India. The number of individuals with COPD in India is reported at 55.3 million cases in 2016.

The leading risk factors responsible for the DALYs were found to be air pollution, tobacco use and occupational risks. The incidence in the population aged more than 30 years ranged between 1.6% to 28.3% in India, but variations exist across the different states. The prevalence is reported to be higher in North Indian states of Jammu and Kashmir, Himachal Pradesh, Uttarakhand, and Haryana followed by East Indian states and then by the west and South Indian states. Among the percentage of COPD DALYs contributed by various risk factors, ambient air pollution was the most predominant cause followed by household air pollution, smoking, occupational risks, ambient ozone pollution and second-hand smoking [6].

Other reported causes of COPD identified in a systematic analysis and meta-analysis of studies in adult patients aged above 30 years of age include sex, socio-economic status, increasing age, pulmonary impairment due to diseases [7].

Malnutrition specifically being underweight (<18 kg/m^2) is found to be a significant risk factor for COPD in a systematic review of population-based studies on COPD prevalence published between 1990 and 2019 [8]. Malnutrition is a routine finding in patients with stable COPD and with exacerbations. Weight loss is reported in 25 – 40% of patients with COPD and loss of skeletal muscle mass in found in approximately 20-35% of patients [9]. Limited Indian data on malnourished COPD patients have reported malnutrition between 11% to 83% of the subjects evaluated in cross sectional studies [10].

Malnutrition is further known to impair the respiratory muscle function, peripheral muscle strength, exercise capacity and leads to higher mortality and morbidity, susceptibility to infections, exacerbations and poor health related quality of life (HRQOL). Malnutrition is also associated with depression and increased costs on health care owing to frequent hospital visits and admissions [11, 12]. Although there are mixed results in terms of the effectiveness of nutritional supplementation, oral nutritional support is able to modify the body weight, fat-free mass, fat mass, lung function, oxygenation, dyspnea severity, inflammatory markers, muscle strength, HRQOL and exercise capacity & tolerance [13-18]. However, malnutrition is common among people with COPD and is often associated with poor prognosis [19].

The factors leading to weight loss are increased energy expenditure secondary to metabolic changes and chronic low-grade systemic inflammation, reduced nutrient intake due to anorexia and increase in respiratory symptoms associated with food intake, and impaired utilization due to altered nutrient utilization and requirements, either alone or in combination [20].

The assessment of body composition, inflammatory markers, dietary intake, nutritional knowledge, challenges pertaining to food availability, feeding, nutritional deficiencies and exercise capacity is crucial to identify and diagnose malnutrition and intervene where ever possible by providing optimum nutritional counseling and timely nutrition support. It is recommended to assess patients comprehensively for malnutrition using the standard tools, provide nutritional advice along with the use of ONS for those with high risk of malnutrition and in patients who complain of difficulty to consume optimal quantity of food due to breathlessness or other symptoms Routine follow-up of these patients to assess for the need for dose adjustment or continuation of the ONS is recommended [21].

Timely oral nutrition support is known to improve energy, protein and micronutrient intake (use of small frequent high-energy and protein meals, ONS, snacks and drinks) in chronically ill patients without compromising food intake and can induce weight gain [22]. Exercise training combined with nutrition intervention to increase protein and branch chain amino acid intake, omega 3 poly unsaturated fatty acids and vitamin D among patients with sarcopenia is known to aid in modification on muscle mass and strength [23].

Keeping in mind the lack of regional data on malnutrition in COPD patients and the multiple factors leading to malnutrition, the present study aimed to assess the nutritional status using BIA, PGSGA, proportion, and causes of malnutrition. It also sought to study the relationship of nutritional status with nutrient intake, pulmonary function, dyspnea, and health-related quality of life in outpatients with stable COPD.

2 Patients and Methods

2.1 Subject selection

Using a convenient sampling design, subjects with stable COPD, visiting the outpatient Department of Respiratory Medicine, JSS Hospital, Mysuru were selected between March 2015 to December 2016. 110 subjects aged between 40 – 75 years of both sexes with stable COPD were included and 46 subjects with co-morbidities such as heart disease, cirrhosis, uncontrolled diabetes, chronic renal failure, acute infection and an acute exacerbation of COPD were excluded. The stable patients were characterized by well controlled respiratory symptoms without moderate to severe exacerbations that required a visit to the emergency department or hospitalization in the previous year and being treated and monitored routinely to ensure a minimum pulmonary decline. The study included stable COPD patients who did not have significant co-morbidities and had provided their consent to participate.

The study did not involve any interventions, invasive procedures, or frequent follow-ups that might inconvenience these patients. A semi structured questionnaire was developed and used to collect the data. The questionnaire aimed to gather data on age, marital status, occupation, area of residence, education, per capita income, smoking habits, alcohol consumption, nutritional supplement use, exposure to dietary counseling/education, frequency of food group consumption, recent food and beverage intake, preferences, disease stage, duration, hospital admissions, medication usage, and physical activity.

2.2 Anthropometry and body composition analysis

All the subjects were evaluated for the following nutritional and clinical parameters. Height was measured using a stadiometer (wall mounted, retractable type) to the nearest 0.1 cm, and body weight was measured on a digital weighing scale with subjects wearing light clothes. The body composition analysis of all the subjects in phase I was performed using 'Bioscan 916' body composition analyzer (Maltron International Ltd, Essex, U.K) that applied bioelectrical impedance analysis (BIA) technique.

The parameters included impedance, fat free mass, fat free mass index, fat mass (kg), body cell mass (kg) and skeletal muscle mass (kg). Bioelectrical impedance analysis is a widely used, non-invasive method for measuring body composition with established accuracy. Since patients with COPD are known to have alterations in body composition, BIA based instrument was used in this study. The Maltron 916 is a portable tetrapolar bioelectrical impedance analyzer that is non-intrusive and calibrated for all age groups and nationalities.

The subjects were analyzed for body composition in a fasting state of at least four hours. The subjects were made to rest in the supine position for 10 minutes on a non-conducting surface with legs slightly separated and arms slightly away from the trunk. A total of 4 surface electrodes were placed each on the dorsal surface of the hand (metacarpal phalangeal joint of the third finger), dorsal surface of the foot (proximal to the meta-tarsal phalangeal joint), pisiform prominence of the wrist and between the medial and lateral malleoli of the ankle [24].

The body mass index (BMI) and fat free mass index (FFMI) was calculated using height, body weight and fat free mass. Further, using BMI and FFMI, the type of nutritional depletion among the subjects was identified using the criteria defined by Schols et al. [25]. The measurement of mid-upper arm circumference (MUAC) was carried out with the subjects standing in an erect position, and the left arm being held at 90 degrees at the elbow. Using a non-stretchable fiberglass measuring tape, the length between the edge of the acromion process and olecranon process of the ulna was measured, and the midpoint was marked.

The arm was made to hand down in a straight fashion, and the circumference at the marked point was made to the nearest 0.1 mm thrice. The triceps skinfold thickness (TSF) was measured using a Lange skinfold caliper. The measurement was made 1 cm above the mark that was made while measuring the MUAC with the subjects keeping their left arm in an extended position. A vertical pinch of skin was gently grasped, and the skin along with the subcutaneous fat was pulled away from the underlying muscle.

The readings are taken using a caliper in mm at this point after ensuring the stabilization of the dial reading. The mid-upper arm muscle circumference (MUAMC) was derived from the MUAMC and TSF measurements using formula (1) [26]:

$$\text{MUAMC} = \text{MUAC} - (3.1416 \times \text{TSF, cm}) \quad \ldots\ldots (1)$$

2.3 Use of PGSGA and food recall

The subjects were assessed for nutritional status using patient-generated subjective global assessment (PGSGA), which is a validated tool for identifying malnutrition [27]. The PGSGA composed of changes in weight, dietary intake, gastrointestinal symptoms, functional capacity, disease and its relation to nutritional requirements such as fever, use of corticosteroids etc. and physical examination for wasting of fat & muscle mass and presence of edema or ascites.

A recall of foods consumed in the last 24 hours (day) was collected from the subjects. To minimize recall bias, the investigators entered data into the questionnaire. Furthermore, to assist participants in accurately recalling their food and beverage consumption, pictorial references were provided, illustrating the typical serving sizes in the hospital cafeteria. In addition, 5 standard cups, measuring between 80 mL and 330 mL, were used as references. This data was converted into quantity of raw foods consumed, and the nutritive values were further calculated using the Indian food composition database by National Institute of Nutrition (NIN), India. Further, the raw food consumption data was used to derive quantity of food groups consumed.

2.4 Evaluation of nutrient intake and adequacy

The resting energy expenditure (REE) was calculated using the equations for predicting basal metabolic rate (BMR) for Indians by the Indian Council of Medial Research, then appropriate activity factors were added based on the physical activity level (PAL) of the subjects. The PAL of the subjects was derived based on the activity pattern of the subjects over a 24 – hour period and physical activity ratio of activities performed. Further, the subjects were categorized into three groups of level of activity based on the FAO/WHO/UNU criteria [28].

A stress factor of 1.2 was applied for patients with normal weight, 1.5 for nutritionally depleted patients, and 1.0 for overweight and obese subjects (adjusted body weight). A factor of 1.1 was applied to account for the thermic effect of food and total energy requirement per day was obtained. Protein requirement was calculated at 1.5 g/kg for subjects with moderate and severe malnutrition. For normally nourished and obese subjects, protein needs were estimated at 1.2 g per kg body weight and adjusted body weight respectively. These needs were derived from recommendation of protein intake between 1.2 – 1.7 g/kg body weight in COPD subjects [29]. The required daily fat intake was calculated at 20 – 25 % of the total calories [30].

The sum of calories provided by protein and fat was subtracted from the total energy requirement of the subject and the remaining calories were divided by a value of 4 to obtain the percentage of calories derived from carbohydrates and the amount of carbohydrate to be consumed per day. The RDA for Indians recommended by the ICMR was used as a reference for the required daily intake of micronutrients [30].

The macronutrient and micronutrient adequacy were evaluated on comparison with the estimated nutrient needs. The percent nutrient adequacy (PNA) was calculated for as percentage of nutrient consumed out of the estimated need. Further, nutrient adequacy ratio (NAR), which is a ratio of an individual's intake per day to the estimated needs. A NAR ratio ≤ 0.66 was considered to be inadequate, 0.66-1.0 as fairly adequate and ≥ 1.0 as an adequate level of intake [31].

Formula (2) used to derive NAR is as follows:

Nutrient adequacy ratio (NAR) = actual intake of a particular nutrient per day/RDA/RDI of the nutrient per day …….. (2)

Once the NAR is calculated for each nutrient, the Mean Adequacy Ratio (MAR) was calculated by averaging all the NAR values together, shown in the equation below. The NAR values were capped to 100% for nutrients with PNA more than 100% before calculating MAR [32]

Mean Adequacy Ratio (MAR) = (Sum of NAR/Number of nutrients) *100 expressed as percentage

2.5 Evaluation of pulmonary function, dyspnea severity and quality of life

The subjects were evaluated for pulmonary function by spirometry. Spirometry (Easy one PC, NDD, Medizintechnik AG, Zurich, Switzerland) was done by trained staff as per American Thoracic Society (ATS) guidelines [33]. Pre and post bronchodilator tests were done for all patients. Post bronchodilator test was performed after using 15 minutes of administration of 400 mcg of nebulized or inhaled salbutamol. The predicted values for FEV_1 and FVC were obtained using corrected Knudson's predicted equation for Asian population (Knudson 83 × 0.87). A record of post bronchodilator FEV_1/FVC ratio less than 0.70 was categorized as obstructive pattern and confirmed COPD according to GOLD criteria.

The severity of airflow limitation was classified as mild (FEV_1 > 80% of predicted), moderate (FEV_1 50 – 80% of predicted), severe (FEV_1 30 – 50% of predicted), and very severe (FEV_1 < 30% of predicted) as per GOLD criteria [34]. The severity of dyspnea was assessed in the subjects using the modified Medical Research Council scale (mMRC), which is used to assess the breathlessness and exertion induced dyspnea [35]. The health-related quality of life (HRQOL) of the subjects with COPD was assessed using St. George's respiratory questionnaire (SGRQ), which is a validated self-reported disease specific questionnaire containing 76 weighted responses to questions on overall health, daily living and perceived well-being [36].

2.6 Statistical analysis

The demographic data and the parameters assessed using PGSGA tool in the study population was expressed as mean and standard deviation (SD) or number and percentage as appropriate. The smoking pack years was expressed as median and interquartile 1 and 3 values. The normality of distribution of all the parameters was assessed by the Shapiro-Wilk test. Differences in PGSGA scores, MAR between the sub-groups classified based on GI symptoms was evaluated by independent t-test. Mann Whitney U test was used to evaluate the differences between MMRC score among the same sub groups.

The association between PGSGA score and pulmonary function parameters were evaluated using Pearson's correlation analysis. Differences in body composition, anthropometry, pulmonary function, physical activity level, nutrient adequacy and food group intake between the three sub groups classified as per the nutritional status was evaluated using one-way ANOVA followed by Bonferroni correction. A bivariate analysis followed by multiple logistic regression was performed to identify the predictors of malnutrition and Nagelkerke R square was used as a measure of efficiency of the model. A p-value less than 0.05 was considered to be statistically significant. The data analysis was carried out using SPSS version 19.0 for windows.

The study was approved by the Institutional Human Ethics Committee of University of Mysore (IHEC-UOM No.100 Ph.D./ 2014 – 15 dated 07.08.2014) and JSS Hospital Mysore (JSS/MC/IEC/01/6903/2014-15 dated 03.03.2015).

3 Results

3.1 Baseline characteristics

The study group consisted of 105 (95.45%) men and 5 (4.55%) women were included in the study. The prevalence of COPD among women in India is reported at 2.6%, in a 2012 study conducted by Jindal SK et al. in a nationwide study across 12 districts in India, which included 42506 women among 86478 subjects in the study group [37]. Mahesh et al. (2009) have reported a prevalence of 4.5% of the 447 female subjects enrolled in the study comprising a total of 900 subjects in Mysuru [38]. Although the current percentage of women with COPD matches the reported prevalence by Mahesh et al. (which is in the same geographical area where the current study was conducted), the number of female subjects in our study is smaller to generalize the outcome of assessment.

81% of the subjects in our study group were residing in rural areas in Mysuru district. Majority of them (78%) were not actively involved in any occupation due to their health condition or were retired from their previous employment. Among the subjects who were involved in a professional work, 11 were farmers, 12 were self-employed, and one of them was a laborer. Half of the subjects had education up to higher secondary school, whereas 46% of them had no formal education. The habit of occasional alcohol consumption was reported in 19 subjects. Among the subjects with COPD, 91% of the subjects were smokers (n-25 active, n-75 ex-smokers).

The median pack years (Q1, Q3) was 25 (11.40) years. None of the women subjects had history of smoking but had a history of biomass smoke exposure ranging from 10-40 years. 89% of the subjects lived in nuclear families. Among the men, 8 % of them had mild disease, 44% of them had moderate COPD, 37% had severe COPD, and 11 % had very severe COPD. Among the women, 2 of them had severe COPD, 2 of them had moderate COPD, and one subject had very severe COPD. The mean disease years were 4 ± 2 years. 74% of them were diagnosed with COPD in the past 1 – 5 years. 61% of them had one exacerbation in the last year, 15% of them had had 2 – 3 exacerbations and 25% of them had reported no absence of exacerbation in the previous year. 78% of them were on a combination drug of inhaled LABA and corticosteroid; whereas 5% of them were on home oxygen support. Five (5) subjects had hypertension and were on medications. The characteristics of the subjects classified based on their nutritional status in presented in Table 1.

3.2 Nutritional status of subjects

The classification of subjects based on PGSGA is shown in Figure 1. Among the 105 men and five women included in the study, 41% were normally nourished whereas, 35% and 24% of them were found to be moderately malnourished and severely malnourished, respectively.

The normally nourished subjects had a significantly lower mean impedance values and PGSGA score compared to the malnourished subjects. The BIA is based on resistance and reactance to electrical current in the body. Higher impedance values infer high resistance to flow of current and depicts lesser muscle mass in proportion to fat mass. The malnourished subjects had significantly lower percentage of ideal body weight, MUAC, TSF, MUAMC, fat free mass, fat mass, body cell mass and skeletal muscle mass and % FEV_1/FVC than normally nourished subjects. All these parameters decreased linearly with increasing severity of malnutrition. The per capita household income (PCHI) and PAL were found to decline with state of malnutrition.

Table 1. Characteristics of subjects based on nutritional status

Nutritional status	Normally nourished – A (n-49)	Moderately malnourished/suspected malnutrition – B (n – 39)	Severely malnourished - C (n-26)	*p* value
	Mean ± SD	Mean ± SD	Mean ± SD	
No of subjects - Total (Men/Women)	45 (43/2)	39 (37/1)	26 (25/2)	--
Age (years)	60 ± 9	61 ± 9	62 ± 8	>0.87
PGSGA score	2.64 ± 1.61	7.41 ± 2.29	13.35 ± 6.86	<0.001
Percentage of IBW	112.29 ± 15.53	95.71 ± 14.22	76.77 ± 9.43	<0.001
BMI (kg/m^2)	23.09 ± 3.69	19.19 ± 2.98	18.28 ± 3.97	<0.001
MUAC (cm)	27.19 ± 1.89	24.32 ± 2.87	21.05 ± 2.39	<0.001
TSF (mm)	12.98 ± 2.93	9.2 ± 3.96	6.36 ± 2.93	<0.001
MUAMC (cm)	23.12 ± 1.52	21.43 ± 2.23	19.05 ± 2.03	<0.001
Bioelectrical impedance (Ohms)	649.78 ± 79.14	717.03 ± 102.96	720.85 ± 136.52	0.004
Fat free mass (kg)	47.07 ± 5.50	41.07 ± 6.34	39.41 ± 8.24	<0.001
Fat Free Mass Index (kg/m^2)	16.87 ± 1.48	15 ± 1.66	14.31 ± 2.58	<0.001
Fat mass (kg)	17.44 ± 7.01	10.9 ± 5.10	10.68 ± 4.08	<0.001
Body cell mass (kg)	26.33 ± 3.53	21.89 ± 3.64	21.56 ± 4.98	<0.001
Skeletal Muscle Mass (kg)	23.80 ± 3.01	19.96 ± 4.04	19.39 ± 4.04	<0.001
Per capita household income (INR)	3233 ± 1881	2722 ± 1427	2647 ± 1039	>0.20
FVC (L)	2.13 ± 0.49	2.26 ± 0.75	2.01 ± 0.6	>0.28
FEV_1 (L)	1.22 ± 0.37	1.31 ± 0.58	1.04 ± 0.45	>0.10
FEV_1/FVC ratio	0.57 ± 0.08	0.55 ± 0.13	0.51 ± 0.11	0.065
% of ideal FVC	69.07 ± 17.22	77.87 ± 21.64	67.77 ± 20.62	>0.09
% of ideal FEV_1	49.04 ± 15.91	55.03 ± 20.56	45.12 ± 19.06	>0.09
% FEV_1/FVC ratio	71.07 ± 10.1a	69.54 ± 11.19	63.04 ± 13.01a	0.014
PAL	1.41 ± 0.13	1.39 ± 0.12	1.37 ± 0.13	>0.37

PGSGA -Patient generated subjective global assessment, IBW- Ideal body weight, BMI- Body mass index, FEV_1- Forced expiratory volume in 1 second, FVC- Forced vital capacity, PAL- Physical activity level, INR – Indian rupees

The parameters used in the assessment of nutritional status of subjects as defined in the PGSGA tool, that depicts presence of malnutrition are presented in Table 2. 37% of the subjects reported weight loss in the past one-to-six-month duration. 49% of them reported reduction in usual food intake. Lack of appetite and early satiety were the major nutrition impact symptoms found to affect the food intake. The limitation to perform routine activities was affected to various extents in 94% of the subjects. Pulmonary cachexia and old age (> 65 years) were the major disease conditions identified to affect the nutritional status. Compared to depletion of fat status (37%), a higher proportion of them were found to have varying severity of muscle depletion (49%).

Table 2. Indicators of nutritional status and malnutrition assessed using PGSGA

A. Changes in body weight	No (%)
Unchanged	69 (63)
Decreased in a month	7 (6)
Decreased in 6 months	34 (31)
B. Status of food intake	
Unchanged	54 (49)
less than usual	56 (51)
Type of foods consumed	
- Normal food in lesser quantities than usual	44 (40)
- Little solid food	9 (8)
- Very little food	1 (1)
C. Nutrition impact symptoms related to food intake	
- No problems	32 (29)
- No appetite	50 (46)
- Feel full quickly	44 (40)

- Fatigue	6 (6)	
- Nausea	2 (2)	
- Fear of dyspnea	1 (1)	
- More than one symptom	30 (27)	
D. Physical activity and daily function		
- Normal without limitations	7 (6)	
- Not normal, able to perform fairly normal activities	39 (36)	
- Not feeling up to most things, but in bed/chair less than half a day	42 (38)	
- Able to do little activity and spend most of the day in bed/chair	20 (18)	
- Rarely out of bed	2 (2)	
E. Nutritionally important disease conditions/ old age		
- Pulmonary cachexia	33 (30)	
- Aged > 65 years	39 (36)	
- Combined symptoms	7 (6)	
F. Physical examination	**Muscle status**	**Fat status**
- No depletion	56 (51)	69 (63)
- Mild depletion	27 (25)	16 (15)
- Moderate depletion	16 (15)	22 (20)
- Severe depletion	11 (10)	3 (3)

3.3 Nutrient intake

The mean percent nutrient adequacy of nutrient intake of 10 nutrients, energy and MAR of the subjects grouped based on their nutritional status is shown in Figure 2. Normally nourished subjects had significantly higher mean daily intake of calories ($F = 11.224$, $p < 0.001$), carbohydrates ($F = 12.527$, $p < 0.001$), thiamine ($F = 15.020$, $p < 0.001$), riboflavin ($F = 6.504$, $p = 0.02$), niacin ($F = 9.303$, $p < 0.001$), iron ($F = 13.431$, $p < 0.001$), calcium ($F = 3.814$, $p = 0.025$), vitamin C ($F = 4.288$, $p = 0.016$) and MAR ($F = 16.478$, $p < 0.001$) than moderately malnourished and severely malnourished subjects. Normally nourished subjects had a better adequacy of nutrient intake than malnourished subjects. The two dotted lines in the graph are marked at 67% and at 100%, based on NAR classification. Adequate intake was found only for calcium (in all the groups), thiamine (in stage B and A) and carbohydrates in the normally nourished group. Protein intake was found to be inadequate in all the groups and fat intake was fairly adequate only in the normally nourished group. The trend indicates that the subjects followed a predominantly carbohydrate rich diet. The adequacy of calorie intake was found to decrease significantly with severity of malnutrition.

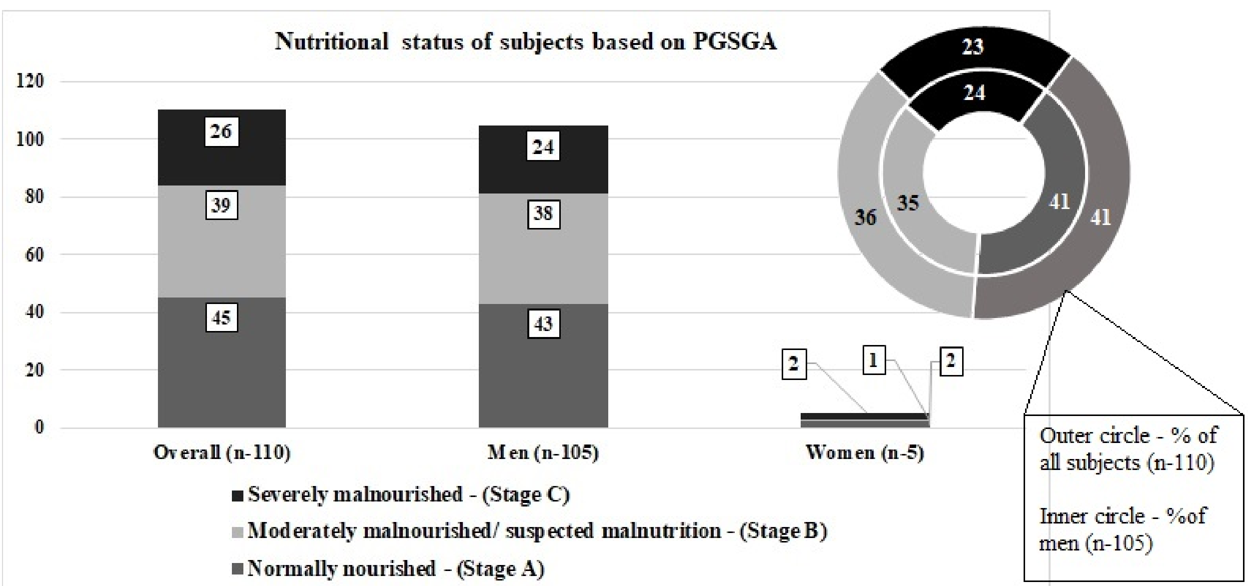

Figure 1. Classification of subjects based on nutritional status using PGSGA

The proportion of subjects with normal nutritional status and malnutrition on assessment using PGSGA tool are presented in both number and percentage. The depiction of nutritional status of women subjects is not made in percentage due to their smaller number

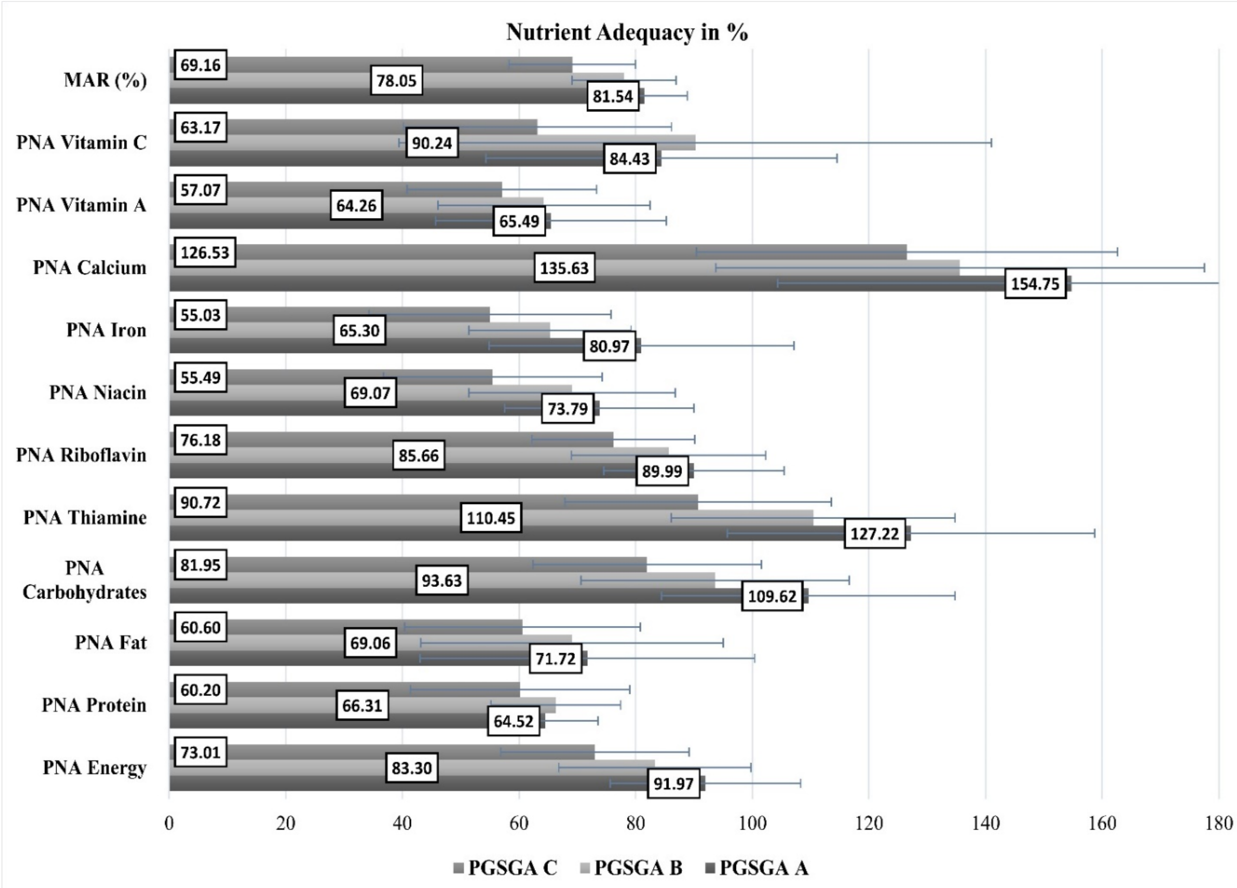

Figure 2. Nutrient adequacy of subjects classified based on nutritional status

This graph depicts the adequacy of intake of eleven nutrients and calories of the subjects as compared to their recommended daily intake after categorizing them based on their nutritional status.

3.4 Food group intake

The food group intake was compared among the subjects classified based on their nutritional status. The results are presented in Table 3. Malnourished subjects had significantly lower mean intake of cereals and cereal products, vegetables and fats & oils, compared to normally nourished subjects. It is evident that the subjects followed a predominantly carbohydrate rich diet with cereals and products being the major source of calories. The pattern of food group indicates that the decrease in consumption of cereals and products as the chief cause of changes in energy intake. The diet pattern was characterized by reduced consumption of fatty foods due to the fear of increase in respiratory symptoms such as cough or phlegm formation. The decrease seen in the intake of fats and oils is proportional to the food quantity consumed rather than consumption of fat rich foods. With decreasing vegetable intake, it can be understood that phytochemical intake is also decreasing with increasing severity of malnutrition.

3.5 Impact of NIS

The subjects were further classified based on the presence or absence of nutrition impact symptoms and parameters related to nutritional status, body composition and adequacy of nutrient intake were analyzed. The results are presented in Table 4. Subjects with nutrition impact symptoms had significantly lower PGSGA score, fat free mass, fat mass, BMI and adequacy of nutrient intake. PGSGA score indicates the need for specific type of one or more nutrition interventions among the patients assessed. The score guides the use of multiple strategies such as nutrition education, counseling, need for interdisciplinary interventions, use of oral nutrition supplements or nutrition support systems comprising of enteral or parenteral therapy to manage malnutrition.

Table 3. Characteristics of subjects based on nutritional status

Nutritional status/Food groups	Normally nourished – A (n-49)	Moderately malnourished/suspected malnutrition – B (n – 39)	Severely malnourished - C (n-26)	*p* value
	Mean ± SD	Mean ± SD	Mean ± SD	
Cereal grains and products (g)	291.44 ± 66.4	235.16 ± 57.99	184.46 ± 58.88	<0.01
Pulses (g)	47.88 ± 18.08	55.41 ± 26.08	46.34 ± 17.81	0.168
Vegetables (g)	151.22 ± 61.82	144.66 ± 57.46	105.38 ± 60.85	0.008
Fruits (g)	69.23 ± 50	66.68 ± 55.31	66.68 ± 53.15	0.495
Milk and Curds (g)	233 ± 77.65	240.74 ± 72.03	244.93 ± 76	0.794
Fats and Oils (g)	14.6 ± 9.5	13.66 ± 8.23	8.53 ± 6.53	0.013
Sugar/Jaggery (g)	12.84 ± 6.4	15.48 ± 8.14	14.84 ± 7.49	0.235

Higher scores indicate the presence of several and severe nutritional problems that may require aggressive intervention. The presence of NIS in the subjects can be the primary cause for chronic reductions in food and nutrient intake, depletion of FFM and FM and malnutrition. The proportion of subjects with cachexia was found to be higher in the group with nutrition impact symptoms (73%) than without nutrition impact symptoms (27%). With the persistent effects of the disease on metabolism, presence of NIS and related decrease in food and nutrient intake, alterations in body composition can be linked with higher prevalence of cachexia.

3.6 Nutritional status and pulmonary function

A correlation analysis between lung function measurements and PGSGA score revealed and statistically significant weak negative correlation between PGSGA score with FEV1 (r-0.190), FEV1/FVC ratio (r-0.225), percentage of predicted and FEV1/FVC ratio (r-0.213). MAR was found to be negatively correlated with FVC (r-0.216). These values indicate the absence of a profound effect of malnutrition and nutrient adequacy on lung function or vice versa. Hence, an association between the presence of malnutrition and lung function or the decrease in nutrient adequacy was not associated with the deterioration in pulmonary function alone as measured by spirometry in the subjects.

3.7 Regression analysis

A multiple logistic regression was performed to evaluate the effects of age, socioeconomic status, education, physical activity status, inadequacy of calorie intake, presence of nutrition impact symptoms, severity of COPD, severity of dyspnea, exacerbations in the previous year and disease years on the likelihood of subjects with malnutrition.

Table 4. Mean nutrient adequacy, body composition and PGSGA score of subjects classified based on presence of nutrition impact symptoms.

Parameters	Nutrition impact symptoms absent (n-54)	Nutrition impact symptoms present (n-56)	*p value*
	Mean ± SD	Mean ± SD	
PGSGA Score	3.5 ± 2.6	10 ± 4	<0.001
Fat free mass (kg)	46.3 ± 6.42	40.08 ± 6.78	<0.001
Fat mass (kg)	16.57 ± 7.22	10.59 ± 4.24	<0.001
BMI (kg/m^2)	22.55 ± 3.93	18.67 ± 3.32	<0.001
MAR (%)	81.59 ± 0.7	73.29 ± 1	<0.001

PGSGA – patient-generated subjective global assessment; BMI: Body mass index; MAR - Mean adequacy ratio

The results are presented in Table 5. The logistic regression model was statistically significant, $\chi 2(14) = 66.487$, $P<0.001$. The Hosmer-Lemeshow test was used to determine the goodness of fit of the model, with a p-value of 0.117 and $\chi 2$ value of 12.867 (df 4) indicating acceptable goodness of fit. The -2-log likelihood was 81.575 and Nagelkerke R square was 0.613 for the model. The model explained 61.3% of variance in the occurrence of malnutrition and correctly classified 84.5 % of the cases.

The presence of nutrition impact symptoms, grade 4 dyspnea and increasing disease years were found to be significantly associated with malnutrition at the 5% level of significance. The presence of nutrition impact symptoms, grade 4 dyspnea and increasing disease years were found to increase the odds of malnutrition in our subjects.

Table 5. Predictors of malnutrition in subjects with COPD

Variable	OR with 95%CI (univariate)	*p value*	OR* with 95%CI (multivariate)	*p value*
Age	0.959 (0.960 – 1.044)	0.58	0.992 (0.930 – 1.058)	0.800
PCHI	1.000 (1.000 – 1.000)	0.104	1.000 (0.999 – 1.000)	0.519
Physical activity level	0.103 (0.005 – 2.139)	0.142	5.836 (0.019 – 1795.823)	0.546
MAR	0.000 (0.000 – 0.026)	0.037	0.062 (0.000 – 100.141)	0.461
Presence of nutrition impact symptoms	26.520 (8.875 – 79.244)	<0.001	33.529 (7.631 – 147.313)	<0.001
Stage of COPD				
- Mild	1.000		1.000	
- Moderate	0.406 (0.076 – 2.173)	0.292	0.113 (0.007 – 1.954)	0.134
- Severe	0.403 (0.074 – 2.186)	0.292	0.084 (0.004 – 1.619)	1.619
- Very severe	0.381 (0.057 – 2.534)	0.318	0.016 (0.000 – 0.568)	0.023
Dyspnea severity				
0	1.000		1.000	
1	3.500 (0.320 – 38.232)	0.304	8.948 (0.381 – 210.159)	0.174
2	1.846 (0.163 – 20.939)	0.621	11.570 (0.489 – 273.658)	0.129
3	7.154 (0.680 – 75.314)	0.101	14.007 (0.579 – 339.919)	0.104
4	12.000 (0.898 – 160.414)	0.060	69.063 (1.673 – 2850.559)	0.026
No of exacerbations in the previous year	1.356 (0.813 – 2.261)	0.243	1.416 (0.699 – 2.868)	0.335
Disease years	1.054 (0.976 – 1.140)	0.181	1.141 (1.017 – 1.281)	0.025

PCHI – Per capita household income, MAR – Mean adequacy ratio, COPD- Chronic obstructive pulmonary disease

3.8 Health related quality of life

The mean rank of dyspnea score, the average total SGRQ score and sub component scores are presented in Table 6. A statistically significant difference in the severity of dyspnea among subjects with varying nutritional status was observed. The mean rank increased linearly with worsening nutritional status.

A chi-square test of independence showed that there was a significant association between presence of nutrition impact symptoms and severity of dyspnea, $X^2(N = 110) = 14$, $p = 0.007$. The HRQOL scores were evaluated after classification of the subjects based on their nutritional status. Malnourished subjects had lower HRQOL than normally nourished subjects. The total SGRQ scores, activity and impact sub-scores of the normally nourished subjects was significantly lower compared to the malnourished groups. Normally nourished subjects were able to perform routine activities such as lying, sitting, bathing, walking on a level or stairs better than malnourished subjects. The impact of respiratory symptoms such as breathlessness during talking, bending over sleeping etc. was higher among the malnourished subjects as well. Disturbances in social life and psychological health assessed as an impact score also was higher in the malnourished group. These disturbances include effect on ability to work or earn, problems caused due to the disease condition, feeling embarrassing in public, feeling frail, feeling exertion in the simplest tasks etc.

4 Discussion

Nutrition is an integral part of a healthy life and it is an important aspect of disease prevention as well as recovery from conditions that modify the nutritional status of an individual. An alteration in the metabolism due to COPD is known to cause malnutrition in a significant proportion of patients with COPD. Malnutrition is a frequent finding and leads to detrimental consequences on the prognosis of the disease, psychology and quality of life [39]. This study was the initial step in the development of a disease specific affordable nutritional formulation using locally available foods for malnourished COPD patients. Hence, the stimulus to conduct this study was to determine the presence and proportion of nutritional problems related to food and nutrient intake.

Table 6. Health-related quality of life and dyspnea severity scores of subjects

Nutritional status	Normally nourished (n-45)	Moderately malnourished (n-41)	Severely malnourished (n-24)	*p value*
	Mean ± SD	Mean ± SD	Mean ± SD	
SGRQ Total score	41 ± 14[a]	43 ± 14[b]	54 ± 17[ab]	0.003*
Activity score	58 ± 23	59 ± 22	72 ± 22	0.033*
Symptom's score	49 ± 18	52 ± 17	59 ± 20	0.11*
Impact score	28 ± 12	42 ± 18	33 ± 15	0.001*
MMRC dyspnea score (Mean rank)	46.22	55.6	71.4	0.004**

SGRQ - St. George's Respiratory Questionnaire, MMRC- Modified Medical Research Council. *One way ANOVA; ** Kruskal Wallis test with post hoc analysis, (H (2) = 11.199, p value = 0.004); Groups with the same superscripts are statistically different from each other.

The results of our study also indicate a similar trend of higher prevalence of malnutrition. Pulmonary cachexia (BMI - < 21 kg/m^2 and FFMI < 16 kg/m^2) was found in 50% of the subjects. The observed degree of malnutrition in our study is comparatively lower than previous studies where SGA/PGSGA was used as a tool for assessment. Gupta et al. [10] have reported 83% malnutrition among 106 subjects with stable COPD (male/female = 92/14). The assessment was using SGA found 59.5% of them as moderately malnourished and 23.5% as severely malnourished [10]. Nguyen et al. have reported 74.45 % malnutrition (SGA B/C) among 168 subjects with COPD. Energy intake was less than the estimated needs in 85.7% of the subjects [40]. However, cachexia was higher than values reported earlier in two studies in Netherlands. Schols et al. [25] have reported 28% cachexia among 412 subjects with stable COPD and Vermeeren et al. [41].reported cachexia in 27% of the 389 subjects with moderate to severe COPD. Cachexia in COPD is due to alterations in muscle fiber physiology (protein turnover, increased activity of ubiquitin proteasome system) which may me triggered by negative energy balance, inflammation, oxidative stress and hormonal alterations [42]. Muscle wasting in COPD patients further contributes to skeletal muscle dysfunction, diminished exercise capacity, health status, and poor quality of life as well as impacts the mortality rate [43].

Food intake is affected by various factors such as nutrition impact symptoms (nausea, vomiting, diarrhea, lack of appetite, early satiety, dysgeusia, dry mouth, ulcers in the mouth etc.), dysphagia and fatigue related to consumption of adequate quantity of food. These are known to be secondary effects of several acute and chronic diseases other than psychological factors affecting food intake. Early satiety, lack of appetite and fatigue were the commonly reported nutrition impact symptoms among 56 subjects in our study. Disturbance in the energy balance is the main driving factor of malnutrition in COPD patients. When the energy expenditure exceeds calorie intake, weight loss occurs. The factors leading to weight loss are increased energy expenditure, reduced nutrient intake, and impaired utilization either alone or in combination [44]. Malnutrition seen in patients with COPD is understood as chronic disease related malnutrition with inflammation otherwise termed cachexia. This state of deranged inflammatory milieu is known to induce anorexia secondary to alterations in the hormonal control of orexigenic and anorexigenic factors [45]. Cachectic COPD patients were found to have higher Interleukin 6 to Interleukin 10 ratio, decreased insulin-like growth factor to growth hormone ratio, insulin resistance and decreased desire to eat as compared to non-cachectic patients in a case control study including 103 patients with COPD [46]. The common respiratory symptoms seen in patients with COPD are dyspnea, which is a sense of increased effort to breathe, chronic cough (productive or nonproductive) and sputum production. Dyspnea is one among the additional factors other than lack of appetite due to anorexia, early satiety and bloating which are known negatively impact food intake [43]. Hyperinflation, flattened diaphragm and reduced abdominal volume seen in COPD patients are known to contribute to decreased food intake by resulting in abdominal discomfort, bloating and early satiety [41]. Fatigue during food consumption and early satiety are also known to limit the food intake [47]. Eating food is known to adversely affect the oxygen saturation and partly increase the symptom of dyspnea in subjects with severe COPD [48].

Malnutrition is known to increase the risk of development of cachexia, which is characterized by anorexia, severe loss of fat free mass, fat mass and poor exercise tolerance [49, 50]. A similar trend was observed in our study, with respect to presence of nutrition impact symptoms & proportion of cachectic subjects. The lower fat free mass and fat mass among malnourished subjects justifies this association. The presence of nutrition impact symptoms could be the consequence of effects of the disease, mainly dyspnea, severe COPD, cachexia and is significantly associated with poor nutrient intake. Chronic deficits in energy and nutrient intake could be associated with lower body weight, fat free mass and fat mass among our subjects. The chronic energy deficit is important in weight losing patients or who are already underweight. Thus, energy needs in these patients may be higher than weight stable patients or with a normal/higher BMI and the energy needs are further affected by the expenditure due to physical task/activity other than increased basal metabolic rate [51]. It is also necessary to include appropriate nutrient composition with respect to ratio of energy obtained from carbohydrates, protein and fat and micronutrients when planning for high calorie diets as a mere increase in energy intake may be insufficient to achieve the nutritional objectives.

This highlights the need for routine screening and assessment for involuntary weight loss, changes in body mass index, food and nutrient intake, changes in body composition whenever feasible and for the development of cachexia. The assessment process will aid in timely identification of deficits in food/nutrient intake and facilitate nutrition intervention that may include modification of nutrient quantity & quality, food texture, meal size, meal pattern or use of oral nutrition supplements in non-cachectic patients and also can be a part of the therapy for patients with cachexia, which includes pharmacological therapy as well. PGSGA score defines the need for planning and implementation of patient specific nutrition intervention that includes medical nutrition therapy (ranging from changes in food attributes, use of oral nutrition supplements, enteral & parenteral nutrition support) patient & family education, symptom management. The association of PGSGA score with nutrition impact symptoms in our subjects indicate the need for oral nutrition support using nutrient dense formulations that may enhance nutrient intake without affecting the present respiratory symptoms. Indications for use of enteral or parenteral nutrition support was not found in the subjects in our study. The association of malnutrition and lung function as measured by spirometry was weak among the subjects in the study group which may be due to the smaller sample size. HRQOL relates to perception of individuals or a group about certain aspects of health such as physical, psychological and social aspects. HRQOL is a routinely used measure in clinical practice and research, that provides an understanding of the impact of health and disease on the quality of life as absence of disease alone does not indicate sound health [52]. The SGRQ is designed to measure frequency of respiratory symptoms, disturbance to routine physical activities (activity score) and disturbances in psycho-social function (impact score). An impaired HRQOL is detrimental to the physical, psychological and social status of individuals with COPD. Depression, cognitive dysfunction and severe hypoxia is linked with a poor HRQOL due to COPD. Dyspnea and chest pain have been associated with poor HRQOL in a cohort of 93 subjects with COPD in India and the authors emphasize the assessment of HRQOL in routine medical care of patients with COPD [53]. The activity and impact component scores indicate the reduced routine and occupational activity & psychosocial function among malnourished subjects in our study. Such an association is frequently reported in literature. Malnutrition was associated with poor total SGRQ scores, activity and impact scores among 168 patients with COPD in a cross-sectional study by Nguyen et al. [40]. and among 163 stable COPD patients involved in a rehabilitation program as reported by Gunay et al. [54]. Thus, malnutrition can be an additional factor apart from the disease itself that can lead to progressive deterioration in health-related quality of life.

5 Strengths and limitations

The subjects included in the study did not have any other significant disease condition apart from COPD that could have an impact on the nutritional status, thus the outcomes could be related to the manifestations of COPD. No studies were available to compare the proportion of subjects with nutrition impact symptoms and related changes in nutritional parameters. To our knowledge, this is the first study reporting changes in nutritional and clinical parameters based on nutrition impact symptoms in patients with COPD in India. Also, no Indian studies on the use of PGSGA in COPD patients have been published to date. The results also highlight the importance of nutrition screening and assessment of stable COPD patients, as assessment may aid in identification of nutrition related problems and intervention to overcome the problems related to food and nutrient intake using specific nutrition intervention strategies. The study had a few limitations. The sample size was small and there were very few women in the study and the findings are not generalizable to women patients. Subjects were selected from the hospital OPD and may not be representative of the general population i.e., patients with COPD. The energy needs were estimated by predictive equations and the food recall method may have contributed to variation in nutrient related data. In routine clinical practice, it is common to see COPD subjects with multiple co-morbidities. Subjects with significant co-morbidities were excluded in this study and the findings are not generalizable to subjects with COPD and co-morbid conditions such as diabetes and heart disease.

6 Summary & Conclusion

A significant proportion of subjects with stable COPD included in our study were malnourished. The presence of nutrition impact symptoms and the associated reduction in calorie intake appeared to be the factors associated with undernourished subjects. The presence of nutrition impact symptoms that have an impact on the food intake such as lack of appetite and early satiety, severe dyspnea and increasing disease years were associated with malnutrition. The PGSGA scores highlight the need for oral nutritional support among the subjects with nutrition impact symptoms affecting food intake and nutrition counseling for the malnourished subjects without nutrition impact symptoms. Hence, the assessment of the nutritional status of subjects with stable COPD should be performed routinely to identify patients at risk of developing malnutrition or who are already malnourished. Assessment of nutritional status using PGSGA is ideal in identifying malnutrition and initiating nutrition intervention.

Funding: The study was funded under the Special Assistance Program-Phase II (Grant no. UGC No. F 640/1/DRS/2013 (SAP-I), dated July15, 2013) from University Grants Commission, Bahadur Shah Zafar Marg, New Delhi, India.

Acknowledgements: Authors thank the Special Assistance Program-Phase II (Grant no. UGC No. F 640/1/DRS/2013 (SAP-I), dated July15, 2013) from University Grants Commission, Bahadur Shah Zafar Marg, New Delhi, India for providing the financial assistance to conduct the study

Previous submissions: None

Authors' Contribution: C.V.S. undertook conceptualization & literature search, investigation, framing the methodology, formal analysis, writing – original draft and review of manuscript & editing. C.S.K. undertook framing of methodology, formal analysis, writing - original draft, review and editing of the manuscript. J.B.S. undertook formal analysis, writing - original draft, review & editing of the manuscript. M.P.A. undertook framing of methodology, formal analysis, writing - original draft, review & editing of the manuscript. A.U. undertook conceptualization & Literature search, framing of methodology, formal analysis, writing - original draft, review & editing of the manuscript, and the funding acquisition for the study. All authors approved the final version before submission. All authors have read and agreed to the published version of the manuscript."

Conflicts of Interest: The authors hereby declare that there is no conflict of interest.

References

[1] Mirza, S., Clay, R. D., Koslow, M. A., & Scanlon, P. D. (2018). COPD guidelines: A review of the 2018 GOLD report. *Mayo Clinic Proceedings. Mayo Clinic*, *93*(10), 1488–1502. https://doi.org/10.1016/j.mayocp.2018.05.026

[2] Chronic obstructive pulmonary disease (COPD). (2017, December 1) World Health Organization. WHO. Available from: https://www.who.int/en/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd). [Last accessed 2019, February 11].

[3] Naghavi, M., Abajobir, A. A., Abbafati, C., Abbas, K. M., Abd-Allah, F., Abera, S. F., Aboyans, V., Adetokunboh, O., Afshin, A., Agrawal, A., Ahmadi, A., Ahmed, M. B., Aichour, A. N., Aichour, M. T. E., Aichour, I., Aiyar, S., Alahdab, F., Al-Aly, Z., Alam, K., … Murray, C. J. L. (2017). Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*, *390*(10100), 1151–1210. https://doi.org/10.1016/s0140-6736(17)32152-9

[4] Safiri, S., Carson-Chahhoud, K., Noori, M., Nejadghaderi, S. A., Sullman, M. J. M., Ahmadian Heris, J., Ansarin, K., Mansournia, M. A., Collins, G. S., Kolahi, A.-A., & Kaufman, J. S. (2022). Burden of chronic obstructive pulmonary disease and its attributable risk factors in 204 countries and territories, 1990-2019: results from the Global Burden of Disease Study 2019. *BMJ (Clinical Research Ed.)*, e069679. https://doi.org/10.1136/bmj-2021-069679

[5] Cao, B., Stevens, G., Ho, J., & Ma, D. (2020). WHO methods and data sources for global burden of disease estimates. https://cdn.who.int/media/docs/default-source/gho-documents/global-health-estimates/ghe2019_daly-methods.pdf?sfvrsn=31b25009_7

[6] Salvi, S., Kumar, G. A., Dhaliwal, R. S., Paulson, K., Agrawal, A., Koul, P. A., Mahesh, P. A., Nair, S., Singh, V., Aggarwal, A. N., Christopher, D. J., Guleria, R., Mohan, B. V. M., Tripathi, S. K., Ghoshal, A. G., Kumar, R. V., Mehrotra, R., Shukla, D. K., Dutta, E., … Dandona, L. (2018). The burden of chronic respiratory diseases and their heterogeneity across the states of India: the Global Burden of Disease Study 1990–2016. *The Lancet. Global Health*, *6*(12), e1363–e1374. https://doi.org/10.1016/s2214-109x(18)30409-1

[7] Verma, A., Gudi, N., Yadav, U. N., Roy, M. P., Mahmood, A., Nagaraja, R., & Nayak, P. (2021). Prevalence of COPD among population above 30 years in India: A systematic review and meta-analysis. Journal of Global Health, 11(04038), 04038. https://doi.org/10.7189/jogh.11.04038

[8] Adeloye, D., Song, P., Zhu, Y., Campbell, H., Sheikh, A., & Rudan, I. (2022). Global, regional, and national

prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis. *The Lancet. Respiratory Medicine*, *10*(5), 447–458. https://doi.org/10.1016/s2213-2600(21)00511-7

[9] Itoh, M., Tsuji, T., Nemoto, K., Nakamura, H., & Aoshiba, K. (2013). Undernutrition in patients with COPD and its treatment. *Nutrients*, *5*(4), 1316–1335. https://doi.org/10.3390/nu5041316

[10] Gupta, B., Kant, S., & Mishra, R. (2010). Subjective global assessment of nutritional status of chronic obstructive pulmonary disease patients on admission. *The International Journal of Tuberculosis and Lung Disease: The Official Journal of the International Union against Tuberculosis and Lung Disease*, *14*(4), 500–505.

[11] Ezzell, L., & Jensen, G. L. (2000). Malnutrition in chronic obstructive pulmonary disease. *The American Journal of Clinical Nutrition*, *72*(6), 1415–1416. https://doi.org/10.1093/ajcn/72.6.1415

[12] Ferreira, I. M. (2003). Chronic obstructive pulmonary disease and malnutrition: why are we not winning this battle? *Jornal de Pneumologia*, *29*(2), 107–115. https://doi.org/10.1590/s0102-35862003000200011

[13] Khan, N. A., Kumar, N., & Daga, M. K. (2016). Effect of Dietary Supplementation on Body Composition, Pulmonary Function and Health-Related Quality of Life in Patients with Stable COPD. *Tanaffos, 15*(4), 225–235.

[14] Gurgun, A., Deniz, S., Argın, M., & Karapolat, H. (2013). Effects of nutritional supplementation combined with conventional pulmonary rehabilitation in muscle-wasted chronic obstructive pulmonary disease: A prospective, randomized and controlled study. *Respirology (Carlton, Vic.)*, *18*(3), 495–500. https://doi.org/10.1111/resp.12019

[15] Sugawara, K., Takahashi, H., Kasai, C., Kiyokawa, N., Watanabe, T., Fujii, S., Kashiwagura, T., Honma, M., Satake, M., & Shioya, T. (2010). Effects of nutritional supplementation combined with low-intensity exercise in malnourished patients with COPD. *Respiratory Medicine*, *104*(12), 1883–1889. https://doi.org/10.1016/j.rmed.2010.05.008

[16] Broekhuizen, R., Creutzberg, E. C., Weling-Scheepers, C. A. P. M., Wouters, E. F. M., & Schols, A. M. W. J. (2005). Optimizing oral nutritional drink supplementation in patients with chronic obstructive pulmonary disease. *The British Journal of Nutrition*, *93*(6), 965–971. https://doi.org/10.1079/bjn20051437

[17] Vermeeren, M. (2004). Nutritional support in patients with chronic obstructive pulmonary disease during hospitalization for an acute exacerbation; a randomized controlled feasibility trial*1. *Clinical Nutrition (Edinburgh, Scotland)*, *23*(5), 1184–1192. https://doi.org/10.1016/j.clnu.2004.03.008

[18] Cai, B., Zhu, Y., Ma, Y. i., Xu, Z., Zao, Y. i., Wang, J., Lin, Y., & Comer, G. M. (2003). Effect of supplementing a high-fat, low-carbohydrate enteral formula in COPD patients. *Nutrition (Burbank, Los Angeles County, Calif.)*, *19*(3), 229–232. https://doi.org/10.1016/s0899-9007(02)01064-x

[19] Schols, A. M., Ferreira, I. M., Franssen, F. M., Gosker, H. R., Janssens, W., Muscaritoli, M., Pison, C., Rutten-van Mölken, M., Slinde, F., Steiner, M. C., Tkacova, R., & Singh, S. J. (2014). Nutritional assessment and therapy in COPD: a European Respiratory Society statement. *The European Respiratory Journal: Official Journal of the European Society for Clinical Respiratory Physiology*, *44*(6), 1504–1520. https://doi.org/10.1183/09031936.00070914

[20] Congleton, J. (1999). The pulmonary cachexia syndrome: aspects of energy balance. *The Proceedings of the Nutrition Society*, *58*(2), 321–328. https://doi.org/10.1017/s0029665199000439

[21] Bostock-Cox, B. (2017). *Identification of malnutrition in COPD patients: a MUST-do!. The British journal of primary care nursing*.

[22] Stratton, R. J., & Elia, M. (2007). A review of reviews: A new look at the evidence for oral nutritional supplements in clinical practice. *Clinical Nutrition Supplements*, *2*(1), 5–23. https://doi.org/10.1016/j.clnu.2007.04.004

[23] van Bakel, S. I. J., Gosker, H. R., Langen, R. C., & Schols, A. M. (2021). Towards personalized management of sarcopenia in COPD. *International Journal of Chronic Obstructive Pulmonary Disease*, *16*, 25–40. https://doi.org/10.2147/copd.s280540

[24] Bioelectrical impedance analysis in body composition measurement: National Institutes of Health Technology Assessment Conference Statement. (1996). *The American Journal of Clinical Nutrition*, *64*(3), 524S-532S. https://doi.org/10.1093/ajcn/64.3.524s

[25] Schols, A. M., Broekhuizen, R., Weling-Scheepers, C. A., & Wouters, E. F. (2005). Body composition and mortality in chronic obstructive pulmonary disease. *The American Journal of Clinical Nutrition*, *82*(1), 53–59. https://doi.org/10.1093/ajcn.82.1.53

[26] Preedy, V. R. (2012). Handbook of anthropometry: physical measures of human form in health and disease. Springer Science & Business Media: pp 278, 669 and 2210.

[27] Jager-Wittenaar, H., & Ottery, F. D. (2017). Assessing nutritional status in cancer: Role of the Patient-Generated Subjective Global Assessment. *Current Opinion in Clinical Nutrition and Metabolic Care*, *20*(5), 322–329. https://doi.org/10.1097/mco.0000000000000389

[28] *Nutrient requirements and recommended dietary allowances for Indians. A report of the expert group of the Indian Council of Medical Research*. (2012). 19–53.

[29] Nelms, M. N., & Sucher, K. P. (2011). Nutrition Therapy and Pathophysiology. *CENGAGE Learning Custom Publishing*, 657–663.

[30] Dietary guidelines for Indians - A manual. National Institute of Nutrition. (2011). *Indian Council of Medical Research*, 89–117.

[31] Singh, A., Gupta, V., Ghosh, A., Lock, K., & Ghosh-Jerath, S. (2015). Quantitative estimates of dietary intake with special emphasis on snacking pattern and nutritional status of free living adults in urban slums of Delhi: impact of nutrition transition. *BMC Nutrition*, *1*(1). https://doi.org/10.1186/s40795-015-0018-6

[32] Nithya, D. J., & Bhavani, R. V. (2018). Dietary diversity and its relationship with nutritional status among adolescents and adults in rural India. *Journal of Biosocial Science*, *50*(3), 397–413. https://doi.org/10.1017/s0021932017000463

[33] Miller, M. R., Hankinson, J., Brusasco, V., Burgos, F., Casaburi, R., Coates, A., Crapo, R., Enright, P., van der Grinten, C. P. M., Gustafsson, P., Jensen, R., Johnson, D. C., MacIntyre, N., McKay, R., Navajas, D., Pedersen, O. F., Pellegrino, R., Viegi, G., Wanger, J., & ATS/ERS Task Force. (2005). Standardisation of spirometry. *The European Respiratory Journal: Official Journal of the European Society for Clinical Respiratory Physiology*, *26*(2), 319–338. https://doi.org/10.1183/09031936.05.00034805

[34] Singh, D., Agusti, A., Anzueto, A., Barnes, P. J., Bourbeau, J., Celli, B. R., Criner, G. J., Frith, P., Halpin, D. M. G., Han, M., López Varela, M. V., Martinez, F., Montes de Oca, M., Papi, A., Pavord, I. D., Roche, N., Sin, D. D., Stockley, R., Vestbo, J., … Vogelmeier, C. (2019). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease: the GOLD science committee report 2019. *The European Respiratory Journal: Official Journal of the European Society for Clinical Respiratory Physiology*, *53*(5), 1900164. https://doi.org/10.1183/13993003.00164-2019

[35] Launois, C., Barbe, C., Bertin, E., Nardi, J., Perotin, J.-M., Dury, S., Lebargy, F., & Deslee, G. (2012). The modified Medical Research Council scale for the assessment of dyspnea in daily living in obesity: a pilot study. *BMC Pulmonary Medicine*, *12*(1). https://doi.org/10.1186/1471-2466-12-61

[36] Jones, P. W., Spencer, S., & Adie, S. (2009). St George's respiratory questionnaire manual.

[37] Jindal, S. K., Aggarwal, A. N., Gupta, D., Agarwal, R., Kumar, R., Kaur, T., Chaudhry, K., & Shah, B. (2012). Indian study on epidemiology of asthma, respiratory symptoms and chronic bronchitis in adults (INSEARCH). *The International Journal of Tuberculosis and Lung Disease: The Official Journal of the International Union against Tuberculosis and Lung Disease*, *16*(9), 1270–1277. https://doi.org/10.5588/ijtld.12.0005

[38] Mahesh, P. A., Jayaraj, B. S., Prahlad, S. T., Chaya, S. K., Prabhakar, A. K., Agarwal, A. N., & Jindal, S. K. (2009). Validation of a structured questionnaire for COPD and prevalence of COPD in rural area of Mysore: A pilot study. *Lung India: Official Organ of Indian Chest Society*, *26*(3), 63. https://doi.org/10.4103/0970-2113.53226

[39] Shepherd, A. B., & Bowell, K. (2019). 'Mind the gap': the importance of managing malnutrition in chronic obstructive pulmonary disease. *British Journal of Nursing (Mark Allen Publishing)*, *28*(22), 1442–1449. https://doi.org/10.12968/bjon.2019.28.22.1442

[40] Nguyen, H. T., Collins, P. F., Pavey, T. G., Nguyen, N. V., Pham, T. D., & Gallegos, D. L. (2019). Nutritional status, dietary intake, and health-related quality of life in outpatients with COPD. *International Journal of Chronic Obstructive Pulmonary Disease*, *14*, 215–226. https://doi.org/10.2147/copd.s181322

[41] Vermeeren, M. A. P., Creutzberg, E. C., Schols, A. M. W. J., Postma, D. S., Pieters, W. R., Roldaan, A. C., & Wouters, E. F. M. (2006). Prevalence of nutritional depletion in a large out-patient population of patients with COPD. *Respiratory Medicine*, *100*(8), 1349–1355. https://doi.org/10.1016/j.rmed.2005.11.023

[42] Remels, A. H. V., Gosker, H. R., Langen, R. C. J., & Schols, A. M. W. J. (2013). The mechanisms of cachexia underlying muscle dysfunction in COPD. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, *114*(9), 1253–

1262. https://doi.org/10.1152/japplphysiol.00790.2012

[43] Sanders, K. J. C., Kneppers, A. E. M., van de Bool, C., Langen, R. C. J., & Schols, A. M. W. J. (2016). Cachexia in chronic obstructive pulmonary disease: new insights and therapeutic perspective: Cachexia in COPD. *Journal of Cachexia, Sarcopenia and Muscle*, *7*(1), 5–22. https://doi.org/10.1002/jcsm.12062

[44] Donahoe, M., & Rogers, R. M. (1990). Nutritional assessment and support in chronic obstructive pulmonary disease. *Clinics in Chest Medicine*, *11*(3), 487–504. https://doi.org/10.1016/s0272-5231(21)00713-9

[45] Muscaritoli, M., Anker, S. D., Argilés, J., Aversa, Z., Bauer, J. M., Biolo, G. I. A. N. N. I., & Sieber. (2010). Consensus definition of sarcopenia, cachexia and pre-cachexia: joint document elaborated by Special Interest Groups (SIG)"cachexia-anorexia in chronic wasting diseases" and "nutrition in geriatrics." *Clinical Nutrition*, *29*(2), 154–159.

[46] Koehler, F., Doehner, W., Anker, S. D., & John, M. (2009). Anorexia in chronic obstructive pulmonary disease — Association to cachexia and hormonal derangement. *International Journal of Cardiology*, *132*(3), 434. https://doi.org/10.1016/j.ijcard.2007.08.054

[47] Hsieh, M.-J., Yang, T.-M., & Tsai, Y.-H. (2016). Nutritional supplementation in patients with chronic obstructive pulmonary disease. *Taiwan Yi Zhi [Journal of the Formosan Medical Association]*, *115*(8), 595–601. https://doi.org/10.1016/j.jfma.2015.10.008

[48] Wolkove, N., Fu, L. Y., Purohit, A., Colacone, A., & Kreisman, H. (1998). Meal induced oxygen desaturation and dyspnea in chronic obstructive pulmonary disease. *Canadian Respiratory Journal: Journal of the Canadian Thoracic Society*, *5*(5), 361–365. https://doi.org/10.1155/1998/347020

[49] von Haehling, S., & Anker, S. D. (2012). Cachexia as major underestimated unmet medical need: Facts and numbers. *International Journal of Cardiology*, *161*(3), 121–123. https://doi.org/10.1016/j.ijcard.2012.09.213

[50] Morley, J. E., Thomas, D. R., & Wilson, M.-M. G. (2006). Cachexia: pathophysiology and clinical relevance1,2. *The American Journal of Clinical Nutrition*, *83*(4), 735–743. https://doi.org/10.1093/ajcn/83.4.735

[51] Lakhdar, R., & Rabinovich, R. A. (2018). Can muscle protein metabolism be specifically targeted by nutritional support and exercise training in chronic obstructive pulmonary disease? *Journal of Thoracic Disease*, *10*(S12), S1377–S1389. https://doi.org/10.21037/jtd.2018.05.81

[52] de Wit M, Hajos T: Health-Related Quality of Life. In: Orbell, S., Schneider, H., Esbitt, S., Gonzalez, J. S., Gonzalez, J. S., Shreck, E., Batchelder, A., Gidron, Y., Pressman, S. D., Hooker, E. D., Wiebe, D. J., Rinehart, D., Hayman, L. L., Meneghini, L., Kikuchi, H., Kikuchi, H., Desouky, T. F., McAndrew, L. M., Mora, P. A., … Turner, J. R. (2013). *Encyclopedia of Behavioral Medicine* (pp. 929–931). Springer New York.

[53] Ibrahim, S., Manu, M. K., James, B. S., Kamath, A., & Shetty, R. S. (2021). Health Related Quality of Life among patients with Chronic Obstructive Pulmonary Disease at a tertiary care teaching hospital in southern India. *Clinical Epidemiology and Global Health*, *10*(100711), 100711. https://doi.org/10.1016/j.cegh.2021.100711

[54] Günay, E., Kaymaz, D., Selçuk, N. T., Ergün, P., Sengül, F., & Demir, N. (2013). Effect of nutritional status in individuals with chronic obstructive pulmonary disease undergoing pulmonary rehabilitation. *Respirology (Carlton, Vic.)*, *18*(8), 1217–1222. https://doi.org/10.1111/resp.12133