Anthropometric and Nutritional status of Chronic Obstructive Pulmonary Disease presenting in Acute Exacerbation in Tertiary care Hospital in Eastern Nepal.

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ABSTRACT

Background: There is scarcity of data regarding the nutritional status of COPD patients presenting in exacerbation in our setup, thus this observational study was conducted.

Methods: We performed an observational study of patients with acute exacerbation of COPD, who were admitted in the Department of Pulmonary, Critical care and Sleep Medicine in tertiary hospital in eastern Nepal from April 2023 to June 2023.

Results: During the study period, a total of 154 patients of COPD with exacerbations were admitted in our department. The baseline anthropometric parameters, lab parameters as well as the malnutrition scores were determined. The mean BMI was 21.82 ± 3.92 kg/m^2 and only 29% had BMI < 18.5 kg/m^2 .The mean hemoglobin, mean cell volume, serum protein, serum albumin, serum calcium, phosphorus and vitamin D level were 12.43 ± 2.32 g/dL, 84.4 ± 9.41 fL, 6.42 ± 1.74 g/dL, 3.32 ± 0.34 g/dL, 8.98 ± 0.63 mg/dL, 3.02 ± 0.42 mg/dL, 18.48 ± 8.22 pg/mL and 40%, 12%, 28%, 41%, 31%, 42% and 49% of these values were below the lower normal limit respectively. The nutritional status tool used NRS-2002, MUST and MNAS-F screened malnutrition in about 68%, 51% and 54% respectively. There shows a discrepancy between the evaluation of the malnutrition assessed by BMI with that of nutritional assessment score.

Conclusion: COPD who present in exacerbations are malnourished, but use of sole BMI to rule out malnutrition in such group of patients can cause false negative result.

Keywords: Acute Exacerbation of Chronic Obstructive Pulmonary Disease; Malnutrition

INTRODUCTION:

Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, expectoration and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction.[1] The World Health Organization (WHO) reported that 90% of COPD-accounted deaths occurred in low- and middle-income countries and has been projected that COPD-associated mortality will increase by 160% in the Southeast Asian region in the coming decades.[2] Acute exacerbation of COPD (AECOPD) is defined as the significant worsening of respiratory symptoms which exceed the normal daily variations thus requiring changes to the current treatment.[3] The relationship of malnutrition and loss of muscle mass i.e., sarcopenia (malnutrition-sarcopenia syndrome, MSS) has a great impact on mortality of COPD patients.[4] The disease induced energy imbalance because of the change in the metabolism, aging, muscle loss and atrophy, tissue hypoxia, ongoing low-grade systemic inflammation, and medications are thought to be the major cause of the poor muscle kinetics as well as nutritional impairment in the these patients.[5] Many COPD patients are hypermetabolic in nature, but despite being in hypermetabolic

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state, COPD patients reduce their dietary intake. The reason for this discrepancy is partly the effects of systemic inflammation that can alter appetite regulation, and in part to the intrinsic energetic cost of eating. So, they often limit their feeding habits to reduce disease-related symptoms, mostly of dyspnea.[6] As COPD patients also have skeletal muscle hypoperfusion and deconditioning, they develop early exercise intolerance which leads to early onset lactic acidosis, leading to early transition to anerobic metabolism. This warrants a higher need of ventilation, to compensate for the ongoing lactic acidosis, thus, for any specific exercise load or minor exacerbation they have more ventilatory demand. Moreover, in severe COPD patients, exercise tolerance may be constrained even by limb muscle fatigue rather than ventilatory limitation.[7] In comparison to the non-cachexic COPD patient, malnourished COPD patients produce a blunted ventilatory response at maximal exercise. This could be due to more dynamic hyperinflation because the cachexic patients have poor muscles mass which are the effectors of the breathing process. Teopompi et al. demonstrated that fat free muscle loss in COPD patients plays an important role in reducing exercise capacity, irrespective of ventilatory limitation. Fat free muscle depletion was also associated with a limited cardiovascular response to exercise and leg fatigue.[8] Depending on the population studied and indicator used, COPD patients are classified as malnourished in the large range of 19 - 60%.[9] The acute stress of exacerbation in COPD leads in elevation of the energy requirements, which is a limiting factor in malnourished patient. Studies have been conducted in western literature regarding the nutritional status of COPD and even their correlational and prognostic effects. Thus, we aim to study the nutritional status of COPD patients presenting as exacerbation. Our limitation for proper assessment of the feeding habits is the unavailability of the context based and validated score to classify them and corelate with the present nutritional status.

METHODS:

Study Setting: The prospective, observational study was conducted at Department of Pulmonary, Critical Care and Sleep Medicine of B.P. Koirala Institute of Health Sciences, a tertiary care Teaching Hospital in Dharan, Nepal within a span of 3 months, starting from April 2023 to June 2023. COPD was defined as: Patient of age > 40 years presenting with chronic cough, chronic sputum production, dyspnea that is progressive (worsens over time) / persistent (present everyday) / worse on exercise / Worse during respiratory infection & had a history of exposure to risk factors like tobacco smoke, occupational dusts and chemicals or smoke from home cooking and heating fuel. Functional classification and Staging of COPD were done based on severity of airflow limitation based upon the criteria laid down by Global Initiative for Obstructive Lung Disease 2023 (GOLD) criteria. Hypercapnic Respiratory Failure in Acute Exacerbation of COPD (AECOPD) was defined as baseline arterial blood gas analysis (measured with room air in the supine position after at least 30 min of rest), partial arterial carbon-di-oxide pressure (paCO2) > 45mmHg. All the required demographic, anthropometric, clinical and laboratory parameters were recorded in the Performa. To determine the nutritional status, we measured the required parameters and used MUST (Malnutrition Universal Screening Tool), Mini Nutritional Assessment Short-Form (MNAS-F) and Nutritional Risk Screening 2002 (NRS-2002) score. The MNAS-F is the frequently used malnutrition screening tool in institutionalized geriatric patients. It screens as well as assesses the patients. MNAS-F has a total score of 14 which are divided to 0-7, 8-11 and 12-14; such that they are categorized to be malnourished, at risk of malnutrition and normal nutritional status respectively. Unlike the NRS-2002, it includes diverse components thus is contextual for the geriatric population.[10] MUST score identifies malnourished individuals in all the settings, be it hospitals, nursing homes, or home care; and became a basis to develop NRS-2002 score. In the MUST score, the results is presented as 0,1 or ≥2; and are at low, medium and high risk of malnutrition and for which routine clinical care, observation at follow up and treatment of the malnutrition is done respectively.[11] The NRS-2002 was helpful in detecting most of the patients who would utmost benefit from nutritional therapy. Results of NRS-2002 score is divided as either ≥3 or <3; the former needs a nutritional care plan, and the latter needs weekly screening for malnutrition.[12] The collected data was entered in Microsoft Excel 2010 and converted to SPSS-11.5 version for the statistical analysis. Descriptive statistics with, mean, SD, median, minimum to maximum Range was calculated for quantitative variables. Frequency and percentage were calculated for categorical variables and graphical and tabular presentation was done for categorical variables where applicable. The results were presented in tabular and graphical formats.

RESULTS:

During the study period of 3 months, a total of 154 patients were enrolled in this study among which, 41.5% (64) were males and 58.4% (90) were females with the mean age of 68.04 ± 12.12 years. The median age was 69.9 years. The minimum age was 49 years and maximum age was 87 years. About 90% of the enrolled patients were smokers having a significant past or present smoking history. The remaining patients had a history of significant biomass exposure. Four-fifth of the patients had functional status of mMRC 2 and 3. More than half of the enrolled patients had baseline GOLD assessment status of GOLD-E and only a minority of them were GOLD-A. Thirty percent of the population were categorized as under-nutrition according to the WHO-Asian BMI classification and half were having BMI in normal range. Twenty percent were overweight, probably because of the presence of sleep related breathing disorders in COPD, which was estimated to be 34-68% in various studies[13]. The baseline characteristics are demonstrated in the table below (table 1).

Table 1: General characteristics of all patients (N=154).

Mean age	68.04 ± 12.12 years
Age Range	44-87 years
Median age	69.9 years
Male	42%
Female	58%
Smoker	90%
Baseline mMRC status	
▪ mMRC-0	0% (0)
▪ mMRC-1	8% (12)
▪ mMRC-2	39% (60)
▪ mMRC-3	42% (65)
▪ mMRC-4	11% (17)
Baseline GOLD status	
▪ GOLD-E	59% (91)
▪ GOLD-B	28% (43)
▪ GOLD-A	13% (20)
Height (centimeters)	159.2 ± 8.47 cm
Weight (kilograms)	53.6 ± 8.42 kg
BMI range	21.82 ± 3.92 kg/m^2
▪ < 18.5 kg/m^2	29% (45)
▪ 18.5-22.9 kg/m^2	53% (81)
▪ ≥ 23 kg/m^2	19% (28)

The laboratory parameters of the study population were analyzed, and demonstrated the following features, as shown in table 2. The mean hemoglobin of the patient was around 12.43 ± 2.32 g/dL. As per WHO guidelines [anemia in men defined as serum hemoglobin <13g/dL in male and <12g/dL in female] about 40% of our population were anemic. About half of the patients had insufficient level of Vitamin D and about 40% of patients had serum phosphorus and serum albumin level below the lower range.

Table 2: Laboratory parameters of the AECOPD patients regarding their Nutritional Status (N=154)

Parameters	Mean ± SD	Low value
Hemoglobin (g/dL)	12.43 ± 2.32	40%
Mean Cell Volume (fL)	84.4 ± 9.41	12%
Serum Protein (g/dL)	6.42 ± 1.74	28%
Serum Albumin (g/dL)	3.32 ± 0.34	41%
Serum Calcium (mg/dL)	8.98 ± 0.63	31%
Serum Phosphorus	3.02 ± 0.42	42%
Serum Vitamin D (pg/mL)	18.48 ± 8.22	49%

We used multiple validated scores to evaluate the nutritional status of the patients of AECOPD, which depicted that the patients are at a risk of malnutrition as shown below in table 3. This shows that the majority of patients are at risk of malnutrition according to NRS-2002 score. MUST and MNAS-F score qualifies about two-third and half of patients to have malnutrition respectively.

Table3: Nutritional Status Scores of the AECOPD patients. (N=154)

Parameters	%
Nutritional Risk Screening-2002	
▪ ≥ 3 (At Risk)	68%
▪ < 3 (Repeat Screening Weekly)	32%
Malnutrition Universal Screening Tool	
▪ 0 (Low)	18%
▪ 1 (Medium)	31%
▪ ≥ 2 (High)	51%
Mini Nutritional Assessment Short-Form	
▪ 0-7 (Malnourished)	54%
▪ 8-11 (At Risk)	30%
▪ 12-14 (Normal)	16%

DISCUSSIONS:

Nutritional assessment and management are an important part of management of stable as well as exacerbated COPD patients, despite this its detail evaluation is underestimated. As a simple, common and standard method, we generally use body mass index (BMI) for the assessment of the nutritional status but, the practical issue regarding the assessment is that we do not have a gold standard tool or method for it[14]. Despite of it, BMI does not perfectly reflect the nutritional status of the patient especially in COPD, due to various factors.[15] Many other anthropometric measure have been used to predict the malnutrition in COPD, but the role of individual measurement to predict malnutrition is also questionable.

Classically polycythemia has been determined as a describing component in COPD. But, in the last 2 decades there has been an increase in the finding of anemia in COPD. The effect of aging of COPD population, associated renal dysfunction and heart failure, ongoing low-grade inflammation, absolute or relative iron deficiency, use of long-term oxygen therapy and use of renin angiotensin aldosterone system (RASS) blocking drugs play an important role for the upsurge of anemia in COPD patients. Among them, the latter have a pronouncing effect, due to ameliorating the hypoxia related polycythemia and blocking the production of angiotensin-II, which is involved in regulation of erythropoiesis.[16] The mean hemoglobin at our setup was around 12.43 ± 2.32 g/dL, and anemia was seen in 39.6% (61) of the study population. This data was similar to seen in the contemporary study. A study done in Lucknow enrolling 150 COPD patients showed that anemia [defined according to WHO] was prevalent in 31.6% of the patients, which had significant relation with their dyspnea scale.[17] Study

done in Kashmir enrolling 200 COPD patients demonstrated that 18% of the patients had anemia, as they had defined anemia by hemoglobin level <13.5 gm/dl in male patients and <12 gm/dl in female patients. Similarly, anemia would occur frequently in COPD patients and is associated with increased morbidity in the form of increased number of exacerbations and hospital admissions.[18] Along with the data above still, presence of anemia despite being an accentuating factor in dyspnea, couldn't perfectly predict the nutritional status as their lies a gap between the prevalence of anemia in our study and that of the malnutrition as per the assessment score.

The mean MCV at our study was 84.4 ± 9.41 fL which was near to the data found with other studies. Similarly, anemia was present in 40% of patients but microcytic anemia was present only in 12 % of patients. This discrepancy as well as the higher range of the MCV was probably because of the poor nutritional status of these patients, leading to nutritional anemia. Anemia in COPD, is also a anemia of chronic disease and is normocytic normochromic pattern, most likely due to EPO resistance leading to elevated EPO levels in these patients[19]. Ziaei M et al could not demonstrate a significant relationship of MCV with the AECOPD and overall patient outcome, but the MCV in survivals of AEOCPD episodes with a mean of 88.81±6.47 fL was higher than that of non-survivals with a mean of 85.77±11.73 fL.[20] Thus evaluating the MCV in patient of COPD might reveal the concealed pattern of the micronutrient deficiency.

Mean serum calcium level in our study was 8.68 ± 0.63 mg/dL and about one-third patient were hypocalcemia. Krishna et al studied 60 COPD patients in Bangladesh and demonstrated that the serum level of Calcium in COPD patient (8.26 ± 0.95mg/d) was statistically lower than that of the adult healthy population (9.21 ± 1.06mg/dl).[21] T. O. Pertseva compared calcium level of COPD patients with that of healthy individuals and found that 13.63% of COPD patients had lower level of serum calcium.[22] These findings are biologically plausible in presence of systemic inflammation leading to impaired calcium metabolism and also could be in favor of the prevalence of osteoporosis in COPD patient. Further detail evaluation is needed, incorporating parathyroid status in the COPD patients, to exactly find the interplay.

Kundu et al had analyzed 60 AECOPD in mechanical ventilation in Eastern India, which had shown that about one-fourth of them had hypophosphatemia in the presentation. They demonstrated in ROC study that serum phosphate level before the first weaning trial, a cut-off value of ≥3.0 mg/dL was identified to have 86.4% sensitivity, 55.3% specificity, 52.8% positive predictive value, 87.5% negative predictive value, and 66.7% diagnostic accuracy in predicting weaning success.[23] Sayed et al enrolled 50 patients with AECOPD, among which 60% had hypophosphatemia (<2.5 mg/dl). They demonstrated the importance of phosphorus level in AECOPD patients in regard to the need for ventilation, the duration of ventilation, and increase in the rate of mortality.[24] Regarding our study about 40% were having hypophosphatemia, which was comparable with the above-mentioned studies. COPD patients have low phosphate levels in both muscles and the circulation[25]. Stroda et al showed lower serum phosphate levels in COPD patients, as well as level of iFGF23 (phosphate-fibroblast growth factor-23) and PTH (parathormone), the hormone with negative feedback on the serum phosphate level are also reduced in COPD patients. This hypothesizes that lowered serum phosphate could be the primary event resulting in the reduction of the above-mentioned phosphate-lowering hormones. Etiology of lower phosphate level in COPD could be multifactorial, along with nutritional component involved[26] .

Pant et al, had enrolled 77 COPD patients in tertiary care hospital from central Nepal, and found to have mean Vitamin D level of 15.16 ± 7.19 ng/ml, which was statistically different from that of the healthy subjects (33.99 ± 12.37 ng/ml). They also found that serum vitamin D level was decreasing gradient with increasing severity of COPD.[27] Kumar et al, had studied about 74 COPD patients from Madhya Pradesh, India and found to have mean vitamin D level of 27.86 ± 16.47 ng/mL. The level varied significantly between GOLD stages and dyspnea scale. Patients having previous year more than one exacerbation had lower levels than those patients having lower exacerbations.[28] COPD stands as a risk factor for vitamin D deficiency, thought probably due to malnutrition, kidney dysfunction, and high catabolism associated with steroid therapy along with insufficient outdoor activity, among which the former three holds quite true for our setup than the last one. Determining Vitamin D status is important because its lower deficiency is associated with decreased lung function, increased inflammation, and decreased immunity.[29] In our study about half of the population had a lower vitamin D level. But beside of it, more sensible part would be to determine the serum parathormone level as COPD patients having serum 25(OH)D <30 ng/mL and serum iPTH>50 pg/mL i.e., hypo-vitaminosis-D with secondary hyper-parathyroidism had a higher risk of moderate exacerbation than the patients with hypo-vitaminosis- D without secondary hyper-parathyroidism. [30]

A meta-analysis published in 2019, determined the pooled global prevalence of osteoporosis in COPD to be 38%. The etiology of it related to chronic smoking, low physical activity, ongoing systemic inflammation, use of glucocorticoid, low weight and sarcopenia, anemia and vitamin deficiency.[31] Thus, the role of malnutrition can be directly pronounced on the latter three causes. Thus, despite being the limitation of our study it would be prudent to recognize the underestimated osteoporosis in COPD.

Baldemir et al had studied about 400 admitted AECOPD patients and found that about 90% of the patients were at risk of malnutrition as per the NRS-2002 (NRS ≥ 3 risk group),

which wasn't similar to our study population (68%). This could be due to the difference in the patient profile between Turkey and Nepal. They demonstrated a statistically significant negative correlation between NRS-2002 and serum albumin level, but a statistically significant positive correlation was observed between NRS-2002 and serum CRP level and the CAR ration (serum CRP to serum albumin ration).[32] Evaluation of NRS-2002 is a simple and bedside screening test, that allows us to ascertain the nutritional status of patient in regard to the recent stress, use of it routinely could imply in better nutritional care of COPD patients.

Study done in Poland between 2019 to 2020, in a respiratory center analyzed 124 COPD patients aged above 60 years. The malnourished population varied from 18.5% for the MUST score to 27.4% for the MNA-SF score and 57.3% for the NRS-2002 score. This discrepancy between our study was because we analyzed all the exacerbated patients, who are probably on a verge of malnutrition.[33] Study done by Carina Rôlo Silvestre analyzing thirty patients of AECOPD, found that according to NRS-2002 score, half patients were at increased risk of malnutrition, but malnutrition was observed in only 36.7% of patients according to body mass index (BMI).[34]

In our study also only 29% of our population were underweight according to the BMI [South-Asian basis], but the other validated score demonstrated drastically different percentage of the patient to be malnourished. The NRS-2002 score which screens the patient who would probably be benefited from nutrition therapy, found about 68% of the patient to be at risk of malnutrition. Similarly, MUST and MNAS-F found 51% and 54% to be malnourished.

Our study showed that COPD patients presenting in exacerbation are malnourished. With the above literatures depicting malnutrition in COPD to be a risk factor for exacerbation and poor quality of life, the attenuation of the former is warranted. The cause of the malnutrition, up to a part due to poor nutritional intake but a clear picture needs to be framed in view of holistic management of COPD patients. Secondly, our study pointed out that BMI isn't a perfect indicator of malnutrition in COPD patients presenting as exacerbation as there lies a discrepancy on assessing the nutritional status, so a further detail workup is needed to evaluate the patients.

CONCLUSIONS:

Comparing our study population with the previously conducted studies, our patients with COPD who present with exacerbations are in a state of malnutrition as depicted by the nutritional scores. Similarly, depending upon only BMI to tag a patient as malnourished might be misleading in chronic diseases like COPD. The cause of malnutrition, which is pertinent to our setup, needs further detailed evaluation. Plausibly, the correction of it might have a beneficial effect on the overall progression of the disease, albeit the real clinical impact of it needs a study deemed to it.

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