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TO PREDICT THE ASSOCIATION OF BLOOD UREA NITROGEN TO CREATININE RATIO WITH SARCOPENIA IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

General Medicine

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ABSTRACT

Background: Chronic Obstructive Pulmonary Disease (COPD) is a major global health burden, often complicated by sarcopenia, a condition characterized by progressive muscle mass and strength loss. The blood urea nitrogen (BUN) to creatinine ratio, typically used to assess renal function, may serve as a marker for muscle wasting in COPD patients. This study investigates the association between the BUN/creatinine ratio and sarcopenia in COPD patients, alongside pulmonary function and inflammatory markers. **Methods:** A hospital-based, cross-sectional study was conducted at Sawai Man Singh Medical College, Jaipur, India, from March 2023 to April 2024. A total of 120 COPD patients (aged >40 years, diagnosed per GOLD guidelines) were assessed. Sarcopenia was evaluated using the SARC-CaLF score, with scores ≥11 indicating sarcopenia. BUN and creatinine levels, pulmonary function tests (FEV1, FVC, FEV1/FVC, PaO2, PaCO2, SpO2). Statistical analyses included Chi-square tests, t-tests, and ANOVA to explore associations. **Results:** Sarcopenia was present in 33.3% of participants, with higher prevalence in severe (30.0%) and very severe (47.5%) COPD cases (p=0.003). The BUN/creatinine ratio was significantly higher in sarcopenic patients (29.25 ± 14.91 vs. 23.77 ± 10.26, p=0.030), driven by elevated BUN levels (16.79 ± 4.11 mg/dL vs. 15.14 ± 4.22 mg/dL, p=0.044). Sarcopenic patients exhibited poorer pulmonary function (lower FEV1, FVC, FEV1/FVC, PaO2, SpO2; higher PaCO2, all p<0.05). No significant associations were found with sex or sociodemographic status. **Conclusion:** The BUN/creatinine ratio is significantly associated with sarcopenia in COPD patients, particularly in severe cases, and correlates with systemic inflammation and impaired pulmonary function.

KEYWORDS

COPD, Sarcopenia, BUN/creatinine Ratio, Pulmonary Function, Systemic Inflammation

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory disorder characterized by persistent airflow limitation and respiratory symptoms, affecting approximately 11.7% of the global population, with a prevalence of 4.2% in India.[1,2] In regions like Rajasthan, India, risk factors such as air pollution, biomass fuel use, and smoking exacerbate COPD prevalence and severity.[3-5] Sarcopenia, the age-related loss of skeletal muscle mass and strength, is a frequent comorbidity in COPD patients, worsening physical function, increasing fall risk, and elevating mortality rates.[6] The blood urea nitrogen (BUN) to creatinine ratio, traditionally a renal function marker, has emerged as a potential indicator of muscle mass and function, particularly relevant in assessing sarcopenia in COPD patients.[7-9]

The pathophysiology of sarcopenia in COPD is multifactorial, involving systemic inflammation, oxidative stress, hypoxia, and nutritional deficiencies.[10-14] Chronic inflammation, driven by pro-inflammatory cytokines like TNF-α and IL-6, promotes muscle catabolism and impairs regeneration. Oxidative stress, resulting from an imbalance between reactive oxygen species (ROS) and antioxidants, damages muscle tissue. Hypoxia, common in advanced COPD, restricts oxygen delivery to muscles, accelerating wasting. Nutritional deficiencies, particularly in protein and vitamin D, further contribute to sarcopenia.[12-14]

While the BUN to creatinine ratio is well-established in renal assessment, its association with muscle health in COPD remains underexplored.[15,16] Elevated BUN relative to creatinine may indicate muscle wasting, but the mechanisms are unclear, necessitating further investigation. Given the high prevalence of COPD and sarcopenia in regions like Rajasthan, this study addresses a critical gap by examining the BUN to creatinine ratio as a predictive marker for sarcopenia in COPD patients.

Aim

To investigate the association of the blood urea nitrogen to creatinine ratio with sarcopenia in patients with chronic obstructive pulmonary disease.

Objectives

1. Measure the BUN to creatinine ratio in COPD patients.
2. Correlate the BUN to creatinine ratio with sarcopenia presence and severity.
3. Evaluate pulmonary function tests (PFTs) in COPD patients.

MATERIALS AND METHODS

This hospital-based, cross sectional observational study was conducted at the Department of General Medicine, Sawai Man Singh (SMS) Medical College, Jaipur, Rajasthan, India.

Study Population-Patients from the inpatient (IPD) and outpatient (OPD) departments of General Medicine.

Study Period: March 2023 to April 2024.

Sample Size: A sample size of 120 patients was calculated based on a standard deviation of 27.28 for BUN/serum creatinine ratio in mild COPD patients, with 80% power, 95% confidence level, and 5% absolute error, using the formula: $N = Z^2 \times SD^2 / E^2$, where $Z = 1.96$, $SD = 27.28$, and $E = 5\%$.[17]

Sampling Method: Convenience sampling.

Inclusion Criteria

- Diagnosed with COPD per GOLD guidelines (FEV1/FVC < 0.7 post-bronchodilator).
- Age > 40 years, both sexes.
- Provided informed consent.

Exclusion Criteria

- Inability to complete pulmonary function tests.
- Presence of chronic renal disorders, acute kidney injury, malignancies, or severe neuromuscular/orthopedic conditions affecting frailty.

Data Collection

- Participants completed a pre-designed, pre-tested, semi-structured questionnaire covering sociodemographic details, clinical history, smoking status, alcohol consumption, and physical examination findings.
- Blood pressure was measured using a calibrated Omron device, averaging two readings after a 5-minute rest.
- A 5 ml blood sample was collected aseptically from the antecubital fossa for laboratory analysis.
- Baseline demographics (age, gender, etc.) and routine investigations (CBC, RFT, LFT, CXR PA view) were recorded.
- COPD diagnosis was confirmed via post-bronchodilator spirometry (400 mcg salbutamol) per GOLD guidelines.
- Sarcopenia was assessed using the SARC-CaLF score, comprising six components: strength, assistance in walking, rising from a chair, climbing stairs, falls, and calf circumference (CC). Scores of 0–10 indicate normal status, while 11–20 indicate sarcopenia.[18]

Study Tools

- **Questionnaire:** Included sociodemographic, clinical, and

lifestyle data.

- **Anthropometric Measurements:**
  - **Height:** Measured using a stadiometer to the nearest 0.01 m.
  - **Weight:** Measured using a standardized SECA electronic weighing machine.
  - **Waist Circumference:** Measured at the midpoint between the last palpable rib and the top of the hip bone.
  - **Calf Circumference:** Measured with a non-stretchable tape, with cutoffs of ≤33 cm (females) and ≤34 cm (males) indicating sarcopenia risk.
- **Digital Blood Pressure Apparatus:** Used to measure blood pressure after a 5-minute rest, averaging two readings.
- **Spirometry:** Conducted to assess pulmonary function (FEV1, FVC, FEV1/FVC).

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 25. Descriptive statistics summarized demographic and clinical characteristics.Independent samples t-tests or Mann-Whitney U tests compared BUN/creatinine ratios between sarcopenic and non-sarcopenic groups. ANOVA evaluated differences across sarcopenia severity levels. A p-value < 0.05 was considered significant.

RESULTS

Of the 120 participants, 78 (65.0%) were male, and 42 (35.0%) were female, indicating male predominance. The mean age was 58.88 years (SD = 12.37), with 40.0% aged >60 years, 31.7% aged 51–60, and 28.3% aged 40–50. Smoking was prevalent, with 108 (90.0%) participants being smokers. Sociodemographic status was predominantly middle (51.7%), followed by low (31.7%) and high (16.7%). Mean height was 1.64 m (SD = 0.09), body mass was 58.86 kg (SD = 12.50), and BMI was 22.14 kg/m² (SD = 5.31).

Sarcopenia Prevalence

Sarcopenia was present in 40 participants (33.3%), with 80 (66.7%) scoring 0–10 (normal) and 40 (33.3%) scoring 11–20 (sarcopenia) on the SARC-CaLF scale.

COPD Severity

COPD severity varied: 37.5% had very severe COPD, 28.3% severe, 19.2% moderate, and 15.0% mild.

Table 1: Distribution of BUN (mg), Creatinine, BUN/Cr According to Sarcopenia Status

Variables	Sarcopenia	Mean	Std. Deviation	P Value
BUN (mg/dl)	Present	16.785	4.1141	0.044
	Absent	15.135	4.2165	
Creatinine(mg/dl)	Present	0.675	0.1836	0.741
	Absent	0.686	0.1712	
BUNCr_ratio	Present	29.250	14.9136	0.03
	Absent	23.770	10.2632	

- **BUN:** Significantly higher in the sarcopenia group (16.79 ± 4.11 mg/dL) compared to the non-sarcopenia group (15.14 ± 4.22 mg/dL, p = 0.044).
- **Creatinine:** No significant difference between sarcopenia (0.68 ± 0.18 mg/dL) and non-sarcopenia groups (0.69 ± 0.17 mg/dL, p = 0.741).
- **BUN/Creatinine Ratio:** Significantly higher in the sarcopenia group (29.25 ± 14.91) compared to the non-sarcopenia group (23.77 ± 10.26, p = 0.030).

COPD Severity and Sarcopenia: Significant association (p = 0.003), with sarcopenia more prevalent in severe (30.0%) and very severe (47.5%) COPD groups.

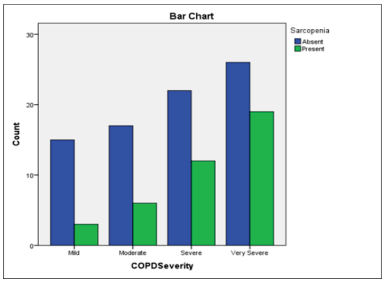

Figure 1: Distribution of COPD Severity Sarcopenia

Pulmonary Function Tests

- **FEV1:** Lower in the sarcopenia group (0.70 ± 0.41 ml) compared to the non-sarcopenia group (1.37 ± 0.37 ml, p = 0.002).
- **FVC:** Lower in the sarcopenia group (1.37 ± 0.82 ml) compared to the non-sarcopenia group (2.72 ± 0.66 ml, p < 0.001).
- **FEV1/FVC:** Lower in the sarcopenia group (45.72 ± 6.60) compared to the non-sarcopenia group (61.20 ± 8.57, p < 0.001).
- **PaO2:** Lower in the sarcopenia group (69.65 ± 7.71 mmHg) compared to the non-sarcopenia group (74.68 ± 8.17 mmHg, p = 0.021).
- **PaCO2:** Higher in the sarcopenia group (47.92 ± 8.69 mmHg) compared to the non-sarcopenia group (39.72 ± 7.36 mmHg, p = 0.043).
- **SpO2:** Lower in the sarcopenia group (93.3 ± 1.97%) compared to the non-sarcopenia group (97.6 ± 1.79%, p = 0.003).

DISCUSSION

This study investigated the association between the BUN to creatinine ratio and sarcopenia in 120 COPD patients, revealing significant findings. Sarcopenia was present in 33.3% of participants, consistent with Costa et al. (32.6%)[16] but higher than Jones et al. (21%)[20], possibly due to differences in age or COPD severity. The higher prevalence in severe (30.0%) and very severe (47.5%) COPD aligns with Spruit et al.[17] and Vestbo et al[19]., who noted increased sarcopenia risk with advanced COPD due to systemic inflammation and reduced physical activity.

The BUN/creatinine ratio was significantly higher in sarcopenic patients (29.25 ± 14.91) compared to non-sarcopenic patients (23.77 ± 10.26, p = 0.030), supporting Byun et al[18].'s findings that elevated BUN reflects muscle catabolism in COPD.[70] Higher BUN levels (16.79 ± 4.11 mg/dL vs. 15.14 ± 4.22 mg/dL, p = 0.044) in the sarcopenia group further corroborate this, aligning with Costa et al.'s association of elevated BUN/creatinine ratios with poor nutritional status and muscle wasting.[16] Creatinine levels showed no significant difference (p = 0.741), suggesting BUN's specific role in reflecting muscle breakdown.

Pulmonary function was significantly worse in sarcopenic patients, with lower FEV1 (0.70 ± 0.41 ml vs. 1.37 ± 0.37 ml, p = 0.002), FVC (1.37 ± 0.82 ml vs. 2.72 ± 0.66 ml, p < 0.001), FEV1/FVC (45.72 ± 6.60 vs. 61.20 ± 8.57, p < 0.001), and SpO2 (93.3 ± 1.97% vs. 97.6 ± 1.79%, p = 0.003), and higher PaCO2 (47.92 ± 8.69 mmHg vs. 39.72 ± 7.36 mmHg, p = 0.043). These findings align with Costa et al. and Jones et al[20]., indicating that impaired lung function exacerbates muscle wasting via reduced oxygen delivery.

The SARC-CaLF score effectively identified sarcopenia risk, with 33.3% of participants scoring 11–20, similar to Hirai et al[21]. and Amado et al[22]'s findings of high sarcopenia prevalence in COPD patients. In contrast, Chen et al[23].'s focus on acutely ill COPD patients linked elevated BUN to mortality rather than sarcopenia, highlighting contextual differences.[23]

SUMMARY AND CONCLUSION

The BUN/creatinine ratio was significantly higher in sarcopenic patients (p = 0.030), driven by elevated BUN levels (p = 0.044), suggesting muscle catabolism. No significant associations were found with sex or sociodemographic status, but older age and lower BMI were linked to sarcopenia risk. The BUN to creatinine ratio is a promising biomarker for identifying sarcopenia in COPD patients, particularly those with severe disease. Its association with muscle wasting, systemic inflammation, and impaired pulmonary function underscores its potential for early sarcopenia detection. Routine monitoring of this ratio could facilitate timely interventions, such as nutritional support and resistance training, to mitigate muscle loss and improve outcomes in COPD patients.

Recommendations

1. Implement integrated COPD management strategies, including resistance training, nutritional support, and patient education on muscle preservation.
2. Incorporate the BUN/creatinine ratio into routine clinical assessments for personalized sarcopenia management in COPD patients.

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