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RESEARCH ARTICLE
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DETERMINATION OF DISEASE SEVERITY AND INFLAMMATORY BIOMARKERS NAMELY C-REACTIVE PROTEIN TO ALBUMIN RATIO AND FIBRINOGEN TO ALBUMIN RATIO AMONG PATIENTS WITH COMMUNITY ACQUIRED PNEUMONIA AT A TERTIARY HEALTHCARE FACILITY IN ETAWAH DISTRICT: A CROSS SECTIONAL STUDY

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ABSTRACT

Background: To determine disease severity and inflammatory biomarkers namely C-Reactive Protein to Albumin ratio and Fibrinogen to Albumin ratio among patients with Community Acquired Pneumonia.

Material and Method: In this observational cross-sectional study the CURB-65 score was used to assess the severity of CAP at the time of admission, after which patients were divided into three groups based on their scores: the low-risk CAP group (scores 0-1), the moderate-risk CAP group (score 2), and the severe CAP group (scores 3-5), CAR and FAR scores were calculated and severity determined and compared with CURB 65.

Result: Total 152 patients were analyzed that nearly half (49.3%) were between 40 and 69 years old. The second-largest group was those aged 70 and above (21.7%), followed by patients aged 25-39 years (20.4%), and those under 25 years (8.6%). Males (66.4%) were more compared to females

(33.6%). CURB-65 severity scores showed 48% of patients had a severity score of 1, 37.5% had a score of 2, and 8.6% had severe pneumonia with scores of 3-5. Higher CAR values were observed in severe cases (mean 77.4±57.6) compared to non-severe low-risk (28.4±25.2) and non-severe moderate-risk (46.4±26.4) groups. Similarly, FAR was significantly higher in severe cases (mean 246.3±130.8) compared to non-severe groups (174.1±75.5 and 204.2±87.7, respectively). **Conclusion:** Elevated biomarkers such as C-reactive protein (CRP) ($p<0.001$), CRP to albumin ratio (CAR) ($p<0.001$), and Fibrinogen to albumin ratio (FAR) ($p=0.009$) were significantly associated with severe CAP, highlighting their potential as indicators for disease severity and prognosis.

Keywords: Disease Severity, Inflammatory Biomarkers, C-Reactive Protein (CRP), Fibrinogen Albumin Ratio (FAR), Community Acquired Pneumonia (CAP), C-Reactive Protein to albumin ratio (CAR)

INTRODUCTION

Community-acquired pneumonia (CAP) is a significant cause of morbidity and mortality worldwide, particularly affecting children, the elderly, and individuals with chronic health conditions. Defined as an infection of the pulmonary parenchyma occurring in individuals who have not been recently hospitalized and not had regular exposure to the healthcare system, CAP presents a major public health concern due to its high incidence and substantial burden on healthcare resources.

CAP is an acute infection of the lung parenchyma acquired outside of hospital settings or within 48 hours of hospital admission in a patient who has not been in a long-term care facility or hospital for 14 days before the onset of symptoms.[1]

Several prediction scores have been developed to classify the severity of CAP; with the most widely used being the CURB-65 and the pneumonia severity index (PSI).[2] Without timely and effective treatment, patients with CAP are at a higher risk of developing severe complications, which can significantly impact their quality of life and even pose a life-threatening danger. Thus, the ability to evaluate the severity of CAP and provide appropriate treatment is crucial in clinical practice.[3] The CAP severity index scoring system is commonly used to determine whether patients can be treated as outpatients or require inpatient care. Additionally, the CURB-65 scoring system is another important tool used to predict the severity of CAP.

The CURB-65 scoring system includes five clinical variables: Confusion, Urea levels ≥7 mmol/L, Respiratory rate ≥30 breaths per minute, low Blood pressure (diastolic ≤60 mm Hg or systolic <90 mm Hg), and age ≥65 years. The CURB-65 score ranges from 0 to 5, with higher scores indicating an increased risk of mortality. Specifically, a score of 0 or 1 corresponds to a low risk of mortality, suggesting that the patient can be managed in an outpatient setting. A score of 3 or higher indicates a need for hospital admission.[4]

Inflammatory markers such as the C-reactive protein to albumin ratio (CAR) and the fibrinogen to albumin ratio (FAR) have emerged as significant predictors in various medical conditions. CAR is a composite marker combining C-reactive protein (CRP), an acute-phase reactant, with albumin, a negative acute-phase reactant, reflecting the balance between inflammation and nutritional status. FAR, on the other hand, integrates fibrinogen, another acute-phase reactant involved in coagulation, with albumin.[5] While these biomarkers have been evaluated to have potential in the identification of disease severity in CAP, research on them is few and far between, especially in the Indian context.

AIM AND OBJECTIVES

Aim

To determine disease severity and inflammatory biomarkers namely C-Reactive Protein to Albumin ratio and Fibrinogen to Albumin ratio among patients with Community Acquired Pneumonia.

Objectives

1. To find out the severity of community acquired Pneumonia using Confusion, Uremia, Respiratory rate, Blood pressure and Age (CURB-65) score in study subjects.
2. To determine and compare the C-Reactive Protein to albumin ratio (CAR) and Fibrinogen to Albumin ratio (FAR) with various categories of severity of community acquired Pneumonia.

MATERIAL AND METHODS

Study type and design

An observational study with a cross-sectional design.

Inclusion criteria

The inclusion criteria for the study population were –

- All patients with an ICD-11 code 'community acquired pneumonia' as the admission diagnosis.[6]
- Patients presenting with clinically typical pneumonia with at least two clinical symptoms suggestive for respiratory tract infection (i.e. fever>38.0◦C, cough, dyspnoea, new or purulent sputum).
- Atypical cases were included when a newly manifest infiltrate is verified and no other cause sufficiently explaining the clinical condition of the patient detected.

Exclusion criteria

The exclusion criteria for the participants that were considered for the current study were as follows

- Cases with aspiration pneumonia, ARDS, pulmonary embolism or receiving chemotherapy or irradiation within 4 weeks before hospitalization.
- Patients hospitalized within the previous four weeks, lack of radiological confirmation of an infiltrate within the first 24 hours after admission or received palliative treatment modalities.
- Patients with CAP complicated by diagnosed malignant tumors, other chronic diseases, infection or inflammatory diseases and systemic autoimmune diseases.
- Patients with Tuberculosis, Exacerbation of COPD, Exacerbation of ACO, Viral Pneumonia, severe malnutrition
- Patient not giving consent to be the part of study.

Sample size and sampling technique

All patients presenting to UPUMS, Saifai, Etawah during January 2023 to June 2024 with a diagnosis of community acquired pneumonia were recruited if they provided written informed consent to take part in the study. A total of 152 patients were included.

Data collection methodology

A detailed history and physical examination were conducted for each subject enrolled in the study, who met the inclusion and exclusion criteria. Samples were collected from the outdoor and indoor wards as well as the respiratory ICU of the study institution. The examination included a thorough physical assessment, evaluation of vital parameters, and measurement of anthropometric data such as height, weight, and body mass index (BMI) using WHO classification. A systemic examination was performed to assess signs of community-acquired pneumonia (CAP).

The CURB-65[7,8] score, a crucial tool used to predict the severity of CAP, assigns different scores to patients based on disturbances in consciousness, blood urea nitrogen level, respiratory frequency, blood pressure, and age. The CURB-65 score was used to assess the severity of CAP at the time of admission, after which patients were divided into three groups based on their scores: the low-risk CAP group (scores 0-1), the moderate-risk CAP group (score 2), and the severe CAP group (scores 3-5).

The clinical evaluation and laboratory data for all patients included the following:

- Random blood sugar (RBS), Complete blood count (CBC), Liver function tests (LFT), Kidney

function tests (KFT), C-reactive protein (CRP), Albumin (ALB), Fibrinogen levels
- Sputum analysis for acid-fast bacilli (AFB) using the Cartridge Based Nucleic Acid Amplification Test (CBNAAT), Sputum Gram stain and bacterial culture and sensitivity, Sputum mycobacterial culture, Sputum fungal culture.

Statistical analysis

Data was analyzed using the statistical software Statistical Package for Social Sciences SPSS, IBM Inc., Chicago, USA, version 25. For analytical statistics, Chi-square test was used for categorical data and student's t-test was used for continuous data.

Ethical consideration

It was carried out with reference number 538/UPUMS/DSW/Ethical/2022-23 and ethical clearance number 89/2022-23 dated 22/12/22.

RESULTS

In the present study, a total of 39.5% patients had bilateral pneumonia followed by 37.5% patients having right sided pneumonia and 23% patients had left side pneumonia.

Figure 1: Distribution of patients according to their diagnosis (N=152)

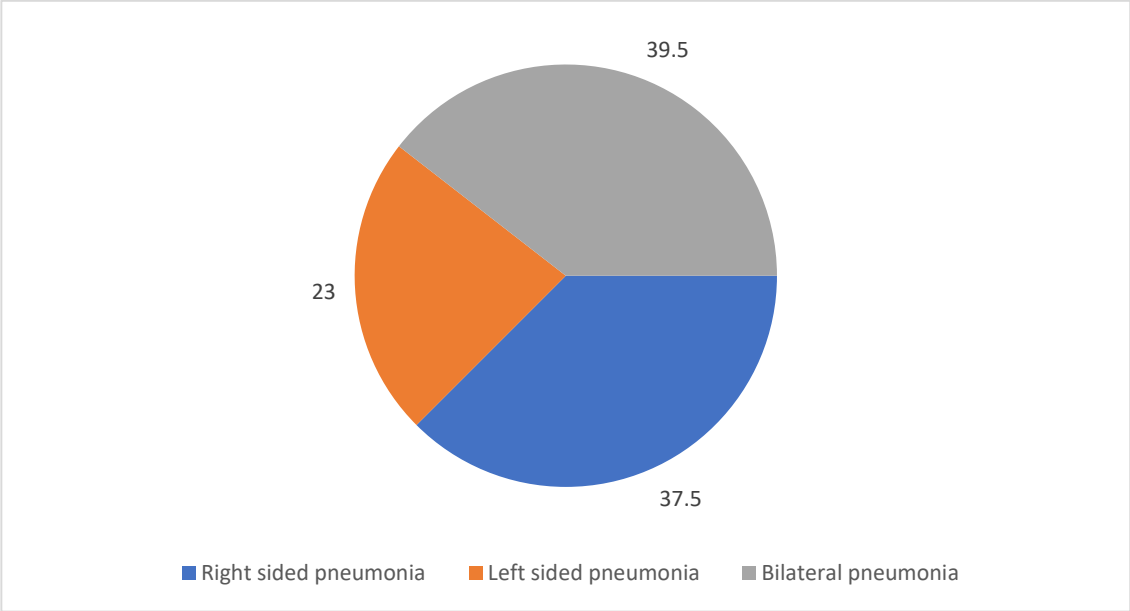

Table 1: Distribution of patients according to age groups (years) (N=152)

Age groups (years)	Frequency (n)	Percentage (%)
<25	13	8.6
25-39	31	20.4
40-69	75	49.3
70 and above	33	21.7
Total	152	100

Table 1 shows distribution of patients according to different age groups. Out of total 152 patients, 13(8.6%) had age <25 years, 31(20.4%) were between 25-39 years and majority of patients were between 40-69 years i.e. 75(49.3%). In elderly age group, a total of 33(21.7%) patients were 70 years or above age.

Table 2: Distribution of patients according to sex (N=152)

Sex	Frequency (n)	Percentage (%)
Female	51	33.6
Male	101	66.4
Total	152	100

Table 2 shows that maximum patients of patients were male i.e. 101(66.4% followed by 51(33.6%) were female.

Table 3: Distribution of patients according to CURB-65 score domains (N=152)

CURB-65 domain	Frequency (n)	Percentage (%)
Confusion	7	4.6
Uremia	140	92.1
Respiratory rate ≥30	11	7.2
SBP <90 / DBP ≤60	20	13.2
Age ≥65	5	33.6

Table 3 shows distribution of patients according to CURB-65 score domains. In the present study, confusion was observed in 7(4.6%) patients, uremia in 140(92.1%), respiratory rate ≥30 in 11(7.2%), SBP <90 / DBP ≤60 in 20(13.2%) patients and age ≥65 years in 5 (33.6%) patients.

Table 4: Distribution of patients according to CURB-65 score (N=152)

CURB-65	Frequency	Percentage
0	9	5.9
1	73	48
2	57	37.5
3	10	6.6
4	3	2

Table 4 depicts distribution of patients according to CURB-65 score. CURB-65 score 1 was observed in majority of patients i.e. 73(48%) followed 2 i.e. 57(37.5%) patients.

Table 5: Distribution of patients according to severity of pneumonia (N=152)

Severity of pneumonia	Frequency(n)	Percentage(%)
Severe	13	8.6
Non-severe moderate risk	57	37.5
Non-severe low risk	82	53.9
Total	152	100

Table 5 illustrates distribution of patients according to severity of pneumonia. A total of 82(53.9%) patients were non-severe low risk, 57(37.5%) patients had non-severe moderate risk and 13(8.6%) patients had severe risk of penumonia.

Table 6: Correlation between different markers and severity of pneumonia (N=152)

Markers	Non-severe low risk	Non-severe moderate risk	Severe	p-value#
CRP (mg/L)	83.2±63.9	127.9±61.4	187.2±130.7	<0.001*
Albumin (gm/dl)	3.2±0.6	2.9±0.6	2.7±0.7	0.002*
CAR	28.4±25.2	46.4±26.4	77.4±57.6	<0.001*
Fibrinogen (mg/L)	536.3±160.2	578.9±189.9	600.4±137.6	0.226
FAR	174.1±75.5	204.2±87.7	246.3±130.8	0.009*
LDH (U/L)	357.6±475.9	322.1±170.9	402±494.2	0.761
INR	1.2±0.2	1.2±0.3	1.2±0.3	0.958
D-Dimer (mcg/ml)	2.6±2.7	3.1±2.8	3.4±1.9	0.481

ANOVA test applied

*Statistically significant at 95% CI (p<0.05)

Table 6 shows correlation between different markers and severity of pneumonia. CRP (mg/L), albumin (gm/dl), CAR and FAR were found to be statistically significant.

DISCUSSION

The age distribution of patients with community-acquired pneumonia (CAP) revealed that nearly half of the patients (49.3%) were aged between 40 and 69 years, making this the most affected age group. This finding aligns with the study by Florin et al., who found that 45.7% of CAP cases were in individuals over 50 years of age.[9] The second most affected group, those aged 70 and above (21.7%). Uwaezuoke et al. highlighted that 35% of elderly patients had severe CAP, necessitating precise risk stratification.[10] Karakioulaki et al noted that only 10% of CAP cases occurred in individuals under 30 years, with a mean age of 55.3 years (SD 17.8).[11] Cho et al. found that 42.9% of their CAP patients required intubation, and the mean age was 60 years (SD 17), while Zheng et al. reported elevated serum S100A8 levels correlated with higher severity scores in older patients.[12,13]

The sex distribution of patients with community-acquired pneumonia (CAP) revealed a higher prevalence in males (66.4%) compared to females (33.6%), suggesting a potential gender-related susceptibility or exposure risk. This aligns with findings from Patel et al., who reported that men are more frequently affected by CAP.[14] In their study, 68% of CAP cases were male, with a significant correlation between male gender and severe CAP.

The CURB-65 score domains showed that 92.1% of patients had uremia, indicating significant renal involvement. Putot et al. found elevated urea levels in 89% of severe CAP cases.[15] Low blood pressure (SBP <90 or DBP ≤60) was observed in 13.2% of patients, suggesting hypotension, a marker of severe disease noted by Maleziux-Picard et al., who reported hypotension in 15% of elderly CAP patients.[16] Elevated respiratory rates (>30 breaths per minute) were present in 7.2% of patients, indicating respiratory distress. Sun et al. observed similar rates of tachypnea, with 8% of their CAP cohort presenting with respiratory rates above 30 breaths per minute.[17] Confusion was observed in 4.6% of patients, reflecting severe systemic involvement. Zheng et al. correlated confusion with increased mortality risk, finding it in 5% of their CAP patients.[13]

The distribution of CURB-65 scores among patients with community-acquired pneumonia (CAP) revealed that 48% of patients scored 1, indicating a mild level of severity. This finding is consistent with Bardacki et al., who observed that a significant proportion of CAP patients presented with mild symptoms and lower CURB-65 scores, which correlated with lower mortality rates.[18] Similarly, 37.5% of patients scored 2 on the CURB-65 scale, placing them in the moderate risk category. This aligns with the findings of Sun et al., who reported that patients with moderate CURB-65 scores required closer monitoring due to the increased risk of complications.[17] Additionally, 6.6% of patients scored 3, and 2% scored 4, indicating severe pneumonia. This is consistent with the study by Zheng et al., who noted that higher CURB-65 scores were associated with severe disease and higher

mortality rates, with 7% of their cohort having scores of 3 or above.[13] Only 5.9% of patients scored 0, suggesting a very low risk, as also observed by Li et al., who reported similar low-risk findings in their study.[19] Regarding the severity of pneumonia, 53.9% of patients were classified as non-severe low risk, which is in line with the findings of Maleziux-Picard et al., who reported that the majority of CAP patients fell into the low-risk category, with favorable outcomes.[16] Non-severe moderate risk was observed in 37.5% of patients, emphasizing the need for vigilant monitoring and appropriate treatment, as highlighted by Putot et al., who stressed that patients in this category still require careful management to prevent progression to severe pneumonia.[15]

The correlation analysis of various markers with the severity of community-acquired pneumonia (CAP) revealed significant differences across the severity spectrum. C-reactive protein (CRP) levels were markedly higher in patients with severe pneumonia (187.2±130.7 mg/L) compared to those with non-severe low risk (83.2±63.9 mg/L) and non-severe moderate risk (127.9±61.3 mg/L) pneumonia ($p<0.001$). This finding aligns with the study by Florin et al., who noted that elevated CRP levels are strongly associated with increased disease severity and worse clinical outcomes in CAP patients.[9] Albumin levels were significantly lower in severe pneumonia cases (2.7±0.7 g/dL) compared to non-severe groups (3.2±0.6 g/dL and 2.9±0.6 g/dL, respectively) ($p=0.002$). Dhawan et al. also reported that hypoalbuminemia is a common finding in severe CAP, correlating with higher morbidity and mortality rates. [20]

The CRP to albumin ratio (CAR) was significantly highest in severe pneumonia cases, with a mean value of 77.4 (±57.6), compared to non-severe low-risk cases (28.4 ± 25.2) and non-severe moderate-risk cases (46.4 ± 26.4) ($p<0.001$). This elevation in CAR aligns with Bardacki et al., who reported that patients with higher CAR values were more likely to experience severe disease, with severe cases having a mean CAR of 75.3 (±54.2).[18] Zheng et al. found that high CRP levels (mean 180.3 mg/L in severe cases) and low albumin levels (mean 2.6 g/dL) independently contributed to worse clinical outcomes, corroborating the current study's findings.[13] Maleziux-Picard et al. noted that in elderly patients, a high CAR (mean 80.1 ± 60.5) significantly predicted mortality, with severe cases showing a mortality rate of 40%.[16] Putot et al. also highlighted that CAR is a significant predictor of adverse outcomes, with values above 70 associated with increased ICU admissions and longer hospital stays.[15] Patel et al., also demonstrated similar trends in their study.[14] Luo et al. also found that CAR was significantly associated with increased severity of CAP.[21]

Fibrinogen levels, although elevated in severe pneumonia (600.4±137.6 mg/dL), did not show a statistically significant difference ($p=0.226$). However, the fibrinogen to albumin ratio (FAR) was significantly higher in severe cases (246.3±130.8) compared to non-severe groups (174.1±75.5 and 204.2±87.7, respectively) ($p=0.009$), consistent with findings by Bardacki et al., who noted that higher FAR values are indicative of severe systemic inflammation and poorer outcomes in CAP patients.[18] Similarly, Zheng et al. noted that higher fibrinogen levels combined with lower albumin levels significantly correlated with increased disease severity, with severe cases showing a mean FAR of 250 (±130).[13] Maleziux-Picard et al. emphasized that in elderly patients, a high FAR was predictive of higher mortality rates, with their study showing severe cases had a FAR of 245 (±135), indicating the importance of this ratio in older populations who are more vulnerable to severe CAP outcomes.[16] Putot et al. also supported these findings, demonstrating that FAR values above 230 were linked to increased ICU admissions and longer hospital stays, underscoring the ratio's predictive value for severe CAP.[15] FAR values being significantly associated with the severity of pneumonia has also been reported by Luo et al. in their study.[21]

SUMMARY AND CONCLUSIONS

The study focused on evaluating the severity of community-acquired pneumonia (CAP) using the CURB-65 score and correlating it with various biomarkers to improve diagnosis and treatment strategies. The study was conducted over 18 months at the Department of Respiratory Medicine, UPUMS Saifai, Etawah, involving 152 patients diagnosed with CAP. The findings of the study

concluded that the CURB-65 score is a valuable tool for assessing the severity of community-acquired pneumonia (CAP). The distribution of CURB-65 severity scores showed 48% of patients had a severity score of 1, 37.5% had a score of 2, and 8.6% had severe pneumonia with scores of 3-5. The high prevalence of severe CAP among older adults, particularly those aged 40-69 years and above 70 years, underscores the need for targeted interventions in these age groups. 33.6% were aged over 65 years. Elevated biomarkers such as C-reactive protein (CRP) ($p<0.001$), CRP to albumin ratio (CAR) ($p<0.001$), and Fibrinogen to albumin ratio (FAR) ($p=0.009$) were significantly associated with severe CAP, highlighting their potential as indicators for disease severity and prognosis. Higher CAR values were observed in severe cases (mean 77.4±57.6) compared to non-severe low-risk (28.4±25.2) and non-severe moderate-risk (46.4±26.4) groups. Similarly, FAR was significantly higher in severe cases (mean 246.3±130.8) compared to non-severe groups (174.1±75.5 and 204.2±87.7, respectively).
Overall, the integration of CURB-65 scores with biomarker assessments provides a comprehensive framework for assessing severity of CAP, ensuring timely and appropriate treatment to improve patient outcomes and reduce healthcare burden.

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