Original Article

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Internal Medicine Section

Clinical and Biochemical Parameters Correlation with Complications and Mortality in Community Acquired Pneumonia in A Tertiary Care Hospital

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ABSTRACT

Introduction: Pneumonia continues to remain a serious health risk despite ongoing efforts. Community Acquired Pneumonia (CAP) is a common respiratory disease often requiring hospitalisation and is a major cause of morbidity and mortality in the population.

Aim: To study clinical and biochemical profile of patient admitted with the diagnosis of community acquired pneumonia and to find the association with various complications and outcomes.

Materials and Methods: In this prospective study, 130 patients of CAP admitted in the institution were enrolled. Data relating to their age, gender, clinical profile, severity score, microbiological details, complications and outcome were recorded. All the laboratory parameters of the patients were compared among the survival and mortality groups using student's t-test and Chi-square test. The analysis was performed using Statistical Packages for the Social Sciences (SPSS Inc, Chicago, IL, version 22.0 for windows). p-value <0.05 was significant.

Results: Out of 130 patients of CAP 109 (83.8%) survived and 21 (16.2%) died. Seventy were male (53.8%) and 60 female (46.1%). Increase mean pulse rate, respiratory rate, lactate and low blood pressure, low oxygen saturation, low GCS scale and acidosis were associated with increased mortality. Sputum cultures were positive in 33 (25.38%), common organism isolated was *E. coli* (8.5%), *pseudomonas* (6.9%) and methicillin sensitive *staphylococcus* (3.1%). The need for ICU admission, mechanical ventilation, inotropes were statistically significant and associated with high mortality (p<0.001). Mean quick Sequential Organ Failure Assessment (qSOFA) score and Systemic Inflammatory Response Syndrome (SIRS) score was higher in mortality group.

Conclusion: Early diagnosis, prompt severity scoring, early sepsis management and monitoring can reduce mortality in CAP. Underlying co-morbid conditions like diabetes, Chronic Obstructive Pulmonary Disease (COPD), hypertension and others need to be managed precisely to prevent adverse outcome.

Keywords: Bacteriology, Mortality, Sepsis, Sputum culture

INTRODUCTION

The Community Acquired Pneumonia (CAP) is defined as acute pulmonary infection in a patient who is not hospitalised or living in a health care facility 2 weeks or more before presentation [1]. CAP is a common and major mortality concern among infectious disease [1,2]. Inflammatory response resulting from CAP may be local or systemic. Sepsis results due dysregulated host response may compromise various vital organs eventually leading to death.

CAP prevalence ranges from 3-4% in developed to 20-30% in developing countries [3]. High incidence rate of 9.7 per 1000 persons have been seen in developed countries with 46.5% is the hospitalisation rate and 12.9% being the 30 day mortality [4]. In developing countries, there is high burden of CAP in adult population [4]. In India, the mortality rate among hospitalised patients diagnosed with the condition has been reported to be around 4% to 21% [3]. The case fatality rate increases to over 50% in patients admitted to ICU with pneumonia-related sepsis and septic shock [5]. Patients with severe pneumonia have highest mortality rate hence, early diagnosis of patients with pneumonia-associated sepsis/septic shock seems paramount [4,5]. The spectrum of pneumonia severity ranges from mild, which can be treated on an out-patient basis, to very severe pneumonia with multiple co-morbidities requiring ICU admission, ventilator support thus resulting in high mortality.

In recent years factors like causative agents, susceptible population, diagnostic methods, emerging antibiotic resistance and treatment of pneumonia have undergone changes. Pneumonia is common among older patients and those with co-morbidity like COPD, diabetes, renal failure, congestive heart failure, chronic liver disease and are also associated with increased mortality [6].

Etiological agent and the type of bacteria causing CAP may vary in different regions of world and may change over time in the same region. This change in bacteriological profile becomes more relevant due to ongoing changes in environment, life expectancy, associated co morbidities, advance detection methods and frequent use of antibiotics. Studies in India also show different bacteria as a predominant causative agent in different regions like *Streptococcus* pneumonia in Shimla [7] and Delhi [8] whereas in Ludhiana [9] it is *Pseudomonas aeruginosa* [9].

Updated data about the incidence of pneumonia may be important to recognise changes in disease patterns, to assess the new aetiological profile according to the new diagnostic technologies, to evaluate preventive interventions, and to allocate health care and research resources [9,10].

Hence the present study was conducted to analyses the various clinical and laboratory parameters and to correlate with different outcome in patient of CAP.

MATERIALS AND METHODS

This was a prospective, observational hospital based study involving patients admitted to emergency and medicine ward at tertiary care centre in Northern India, between January 2018 to August 2019.

Ethical Consideration

The study was conducted among the patients of pneumonia admitted to the Department of General Medicine, Government Medical College, Chandigarh, India, on ethical guidelines for biomedical

research on human subject as given in the "Declaration of Helsinki" and by Central Ethics Committee on Human Research (CECHR) of ICMR, New Delhi. Written informed consent was taken from the patients prior to the study. The interventions involved in the present study were completely safe. Enrolled subjects were informed about the study its purpose, methods and outcome in simple language of their choice. Queries regarding discomfort and risks if any were explained. Personal details of participants were kept confidential. The patients were given the right to opt out of the study at any time they wanted without any impact on the treatment given.

Inclusion Criteria: Age more than 18 years, clinical signs and symptoms suggestive of pneumonia and radiological evidence of infiltrates on chest radiograph consistent with consolidation.

Exclusion Criteria: Referral from another hospital, patients on mechanical ventilation upon admission, hospital acquired pneumonia, aspiration pneumonia, tuberculosis, miliary tuberculosis, cavitary lesion of lung, lung malignancies, immunosuppressed patients (HIV patients, solid organ transplant, post splenectomy, on steroids, on radiotherapy and chemotherapy).

The optimum sample size was calculated on the basis of 95% confidence level and 10% anticipated difference between detection rate of pneumonia. Sample size calculated was 116 which was inflated by 20% further to adjust dropouts, accordingly a total 130 cases were included.

METHODOLOGY

Patients who met the inclusion criteria and were willing for the study were explained regarding the study and its purpose through the patient proforma. The demographic parameters of the all patients were noted at the time of admission. Patients were subjected to initial set of investigations such as complete blood count, urine analysis, renal function tests, liver function test, coagulogram, arterial blood gas analysis, blood culture and sputum culture. Chest radiography, electrocardiogram were done in every patient, echocardiogram and other specialised investigations (like pleural fluid analysis, CT scan, bronchoscopy) were done wherever necessary as per the clinical setting. Patients were followed-up during their stay in hospital. Strict vital monitoring was done during the hospital stay for development of any complication. The aforementioned investigations were repeated on 72 hours of therapy and at time of discharge. Follow-up of the discharged patients was obtained on repeat outpatient visit or via telephone in case patient was not able to come physically on desired date which was usually a period of two weeks. Readmission, if any, in <2 week due to complication was also recorded.

Treatment Protocol

The patients, who were diagnosed radiological on chest X-Ray and those with positive blood culture, or sputum culture were given Intravenous (IV) antibiotics preferably based on culture sensitivity. All patients were monitored for any new complications/death during their hospital stay, and their outcomes were evaluated at discharge/death. The main outcome of interest was in-hospital mortality. Other outcomes that were assessed include need and duration of inotropic support, need and duration of ventilation, type of ventilatory support (invasive or non-invasive), need for dialysis and duration of ICU and hospital stay.

STATISTICAL ANALYSIS

All the laboratory parameters of the patients were compared among the survival and mortality groups using student's t-test and chi-square test. The analysis was performed using Statistical Packages for the Social Sciences (SPSS Inc, Chicago, IL, version 22.0 for windows). The p-value <0.05 was significant.

RESULTS

In the cohort of 130 patients, 70 (53.8%) were males and 60 (46.17%) were females. The mean age (±SD) of patients was 48.63±18.721, with the range from 18-90 years.

Fever was present in 88.5% (115/130) of patients with a mean duration of 6 days. The other symptoms were shortness of breath among 86.9% (113/130), cough with or without expectoration among 65% (50/130), altered sensorium among 8.5% (11/130), chest pain among 1.5% (2/130). There was no statistical difference in symptoms with mortality [Table/Fig-1].

Symptoms	Total (n=130)	Survivors (n=109)	Deceased (n=21)	p-value*
Fever	115 (88.5)	95 (87.2)	20 (95.2)	0.463
Breathlessness	113 (86.9)	92 (84.4)	21 (100)	0.073
Cough	65 (50)	56 (51.4)	9 (42.9)	0.634
Altered sensorium	11 (8.5)	9 (8.3)	2 (9.5)	1.000
Chest pain	2 (1.5)	1 (0.9)	1(4.8)	0.298

[Table/Fig-1]: Bivariate analysis of symptoms among the two groups.
%Percentage in parenthesis *Fisher's-exact test

Higher values of mean pulse and respiratory rate at admission were significantly associated with mortality (p<0.05). However, blood pressure (systolic and diastolic) and oxygen saturation were not significantly associated with mortality [Table/Fig-2].

Parameters	Total (n=130)	Survivors (n=109)	Deceased (n=21)	p-value*
Temperature (in OF) >100	100.51±1.73	100.54±1.71	100.36±1.83	0.665
Pulse (bpm) >90	102.55±17.41	99.41±16.19	118.86±14.43	<0.001
RR>20 (bpm)	26.98±7.74	25.74±5.74	33.4312.52	0.012
GCS<10	14.14±1.90	14.61±1.37	11.71±2.43	<0.001
Systolic BP <100 (mmHg)	108.44±21.75	109.79±21.57	100.11±21.52	0.081
Diastolic BP <90 (mmHg)	68.94±12.72	69.56±12.81	65.71±12.07	0.206
Spo_2<80	85.53±10.99	85.69±9.89	84.66±15.81	0.696

[Table/Fig-2]: Bivariate analysis (Survivors vs Deceased) of vital parameters in patients with pneumonia.
Student' t-test

The most common co-morbidity was diabetes mellitus in 38.5% (50/130) patients followed by hypertension in 21.5% (28/150) patients, Cardiovascular disease in 6.2% (8/130), chronic renal diseases in 5.4% (7/130) and COPD in7.7% (10/130). History of smoking was seen in 39 (30%) of patients [Table/Fig-3].

Comorbidities	Total (n=130)	Survivors (n=109)	Deceased (n=21)	p-value*
Diabetes	50 (38.5)	41(37.6)	9 (42.9)	0.651
Hypertension	28 (21.5)	26 (23.9)	2 (9.5)	0.144
COPD	10 (7.7)	10 (9.2)	0 (0.0)	0.149
CAD	8 (6.2)	8 (7.3)	0 (0.0)	0.200
CKD	7 (5.4)	6 (5.5)	1 (4.8)	0.890
Smoking	39 (30)	36 (33)	3 (14.3)	0.086

[Table/Fig-3]: Group wise comparison of co-morbidities and risk factors with outcome.
Pearson Chi-Square*

Sputum culture was sterile in 74.6%. The most common organism isolated was *E.coli* (8.5%), followed by *Pseudomonas* (6.9%) and *Klebsiella* (3.8%), respectively. Methicillin Sensitive *Staph aureus* (MSSA) was seen in 3.1%, *Acinetobacter* in 2.3% and 0.8% cases had dual infection with both *Citrobacter* and *Acinetobacter*.

Chest X-ray was the main radiological modality used to diagnose pneumonia. Highest mortality was seen in patients with bilateral pneumonia with ARDS followed by pneumonia involving two or more lung lobes.

Although the mean platelets were lower and TLC was higher in patients

who died as compared to the survivors, but it was not statistical significant (p<0.05). The statistically significant parameters were pH (p=0.037), Po_2 (p=0.057), Spo_2 (p=0.003) and lactate (p=0.001). The blood urea and serum creatinine was higher in non-survivors and other variables that correlated with mortality were bilirubin, SGOT, SGPT and albumin but was not statistically significant [Table/Fig-4].

Parameter	Total (n=130)	Survivors (n=109)	Deceased (n=21)	p-value*
Platelets (X10^9/L)	219.87±144.33	225±150.33	193±106.89	0.354
TLC (X10^6/L	15.80±8.944	15.44±8.92	17.70±9.04	0.290
Urea (mg/dL)	56±44.82	53±44.40	72±44.73	0.077
Creatinine (mg/dL)	1.33±0.95	1.30±0.99	1.50±0.71	0.386
pH	7.34±0.10	7.358±0.99	7.299±0.11	0.037
Po_2	84.28±33.64	87.17±32.01	69.30±38.52	0.057
Spo_2	83.70±12.77	85.65±11.16	73.56±15.8	0.003
Lactate	2.12±1.66	1.88±1.53	3.39±1.78	0.001
Bilirubin (mg/dL)	0.89±1.12	0.83±0.89	1.22±1.91	0.144
SGOT (IU/dL)	124.9±316.76	86.02±214.11	326.71±590.44	0.079
SGPT (IU/dL)	109.86±317.59	68.91±201.97	322.43±611.32	0.074
Albumin (gm/dL)	3.21±2.32	3.28±2.52	2.89±0.15	0.093

[Table/Fig-4]: Group wise comparison of laboratory parameters in patients with pneumonia.
Student's t-test*

All patients had one or more organ dysfunction necessitating longer hospitalisation and further interventions [Table/Fig-5]. Most common intervention required was ICU admission, followed by requirement of inotropes and need for mechanical ventilation; were statistically significant and associated with high mortality (p<0.001) [Table/Fig-6].

Complications	Total (n=130)	Survivors (n=109)	Deceased (n=21)	p-value*
Pleural effusion	17 (13.1)	16 (14.7)	1 (4.8)	0.217
Acute Kidney Injury (AKI)	19 (14.6)	6 (5.5)	13 (61.9)	<0.001
Hepatitis	29 (22.3)	15 (13.8)	14 (66.7)	<0.001
Shock	38 (29.2)	17 (15.6)	21 (100)	<0.001
Acute Respiratory Distress Syndrome (ARDS)	42 (32.3)	22 (20.1)	20 (95.2)	<0.001
Disseminated Intravascular Coagulation (DIC)	7 (5.4)	0	7 (33)	<0.001

[Table/Fig-5]: Group wise comparison of various complications among the two group.
Percentage (%) in parenthesis *Pearson Chi-square test

Intervention	Timings	Total (n=130)	Survivors (n=109)	Deceased (n=21)	p-value*
Inotopes	At admission	25 (19.2)	13 (11.9)	12 (57.1)	<0.001
	At 72 hours	29 (22.3)	11 (10.1)	18 (85.7)	<0.001
	At Discharge/Death	19 (14.6)	0	19 (90.5)	<0.001
Minute Vantilation (MV)	At admission	10 (7.7)	2 (1.8)	8 (38.1)	<0.001
	At 72 hours	24 (18.5)	7 (6.4)	17 (81)	<0.001
	At Discharge/Death	20 (15.4)	0	20 (95.2)	<0.001
Noninvasive Ventilation (NIV)	At admission	13 (10)	10 (9.1)	3 (14.2)	0.475
	At 72 hours	18 (13.8)	5 (4.5)	13 (61.9)	<0.001
	At Discharge/Death	0	0	0	-
ICU Admission	At admission	35 (26.9)	14 (12.8)	21 (100)	<0.001
	At 72 hours	53 (29.1)	32 (29.3)	21 (100)	<0.001
	At Discharge/Death	21 (16.1)	0	21 (100)	<0.001
Haemodialysis		5 (38.4)	3 (2.75)	2 (9.5)	0.183

[Table/Fig-6]: Frequency of intervention required and its association with outcome (at Admission, 72 hours, Discharge/Death).
Percentage (%) in parenthesis Pearson Chi square* test

Among the patients with pneumonia, 130 were screened based on a qSOFA score ≥2 and SIRS ≥2 points. The in-hospital mortality rates for the entire cohort was 21 (16.2%) (p-value <0.001). No mortality was seen in qSOFA and SIRS negative group score (<2).

DISCUSSION

The study population comprised of 70 males and 60 females. The mean age cohort was 49 years range (18-90) years and subsequent higher mortality was seen in younger age group which was comparable with previous studies by Waterer GW et al., and colleagues who reported a mean age of 58.1 years (range 18-99 years); suggested a substantial increase in the risk of death in younger patients with CAP [11]. These findings were in contrast to a study where a higher incidence of CAP with increasing age was reported and subsequent higher mortality in older age group [12]. In the index study higher mortality in younger age group could be attributed to delayed presentation with clinical deterioration with ARDS and requirement of mechanical ventilation on presentation, while others presented with hypotension/ multiorgan failure requiring inotropic support.

The majority of patients presented with fever 88.5% (n=115), dyspnea 86.9% (n=113), cough with expectoration in 65% (n=50) followed by altered mental status and pleuritic chest pain, in 8.5%, and 1.5%, respectively as seen in previous studies Shah BA et al., and Bansal S et al., [3,7]. The statistically significant association with mortality was seen with tachycardia (p=0.001), tachypnea (p=0.012) and altered mental status (GCS) (p=0.001). The present results were similar to study by Nagesh Kumar TC et al., [13]. Various haematological and biochemical abnormalities were observed in study population. The laboratory parameters which were of statistical significance at admission were pH, Po_2, Spo_2, lactate and serum creatinine [14].

Most of the patients had one or more risk factor for pneumonia. In present study co-morbidities showed no individual impact on mortality. Diabetes mellitus was present in 38.5% cases and low mortality was seen in diabetics (42.9%) as compared to non-diabetics (57.1%) similar to the results seen in a study by McAlister FA et al., of 2,471 patients of CAP, with 401 diabetics [15]. Kaplan V et al., in a study on 623,718 US patients hospitalised for CAP, aged >65 years reported no association between in-hospital mortality and diabetes: adjusted RR 0.96 (95% CI 0.93-0.99) which corroborates with the present findings [16].

A total of 30% of the patients were smokers in contrast to the study by Abdullah BB et al., concluding that cigarette smoking was the strongest independent risk factor for invasive pneumococcal disease [17]. A 7.7% in the present study were a diagnosed case of COPD. The prevalence of COPD ranges from 15% to 42% in various studies [18]. In the present study there was no significant difference in mortality in patients with history of smoking and COPD as compared to general population. Liapikou A et al., in a study reported similar results [18]. This was in contrast to previous studies, where most of studies have reported, smoking and COPD as an important risk factor for mortality [12,19]

In the present study, the microbiological diagnosis of CAP was confirmed only in 30% (n=39) patients. In 25.3% cases, the culprit organisms were isolated in sputum, and blood cultures were positive in 4.5% which was comparable with previous studies, 29% and 6% respectively in a study by Shah BA et al., [3] and 22% in study by Oberoi A and Agarwal A [9]. The present centre being a tertiary care referral centre, most of the patients who presented to us were already on antibiotics, making it difficult to grow the organism. Even with the use of extensive laboratory testing and various invasive procedures, aetiological confirmation cannot be made in 50% of the cases done in two independent studies [3,20].

The most common organism isolated in the present study was *E.coli*, which accounts for 8.5%. Next common was *Pseudomonas*

accounting for 6.9% followed by *Klebsiella* and *Staphylococcus aureus* 3.8%, 3.1%, respectively and other gram-negative bacilli which include *Acinetobacter*, *Citrobacter* accounting for 2.3% and 0.8% respectively the present results were similar to a study by Prina E et al., [21]. *Streptococcus pneumoniae* has been identified as the commonest organism causing CAP all over the world [22]. Over the last three decades, various studies have reported higher incidence of gram-negative organisms among culture positive pneumonias [7,22,23]. *Pseudomonas aeruginosa* predominates in Ludhiana, Karnataka and Srinagar [23]. Cilloniz C et al., reported *P. aeruginosa* in 4% cases [24]. The radiological data in the present study showed a predominance of lobar pneumonia in 95 (73%) patients followed by bronchopneumonia in 10 (7.69%), pneumonia with pleural effusion seen in 17 (13%), and multilobar in 8 (6.15) patients ($p<0.017$) our results were similar to studies done by Bansal S et al., and Torres A et al., [7,25].

Complications like Acute Kidney injury, Hepatitis, Shock, ARDS, and DIC were found to be significantly associated with mortality ($p<0.001$). Overall, mortality rate was 16.2% in the study. Few studies have reported on complications of CAP. Paganin F et al., in a study on 112 immuno-competent patients with a mean age 54.7 years, reported mortality in 43%, shock 48%, mechanical ventilation 82% [26]. Estenssoro E et al., reported ARDS in 28% cases of CAP [27].

qSOFA and SIRS scores were compared for various outcomes. The mean qSOFA and SIRS score on admission was higher in mortality group (2.571 vs 3.429) compared to survival group (1.064 vs 2.688), respectively. A 46 (35.8%) had positive qSOFA score (≥2) and 117 (90%) had positive SIRS score (≥2). Area Under the Receiver Operating Characteristic Curve (AUROC) of both the scores qSOFA vs SIRS (0.937vs0.73) were also compared. This implies that qSOFA was better than SIRS, in predicting mortality. The present results were similar to previous studies done in pneumonia, with Area Under the Curve (AUC) ranging from (0.7 to 0.81 in hospital mortality. It was found that qSOFA had a relatively high AUROC compared with) have shown that qSOFA has a significant predictive value with respect to in-hospital mortality as compared to other scores [28,29]. Similarly in a study by Jiang J et al., on CAP a qSOFA score ≥2 was found to be strongly associated with mortality in patients with pneumonia, the AUROC curve 0.70, with pooled sensitivity and specificity 0.36 (95% CI, 0.26-0.48) and 0.91 (95% CI, 0.84-0.95), respectively [30].

Limitation(s)

This was a single centred study and the disease spectrum elucidated in the study population is limited to the hospital setting and thus results cannot be extrapolated to other region and those with less severe illness. There was potential for the information bias regarding age, duration of symptoms, co-morbidities and treatment. The decision for ICU care and treatment could have potential biased as it depends on availability of ICU bed and mechanical ventilator. Patients with known co-morbidities affecting the organ functions were included; some patients possibly had decompensated organ dysfunctions that could have affected the complications and the final outcome.

One of the strength of the study was that all patients were followed-up. At two weeks post discharge, all of the patients who survived had shown clinical, biochemical and radiological improvement and none of them had to be readmitted.

CONCLUSION(S)

Mortality due to CAP in the study was 16.2%, with higher mortality in 41-60 year age group. Gram negative organisms were the most common cause of CAP. Outcome and mortality was significantly associated with pH, PO_2, SpO_2, lactate, qSOFA, requirement of ionotrops and ventilation. The most common complication was ARDS followed by shock and AKI.

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