Original Article

Association between Serum CRP Level and CURB-65 Score in Community Acquired Pneumonia Patients

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Abstract: Community acquired pneumonia (CAP) is major cause of morbidity and mortality in adults. The presentation may be varied, in addition, there are some non-infectious respiratory diseases in the differential diagnosis of CAP, such as malignant diseases, interstitial lung diseases, pulmonary edema, and pulmonary hemorrhage. We usually diagnose patients having CAP by comprehensive evaluation of symptoms, vital signs, laboratory examinations, and radiographic examinations. Several severity scores have been proposed to predict patient outcome and to guide initial management of patients with community acquired pneumonia (CAP). Most have been derived as predictors of mortality and CURB-65 (confusion, blood urea nitrogen, respiratory rate, blood pressure and age 65) is commonly used score. To assess the association between serum CRP level and CURB-65 score among patients with community acquired pneumonia cross sectional study was done. A total of 101 consecutive adult patients of either sex admitted in Bir Hospital with the diagnosis of CAP were enrolled. CURB-65 score and serum CRP level were calculated. Data analysis was done using SPSS. A p value <0.05 was considered statistically significant. A total of 101 participants (58 male and 47 females) with maximum age of 92 years and minimum age of 23 years were enrolled. Maximum number of patients were of 61-70 years of age group. Maximum number of patients presented with cough, fever, shortness of breath, pleuritic chest pain, sputum production. Patients enrolled in this study, maximum was of CURB-65 one i.e. 47 and least of CURB-65 five i.e. 5. According to CURB-65 score 1,2,3,4,5 mean Serum CRP level was 27.95, 56.36, 71.79, 77.57, 86.18 respectively. There was a statistically significant association between CURB-65 criteria and serum CRP levels (P=0.000345) which means that the concentration of this inflammatory biomarker increased with an increase in the score of CURB-65 criteria. Mortality in this study was 5.45%. According to the results, the serum level of CRP is a strong prognostic factor for evaluating severity of CAP and suitable factor for the CURB-65 criteria in decision making of whether a patient with CAP in the ICU should be admitted.

Keywords: CAP, CURB-65, Serum CRP

1. INTRODUCTION

Pneumonia is a form of acute respiratory infection that is most commonly caused by viruses or bacteria [1]. Pneumonia is classified as community-acquired pneumonia (CAP), hospital-acquired pneumonia, and ventilator-associated pneumonia [2]. Community-acquired pneumonia (CAP) is defined as an acute infection of the pulmonary parenchyma in a patient who has acquired the infection in the community, as distinguished from hospital-acquired (nosocomial) pneumonia [3]. It was demonstrated that for initial assessment, Qsofa (quick sequential organ failure assessment) outperformed SIRS (systemic

inflammatory response syndrome) and presented better clinical usefulness in patients with CAP in the ED (Emergency Department) [4]. Moreover, CRB (confusion, respiratory rate and blood pressure) and CRB-65 had better predictive performance than qSOFA for initial stratification of patients with CAP in some scenarios [5]. For the comprehensive assessment of CAP, PSI (pneumonia severity index) had the best predictive performance and NB for mortality, whereas SOFA seemed more suitable when considering ICU admission [6]. The parameters such as Confusion (based upon a specific mental test or new disorientation to person, place, or time) Urea (blood urea nitrogen in the United States) >7 mmol/L (20 mg/dL) Respiratory rate ≥30 breaths/minute Blood pressure (BP; systolic <90 mmHg or diastolic ≤60 mmHg) Age ≥65 years (CURB-65) were used as criteria to measure the severity of pneumonia [7]. In clinical practice, one of the indicators of hospital admission whether at indoor or ICU is CURB-65 score. It is suggested that patients with a CURB-65 score of 0 to 1 could probably be treated as outpatients, those with a score of 2 should be admitted to the hospital, and those with a score of 3 or more should be assessed for ICU care, particularly if the score was 4 or 5 Many reviews and studies have been carried out to investigate the risk of mortality due to pneumonia based on these criteria. In a large independent study of 3181 patients with CAP, mortality was 3 percent among 901 patients with a CURB-65 score of 1[8]. According to these criteria, clinician can make decision to treat the patients in outpatient, hospitalization, or intensive care unit (ICU) admission [9]. An increase in the concentration of serum proteins that are referred to as acute phase reactants (APR) accompanies inflammation and tissue injury [10]. Awareness of this phenomenon, termed the acute phase response, first occurred with the discovery of C-reactive protein (CRP) in the serum of patients during the acute phase of pneumococcal pneumonia [11]. CRP is a 118-kDa pentameric protein synthesized in hepatic cells through induction by interleukin-6 (IL-6), IL-1β, and tumor necrosis factor-α (TNF-α) whenever infection or tissue inflammation occurs [12]. In healthy adults, the normal CRP concentration is usually less than 5 mg/L [13]. CRP is inflammatory marker that can be used for the diagnosis of pneumonia, and serum level >40 mg/L in bacterial pneumonia has 70% sensitivity and 90% specificity [14]. The secretion of CRP starts within 4–6 hours, and its level doubles every 8 hours; it then reaches its maximum level within 36–50 hours. After the stimulation is removed, the CRP level falls relatively quickly, with a half-life of 19 hours [15]. In other study, 73% sensitivity and 65% specificity have been reported for CRP, in this regard [16]. Flanders et al. reported that a bedside CRP test was useful for predicting CAP in adults with acute cough [17]. Pneumonia is one of the major causes of death and morbidity with an incidence of 20% to 30% in developing countries and 3% to 4% in developed countries [18]. It is projected that Nepal, India, Bangladesh accounts for 40% of global acute respiratory infections [19]. Bir Hospital is one of the largest tertiary healthcare centres of Nepal, whose unpublished hospital record showed overwhelming burden of pneumonia among adults. Data from FY 2074/75 showed out of 11600 inpatients, 256(2.20%) were among pneumonia patients with mortality of 28(10.9%). In FY2075/76 showed out of 12605 inpatients, 208(1.65%) were among pneumonia patients with mortality of 27(12.9%). In FY 2076/77 showed out of 10560 inpatients, 163(1.54%) were pneumonia patients with mortality of 12(7.36%) [20]. Community acquired pneumonia is a common respiratory problem in Nepal. The mortality rate within this CURB-65 risk group is like that observed for pneumonia severity index (PSI)class III patients; although some of these patients can be safely managed as outpatients, others may warrant brief emergency department or hospital observation or brief inpatient hospitalization. We generally favor hospital admission for patients with a CURB-65 score of 1, although patients with a score of 1 due to being ≥65 years of age who do not have major co-morbidities may not require admission. A number of substances can serve as markers of severe inflammation. The two most commonly in use are C-reactive protein (CRP) and procalcitonin (PCT). Levels of these acute-phase reactants increase in the presence of an inflammatory response [21]. The aim of the study is to assess the association between serum CRP level and CURB-65 score among patients with community acquired pneumonia. To establish the association between serum CRP Level and pneumonia severity (CURB-65 Score) among patients

admitted with diagnosis of pneumonia at IPD and ICU of Bir hospital. To see the age and sex distribution of CAP patients. To see radiological predominance in different zones of right and left lungs. To describe the clinical presentations with respect to patients with community acquired pneumonia. To see prevalence of CAP in different co-morbid conditions. To see mortality and morbidity among severe community acquired patients.

2. MATERIALS & METHOD

The study is a cross-sectional study. The study was conducted in medicine IPD and ICU, admitted cases in Bir Hospital, Kathmandu. The study population was patients admitted with diagnosis of pneumonia in medical ward and medicine ICU in Bir Hospital. The duration study was 1 year. The sample size will be calculated using a single proportional formula taking 60% prevalence rate of the pneumonia with an α level of significance at 5%. The following formula with 95% significance level (Zα/2 = 1.96) at 10% margin error will be used.

$$n=z^2pq/d^2$$

$= (1.96)^2 \times 0.6\ (1-0.6)/\ (0.1)^2$

n=sample size

z=1.96 for 95% confidence intervals prevalence of pneumonia i.e. 60%

q=1-p

d=margin of error taking 10%

The calculated sample size is 92. After adjusting 10% non-response rate, final sample size will be 101.

After enrolment, detailed history and elaborate clinical examination (general and systemic) was done in each case and confusion, respiratory rate and blood pressure were noted. All necessary investigations required for CAP in each case which are already sent by respective consultant was filled up in predesigned proforma such as blood urea and serum CRP Level. All patients were investigated and treated according to guidelines followed by consultants of Bir Hospital. The baseline characteristics like age, sex, registration number, serum urea, serum CRP were noted. Reagents 1 R1 (Tris buffer, alpha ketoglutarate, urease of Jack Bean and GLDH of microorganism) and R2 (NADH and non-reactive filters and stabilizers) which is liquid ready to use was used. This is manufactured by Erba Mannheim XL Sy Spack Co. Ltd. CRP was estimated by the Turbodyne SC (Turbidimetry and nephelometry) machine produced by Tulip group. Before data collection, ethical approval was taken from Institutional Review Board of National Academy of Medical Science (NAMS). After approval from the IRB, NAMS, the data were collected having written consent from the selected respondents. Confidentiality was maintained to the upmost. The participants paid the cost of investigations as long as they are part of their routine investigations that would be ordered whether or not they would be enrolled for the study. For those investigations which are to be ordered solely for the purpose of this study, the cost was borne by the investigator. The data was entered into Excel spreadsheet. Coding of data was done and errors checked. Clean data was transferred to Statistical package for social science (SPSS) software for further statistical analyses. Data was presented on frequency, percentage and table. The ANOVA test was used for continuous variables. The P-value<0.05 was considered statistically significant.

3. RESULTS & DISCUSSION

Table 01: Sex distribution of the patients.

Sex	
Male	58
Female	47

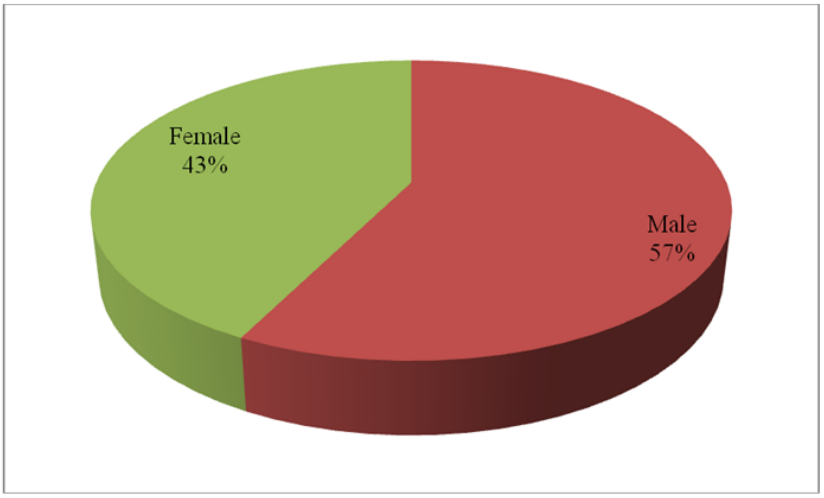

Figure 01: Pie chart showing Gender distribution of CAP patients

Most of the patients enrolled in the study were male, 57% and female were 43%

Table 02: Clinical Presentations

Clinical Presentation	
Fever	88
Dyspnea	83
Cough	91
Chest pain	59
Confusion	16

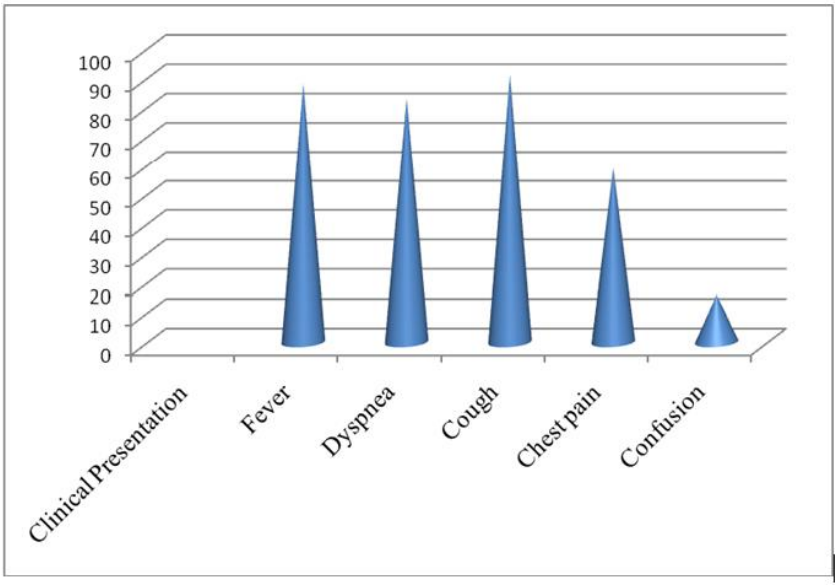

Figure 02: Bar diagram showing clinical presentations of CAP Patients

Most common presentation is cough followed by fever, dyspnea, chest pain and confusion.

Table 03: Variant of cough

Cough variant	
Dry	8
Mucoid	35
Mucopurulent	55

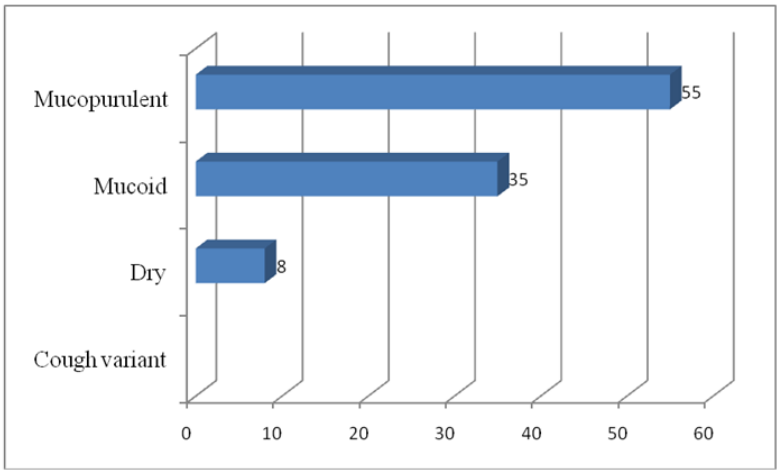

Figure 03: Bar diagram showing Variant of cough

Cough is the most common clinical presentation in CAP Patients and among them mucopurulent is most common followed by mucoid and dry.

Table 04: Patients with tachypnea and normal respiratory rate.

Respiratory rate	
>30	77
<30	24

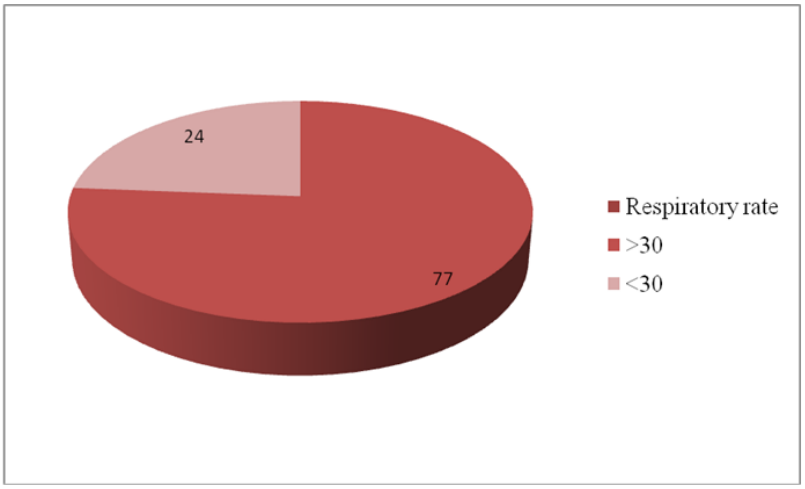

Figure 04: Pie chart showing respiratory rate

Most patients in the study presented with fast respiratory rate

Table 05: Patients on the basis of age group

Age	
18-30	11
31-40	4
41-50	9
51-60	16
61-70	25
71-80	22
80+	14

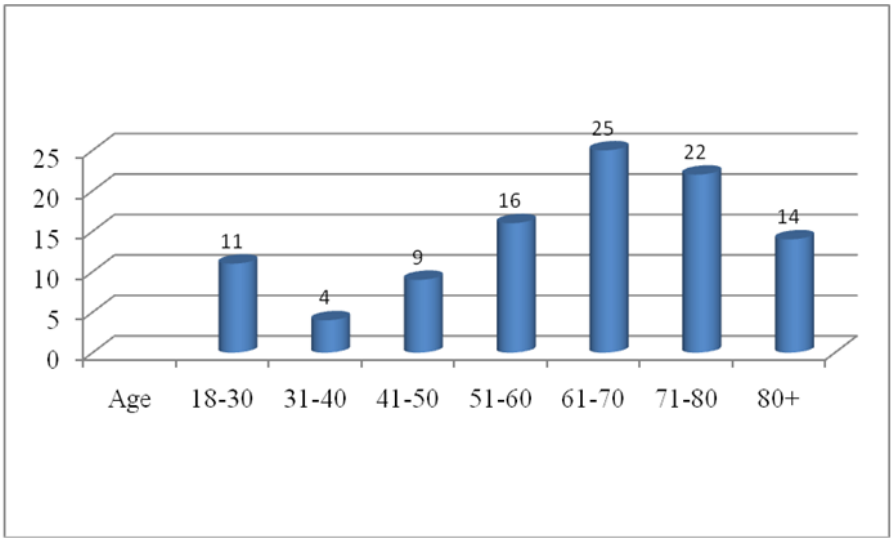

Figure 05: Bar diagram showing age distribution of the patients.

Maximum number of patients are of age group (61-70) followed by (71-80), (51-60) and 80+ so more common in advanced age.

Table 06: Blood pressure at presentation

Blood pressure	
<90/60	9
>90/60	92

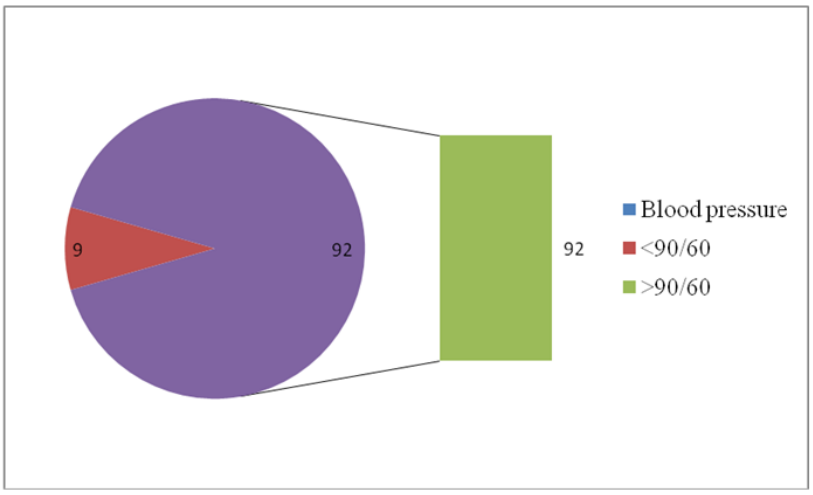

Figure 06: Pie chart showing blood pressure at presentation

Most of the patients presented with normal blood pressure.

Table 07: Different Zones of lung involvement on Chest X-ray

Chest X-ray	
RUZ (right upper zone)	7
RMZ (right middle zone)	10
RLZ (right lower zone)	21
LUZ (left upper zone)	3
LLZ (left lower zone)	11
Bilateral	42

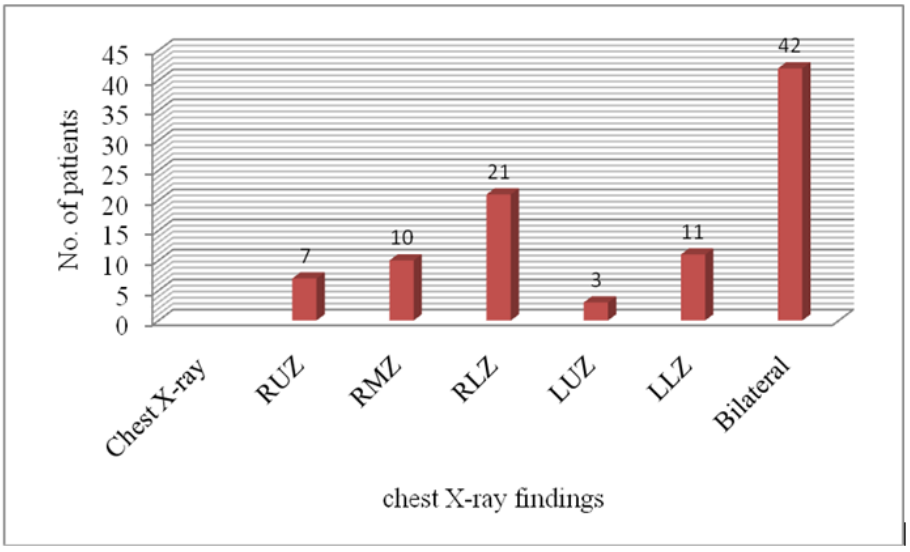

Figure 07: Bar diagram showing involvement of different zones on Chest X-ray

Most of the patients presented with bilateral lung involvement followed by RLZ, LLZ, RMZ, RUZ, LUZ.

Table 08: Different comorbid conditions present in CAP Patients

Comorbid conditions	
COPD	37
DM	8
Hypertension	12
Bronchial Asthma	2
CKD	7
No comorbities	35

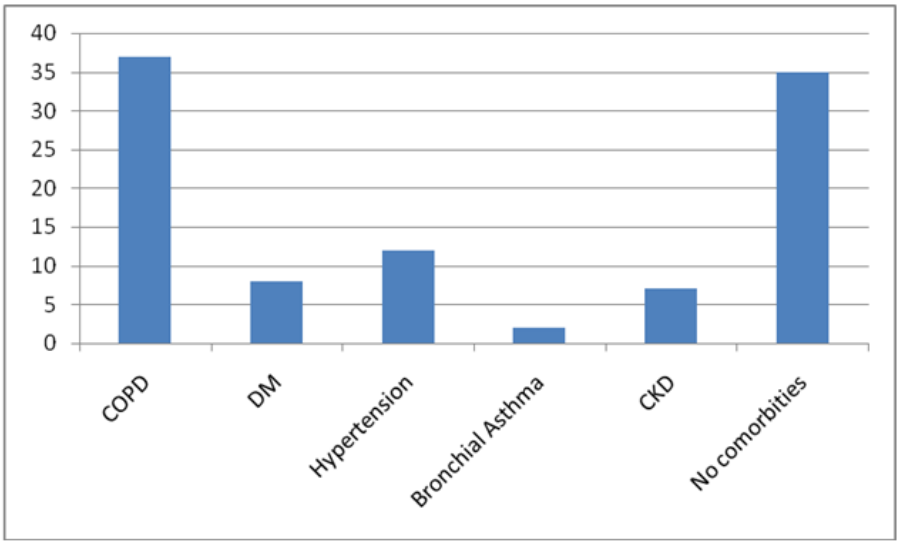

Figure 08: Bar diagram showing different comorbid conditions in CAP

This shows highest prevalence of CAP is among COPD, followed by hypertension, DM, CKD and bronchial asthma.

Table 09: Mortalities among studied patients

Mortalities	
Total no.	6
Total cases	101

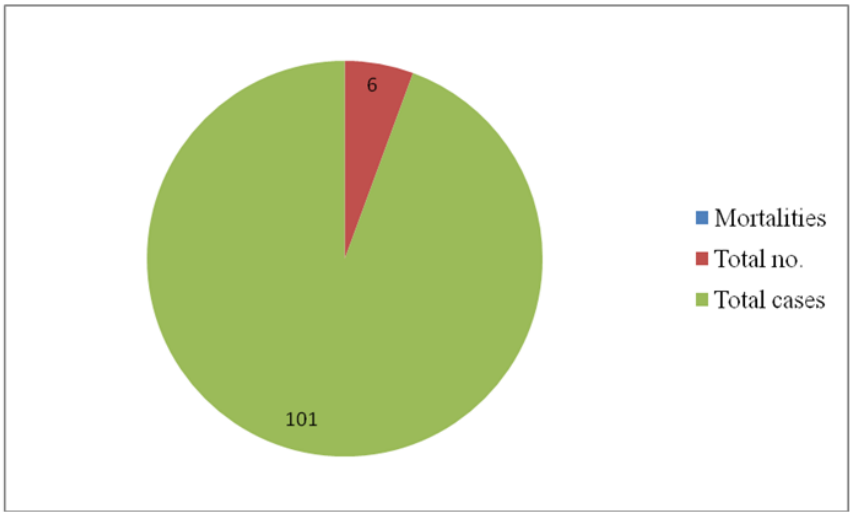

Figure 09: Pie chart showing mortalities among study population

Among studied population 5.96% mortalities were found.

Table 10: CURB-65 Score and number of patients

CURB-65 Score	No. of patients
1	47
2	21
3	21
4	8
5	4

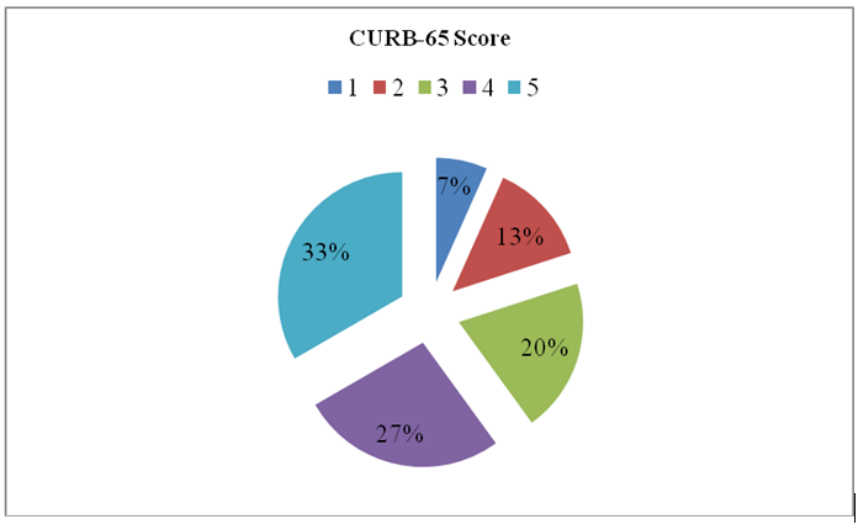

Figure 10: Pie chart showing distribution of patient on CURB-65 Score

In this study maximum no. of patients with CURB-65 Score of 1, followed by 2, 3, 4 and least no. of 5.

Table 11: Relationship between CURB-65 and Mean CRP level

CURB-65	Mean CRP	
1	27.95	
2	56.36	P=0.000345
3	71.79	
4	77.57	
5	86.18	

A statistically significant relationship was observed between the mean CRP in 101 patients who were hospitalized (63.97+/-5.23 mg/dl) (p=0.000345).

DISCUSSION

CAP is the leading cause of infectious disease-related deaths in the United States, and the second most common cause of hospitalizations [22]. It can affect patients of all ages and across all spectrums of health, with most of the hospitalizations occurring in older patients [23]. A cross-sectional study was carried out with the aims of finding association of CURB-65 score with serum CRP level among the patients admitted in the tertiary level Hospital (National Academy of Medical Science, Bir Hospital). The data were collected, analyzed and presented systematically with the help of tables. The main findings of the study are as follows. In this study, 101 patients with acute CAP and mean age of 61.6+/-18.53 years were enrolled, and the majority of them (57.42%) were male. Similar study conducted with male to female ratio was 1.1:1[24]. In a similar study in which mean age of presentation was71.49+/-15.21 years with73.11% male [25]. Maximum number of patients were of 61-70 age groups. The results yielded showed a greater number of hospital admissions in elderly males aged more than 65 years which is similar to the other studies conducted [26]. In this stage, the elderly population is known to have chronic and weakening conditions and the tendency towards males is high. This fact is reported to be a major risk factor for CAP [27]. In our study, the most common clinical symptoms in patients were cough, fever, dyspnea and chest pain. Similar study done by Shrestha R et. al showed the commonest mode of presentation was cough followed by fever. A study [28,29] showed that maximum number of patients presented with cough (99%), fever (95%), sputum production (65%). Moreover, the most common chest X-ray findings in the patients were interstitial infiltration involving both lungs followed by right lower zone and left lower zone. A similar study which showed lobar involvement is more common with right lower zone commonest followed by left lower zone [30]. Research [31] which showed that lobar pneumonia was seen in 99% of cases with the right lower zone being the most commonly involved zone on chest X-ray. In this study, 65.34% had co-morbidities associated with CAP. Research [32] had 63.4% co-morbidities associated with CAP which is similar to our study. The most common co-morbidity was COPD which is identical in this study as well. COPD was followed by hypertension, diabetes mellitus, CKD and bronchial asthma. A study [33]CAP showed that 70-78% had the co-existing co-morbidities. Irfan et.al showed that co-morbid illnesses were present in 63.5%with community acquired pneumonia in developing country [34]. The correlation between co-morbidity and the outcome was not significant. Assessment of severity and site of care decisions for community acquired pneumonia patients (CAP) are very important for patient's safety and optimal use of resources. Late admission to the intensive care unit leads to increase the rate of mortality in CAP [35]. A study [36] has analyzed different severity scores for CAP like PSI, CURB-65 and modified BTS) and its strength and weaknesses that provided comparable information with regard to identifying high risk patients for whom more aggressive management strategy is required. A simple severity assessment tool, the CURB-65 score, accurately classifies patients with CAP into different management groups:

patients with CURB-65 scores of 0 who are at very low risk of mortality (0%) and who, thus, may be suitable for home treatment; patients with scores of 1 who are at a relatively low risk of mortality (1.1%) and who also may be suitable for home treatment, but who need additional criteria for admission decision; patients with scores of 2 who are at intermediate risk of mortality (7.6%) and who should be considered for short-stay inpatient treatment; and patients with scores >2 who are at high risk of mortality (26.7%) and who should be managed as having severe pneumonia[37]. For evaluation of pneumonia severity, CURB-65 criteria and biomarkers including serum levels of CRP were used, which in this study, the frequencies of ranking 1,2,3,4 and 5 of CURB-65 criteria were 46.53%, 20.79%, 20.79%, 7.92%, 3.96% respectively and the rank of 1 had the highest frequency. In [38] study these frequencies were 26%, 25.6%, 9.05% and 0.9% respectively while 19% was of CURB-65 criteria of 1, which were similar to this study. In a study [39] frequency of ranks 0 and 1 of CURB-65 criteria were 31%in total, the rank 2 was 30% in total; and ranks of 3 and more were 39% in total; which is different from this study. It indicates that the patients of the present study were assessed faster for treatment before exacerbation of the disease. A study [40] discussed many other markers of CAP like procalcitonin, soluble triggering receptor expressed on myeloid cells-1, pro-adrenomedullin, and presepsin but in this study CRP only has been done and other tests are difficult to perform due to unavailability of lab facilities and cost also. In the present study, there was statistically significant relationship between the mean serum level of CRP and the CURB-65 criteria ranking in patients with acute CAP. Serum CRP level is a useful marker for establishing the diagnosis of CAP in adult patients with lower respiratory tract infections [41]. High CRP values are especially high in patients with pneumonias caused by S pneumonia or L pneumophila [42]. An author [43] has reported that there was statistically significant relationship between CURB-65 criteria and serum CRP. In a study [44] serum levels of CRP in 62 patients with pneumonia and 96 patients with asthma and 161 patients with COPD were compared and reviewed. They reported that CRP serum levels in the patients with CAP were higher than other two groups and strong correlation with serum CRP was observed. Also, they reported sensitivity of 91% and specificity of 93% for CRP levels greater than 48mg/dl for the diagnosis of pneumonia. In this study, mortality with CAP was 5.94%. The multivariate analysis showed that the presence of altered mental status and low blood pressure at presentation remained the significant risk factor for death. A study [45] showed that mortality of 9.2% with CAP patients admitted at hospital. Similar percent of mortality seen in other studies including hospitalized CAP patients [46]. The presence of COPD has not proved to be risk factor for mortality as other studies showed. Neither the age, nor the severity determined by CURB-65 score have not been assessed as independent risk factors of mortality, as reported in other series.

4. CONCLUSIONS

By considering CRP levels quickly rise in bacterial infections, this is considered as the primary marker in CAP patients during infection. Serum level of CRP is directly correlated with CURB-65 score. Using this test can be effective in rapid evaluation and early assessment of CAP, and good alternative to CURB-65 criteria for making clinical decisions regarding the hospitalization of the patients in ICU ward. Confusion, blood urea nitrogen, respiratory rate and blood pressure which are used for measuring severity of pneumonia, can be influenced by concomitant illness or other medications due to chronic disease in which measurement of CRP can be valuable in evaluating severity of pneumonia.

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