

Aetiology, Clinical Presentation and Outcome in Patients with Community-Acquired Pneumonia Requiring Hospitalisation: A Prospective Study

J. Harikrishna¹, Vasili Pradeep¹, Alladi Mohan¹, K.M. Bhargav¹, Abhijit Chaudhury², B. Vijayalakshmi Devi³ and K.V.S. Sarma⁴

Departments of Medicine¹, Microbiology², Radiodiagnosis³, and Statistics⁴, Sri Venkateswara Institute of Medical Sciences, Tirupati (Andhra Pradesh), India

Abstract

Background. There is paucity of reliable published data from Andhra Pradesh, India regarding aetiology, clinical presentation and outcome in patients with community-acquired pneumonia (CAP) requiring hospitalisation.

Methods. We prospectively studied 100 consecutive adult patients admitted with CAP during the period January 2018 to June 2019 at our tertiary care teaching hospital in Tirupati, Andhra Pradesh, South India.

Results. Their mean age was 54.4±15.7 years; there were 57 (57%) males. Single aetiology was found in 42% with influenza A (H1N1)pdm09 (12%), *Legionella pneumophila* (9%) being the most common; more than one concurrent aetiological agents were found in 31%; and no aetiological agent could be established in 27% patients. Mechanical ventilation (both non-invasive ventilation [NIV] and invasive mechanical ventilation [IMV]) were required in 65 patients. NIV was required in 58 patients, of them 38 had recovered; 20 had NIV-failure and required tracheal intubation and IMV. Sixteen patients died; 12 due to CAP and the rest due to other causes. On receiver-operator characteristic (ROC)-curve analysis acute physiology and chronic health evaluation II (APACHE II) score ≥14 (sensitivity 84.5% and specificity 56.3%), pneumonia severity index (PSI) score ≥98 (sensitivity 72.6% and specificity 68.8%) and erythrocyte sedimentation rate (ESR) ≥76 (sensitivity 73.8% and specificity 62.5%) were predictors of death. On multivariable analysis need for IMV (p<0.001) emerged as an independent predictor of death.

Conclusions. CAP can present with single or multiple concurrent aetiologies. A trial of NIV can obviate the need for IMV. On multivariable analysis, need for IMV is an independent predictor of death in patients with CAP.

[Indian J Chest Dis Allied Sci 2020;62:117-125]

Key words: Community acquired pneumonia, India, Aetiology, APACHE II score, Pneumonia severity index, Outcome.

Introduction

Community-acquired pneumonia (CAP) remains a common and serious illness despite the availability of potent new antimicrobials and effective vaccines.¹⁻⁵ World Health Organization (WHO) Global Burden of Disease study estimated that lower respiratory tract infections (LRTIs), which include CAP, were 429.2 million episodes of illness worldwide and accounts for 94.5 million disability adjusted life years (DALYs). In adults aged over 59 years, it causes 1.6 million deaths annually.¹ In United states, pneumonia is the sixth leading cause of death from the infectious diseases affecting four million cases annually of which more than half a million require hospitalisation.² In a

recent study conducted in Louisville population in USA over a period of two years, in-hospital mortality was 6.5% and when the results were extrapolated to entire US population, the estimated burden remained substantially high accounting for greater than 1.5 million adults being hospitalised annually with a high mortality of one out of three patients being hospitalised with CAP dying annually.³

There are no large studies on epidemiology of CAP from India, but mortality data on total number of deaths caused by LRTIs are available. The number of deaths due to LRTIs was 35.1/100,000 population in the year 2008 compared to 35.8/100,000 population for tuberculosis (TB), while it was 194.9/100,000 for infectious and

Funding: Sri Balaji Arogya Varaprasadini Scheme of Sri Venkateswara Institute of Medical Sciences and Tirumala Tirupati Devasthanams, Tirupati

[Received: January 1, 2020; accepted: May 6, 2020]

Corresponding author: Dr Alladi Mohan Professor and Head, Department of Medicine, Sri Venkateswara Institute of Medical Sciences, Tirupati-517 507 (Andhra Pradesh), India; E-mail: alladimohan@rediffmail.com

parasitic diseases.⁴ Thus, around 20% of mortality due to infectious diseases in India is caused by LRTIs.

In recent years, both epidemiology and treatment of pneumonia have undergone changes. Pneumonia is increasingly being encountered among older patients and those with co-morbidity, like chronic obstructive pulmonary disease (COPD), diabetes mellitus, renal failure, congestive heart failure, chronic liver disease (CLD) and other conditions.⁵ Bacteriological profile of CAP is different in different countries and changes with time within same country, probably due to frequent use of antibiotics, changes in environmental pollution, increased awareness of disease and change in life expectancy. *Streptococcus pneumoniae* has been the most common organism causing CAP in most parts of Europe⁶, United States⁷, United Kingdom (UK)⁸, Iraq⁹ and *Klebsiella pneumoniae* was the most common organism causing CAP in patients admitted to an intensive care unit (ICU) in Singapore.¹⁰ In India also, the aetiological agent of CAP has been observed to vary with geographic distribution.¹¹⁻¹³ While *Streptococcus pneumoniae* was the predominant isolate in Shimla¹¹ and Delhi¹² *Pseudomonas aeruginosa* was the most frequent aetiological agent in Karnataka.¹³

Sparse published data are available regarding aetiology, clinical presentation and outcome in patients with CAP requiring hospitalisation from the state of Andhra Pradesh. Hence, the present study was designed to study the aetiology and clinical presentation in patients presenting with CAP requiring hospitalisation; and to study the predictors of outcome in patients presenting with CAP requiring hospitalisation at our tertiary care teaching hospital.

Material and Methods

Consecutive adult patients (18 years or more) presenting with community-acquired pneumonia (CAP) admitted to medical wards and medical intensive care unit (MICU) at the Sri Venkateswara Institute of Medical Sciences (SVIMS), Tirupati, a tertiary care teaching hospital during the period January 2018 to June 2019 were screened for inclusion in the study. Patients who tested sero-positive for human immunodeficiency virus (HIV), pregnant women, proven malignancy, prior hospitalisation within three months of clinical presentation, on dialysis therapy, on wound care and who were not willing to participate in the study were excluded.

The study was conducted after obtaining clearance by the Institutional Thesis Protocol Approval Committee and Institutional Ethics Committee. Written informed consent was obtained from all the study participants. In

case the patient is unconscious, consent was obtained from the next responsible attendant. A detailed history regarding presence of fever, cough, purulent sputum production, pleuritic chest pain, exposure to critically ill patients, exposure to birds and travel history was obtained. Socio-economic status of the patients was recorded and categorised as per the modified Kuppaswamy's socio-economic scale updated for 2019.^{14,15} A thorough physical examination was carried out in all the study participants. Tachycardia was defined as heart rate >100/min; and tachypnoea was defined as a respiratory rate >20/min. Arterial oxygen saturation (SpO₂) was measured using pulse oximeter (Model DR-50D, Dr Trust, Chandigarh, India).

In all the patients, laboratory and imaging investigations were carried out to establish a diagnosis and for managing the patient. These included complete haemogram, serum biochemistry including renal function, liver function tests, serum electrolytes and random blood glucose. One set of blood cultures were obtained at the time of admission. One mL of heparinised blood sample was procured for arterial blood gas (ABG) analysis from the radial artery and was transported to the laboratory immediately for processing. ABG analysis was done using AVL Compact 2 (Radiometer, Denmark) analyser. Urine sample was sent for routine and microscopy examination. Sputum collection was done at the time of admission for Gram's staining, acid-fast bacilli (AFB) staining and Xpert MTB/RIF testing as was feasible. Sputum was also subjected to bacterial culture on blood-agar and MacConkey-agar. In patients who could not expectorate sputum spontaneously, sputum induction was done by 3% hypertonic saline nebulisation. Throat swab was tested for influenza type A (H1N1pdm09), (H3N2) and influenza type B by reverse transcriptase real-time polymerase chain reaction (RT-PCR) in the Indian Council of Medical Research-Department of Health Research (ICMR-DHR) Virus Research and Diagnostic Laboratory (VRDL) at our Institute, using AriaMx Real-Time PCR system (model 8830 A, Agilent, Germany) using AgPath-ID TM One-step RT-PCR Kit (TaqMan Influenza A Assay Sets, Applied Biosystems, California).

Serum *Mycoplasma pneumoniae*, *Legionella pneumophila* and *Chlamydia pneumoniae* immunoglobulin M (IgM) testing was also carried out by enzyme-linked immunosorbent assay (ELISA) using kits manufactured by NovaTec Immunodiagnostica (GmbH, Dietzenbach, Germany) as per the manufacturer's instructions. All patients underwent chest radiograph (postero-anterior view or antero-posterior view) (bed-side portable); computed tomography (CT) of the chest was done whenever necessary.

Diagnosis of CAP was made as per the British Thoracic Society (BTS) guidelines for the management of community-acquired pneumonia in adults Update 2009.¹⁶ Mechanical ventilation (MV) (both non-invasive ventilation [NIV] and invasive mechanical ventilation [IMV]) were instituted in patients with tachypnoea (respiratory rate >40/min), hypoxaemia who were unable to maintain a partial pressure of oxygen (PaO₂) of >60 mmHg despite supplemental oxygen administration with a high flow gas delivery system delivering a fraction of inspired oxygen (FIO₂) of up to 0.5 to 0.6.

As per the BTS guidelines¹⁶ initial risk stratification was done based on confusion, urea, respiratory rate, blood pressure plus age ≥65 year (CURB-65) score in conjunction with clinical judgement and patients were managed accordingly. In all the patients, at the time of initial admission, acute physiology and chronic health evaluation II (APACHE II) score¹⁷ and the pneumonia severity index (PSI) score^{18,19} were calculated. All these details were recorded in a structured proforma.

Statistical Analysis

Data were recorded on a pre-designed proforma and managed using Microsoft Excel worksheet (Microsoft Corp., Redmond, WA). All the entries were double-checked for any possible error. Patients were followed up until death or discharge from the hospital in order to register their survival status. Descriptive statistics for categorical variables were performed by computing the frequencies (percentages) in each category. For the quantitative variables, approximate normality of distribution was assessed. Variables following normal distribution were summarised by mean ± standard deviation; the remaining variables were summarised as median (interquartile range [IQR]). Categorical variables were reported as percentages.

A mathematical model was developed to predict mortality in patients admitted with CAP to the medical intensive care unit (MICU). In-hospital mortality was the primary outcome studied. "Worst case-scenario" analysis²⁰ was done wherein, the discharged against medical advice (DAMA) patients were considered to have died.

Analysis for prediction of mortality was performed in two stages. Univariate analysis was carried out to compare the demographic, clinical, and laboratory variables between alive and dead patients using unpaired t-test, Mann-Whitney U-test for continuous variables and Chi-square test, Fisher's exact test for categorical variables. A two-tailed P-value of <0.05 was considered statistically significant.

Age (years) was categorised as ≥65 years and <65 years. Receiver-operator characteristic curves (ROC-curve) for APACHE II and PSI scores, and erythrocyte sedimentation rate (ESR) were plotted with (1-specificity) on the X-axis and sensitivity on the Y-axis using different cut-off levels of APACHE II and PSI scores to arrive at the choice of the most appropriate cut-off level to predict mortality in patients admitted with CAP.

Multivariable analysis was carried out considering in-hospital mortality as the "dependent variable", and variables found significant at a P<0.3 on univariate analysis, and the ROC cut-offs derived for APACHE II, PSI scores and ESR as predictor variables (co-variables), using step-wise binary logistic regression (backward-conditional method) to predict mortality in patients admitted with CAP.

The statistical software IBM Statistical Package for Social Sciences (Version 20, IBM Corp., Somers NY, USA); and MedCalc Version 19.1 (MedCalc Software bvba, Ostend, Belgium; <https://www.medcalc.org>; 2016) were used for statistical calculations.

Results

During the study period, 110 consecutive adult patients with CAP requiring admission were recruited. These patients were screened for eligibility for inclusion in the study. Of these, 10 patients were excluded, reasons being prior hospitalisation within prior three months (n=6), patients on dialysis therapy (n=3) and not willing to participate in study (n=1). The remaining 100 patients satisfying inclusion criteria were considered for analysis (Figure 1).

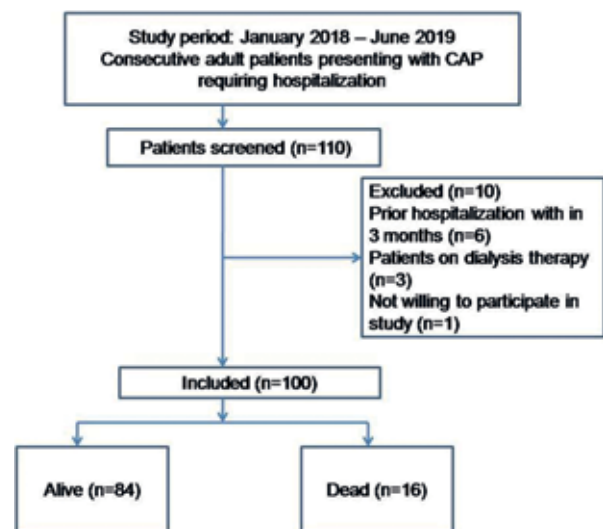


Figure 1. Study plan

Definition of abbreviation: CAP=Community-acquired pneumonia

Their mean age was 54.4±15.7 years. Majority of the patients were within age group 50-64 years (39%); there were 57 (57%) males. Majority of patients belonged to lower middle class (n=58) followed by upper middle class (n=22). Majority of the cases (13%) occurred in the month of November.

Most common presenting symptoms were fever (97%), cough (96%) and shortness of breath (93%) and others were sputum (75%), chest pain (14%), vomiting (7%), altered sensorium (6%), headache (3%) and loose stools (2%). The median (IQR) respiratory rate was 32 (22-40) per min; median (IQR) heart rate was 107 (62-146) per min. Majority of the patients presented with tachycardia (n=62); and tachypnoea (n=99) with co-morbid conditions were evident in 45% of the patients. Most common co-morbid conditions were diabetes mellitus (26%), hypertension (16%), COPD (11%), among others.

In the chest radiograph, unilateral involvement was seen in 47% while bilateral involvement was evident in 53% of patients. Pleural effusion was evident in 11% of patients (unilateral in 5; bilateral in 6 patients). Categorisation of the patients was done according to PSI^{18,19} and majority of the patients (n=38) belonged to class III. Of the 100 patients presented with CAP, single aetiology was found in 42% with influenza A (H1N1) pdm09 (12%), *Legionella pneumophila* (9%) being the

most common; more than one concurrent aetiological agents were found in 31%, which was considered as a result of multiple aetiological agents found in sputum and blood culture, serology; and no aetiological agent could be established in 27% patients (Table 1). In the patients presenting with CAP, intravenous antibiotics and oral antiviral drugs were started based on clinical severity, PSI score at presentation and radiological findings. After definitive diagnosis, antibiotics were changed according to culture sensitivity reports.

Mechanical ventilation (MV) was required in 65 patients. NIV was required in 58 patients, of them 38 had recovered with NIV; 20 had NIV-failure and required tracheal intubation and IMV.

Respiratory failure was the most common complication accounting for 65% followed by the acute kidney injury (AKI) in 29% and septic shock in 15%. Sixteen patients (16%) died; 12 patients died due to complications of CAP and four patients died due to other causes. On univariate analysis of continuous variables, patients who died had a statistically significant higher respiratory rate (P=0.030), ESR (P=0.031), APACHE II score (P<0.001), and PSI score (P=0.016). On univariate analysis of categorical variables, presence of shock (P<0.001), PSI ≥98 (P=0.004), APACHE II ≥14 (P=0.002) and ESR ≥76 (P=0.009) were statistically significant predictors death. On ROC-curve analysis APACHE

Table 1. Number of specific pathogen co-detection combinations in 100 patients with CAP

	Influenza (H1N1) pdm09	Influenza A (Non H1N1)	Influenza B	<i>Staphylococcus aureus</i>	<i>Streptococcus haemolyticus</i>	<i>Escherichia coli</i>	<i>Pseudomonas</i> sp.	<i>Klebsiella pneumoniae</i>	<i>Legionella pneumophila</i>	<i>Mycoplasma pneumoniae</i>	<i>Chlamydiae pneumoniae</i>	<i>Aspergillus</i> sp.
Influenza A (H1N1)pdm09	12	0	0	6	1	2	2	1	7	3	3	0
Influenza A (non H1N1)	0	0	0	1	0	0	0	0	0	0	0	0
Influenza B	0	0	2	0	0	0	0	0	0	0	0	0
<i>Staphylococcus aureus</i>	6	1	0	8	0	0	0	0	1	4	4	0
<i>Streptococcus haemolyticus</i>	1	0	0	0	0	1	0	0	0	0	0	0
<i>Escherichia coli</i>	2	0	0	0	1	0	0	0	0	0	0	0
<i>Pseudomonas</i> sp.	2	0	0	0	0	0	2	0	2	1	0	0
<i>Klebsiella pneumoniae</i>	3	0	0	0	0	0	0	0	1	0	0	0
<i>Legionella pneumophila</i>	7	0	0	6	0	1	2	1	9	3	3	0
<i>Mycoplasma pneumoniae</i>	3	0	0	4	0	0	1	0	3	6	5	0
<i>Chlamydiae pneumoniae</i>	3	0	0	4	0	0	0	0	3	5	2	0
<i>Aspergillus</i> sp.	0	0	0	0	0	0	0	0	0	0	0	1

Definition of abbreviation: CAP=Community acquired pneumonia

II score ≥ 14 , PSI ≥ 98 and ESR ≥ 76 predictors of death. On comparison of performance of APACHE II and PSI scores, both the tools performed similarly in predicting mortality difference between areas=0.0458; standard error (SE)=0.0889 (95% CI [confidence interval] -0.129 to 0.220; z statistic=0.515); P=0.6069 (Figure 2 and Table 2).

On multivariable analysis need for IMV support ($P < 0.001$) emerged as independent predictor of mortality. The model was found to have a -2 Log likelihood = 49.356, Chi-square=89.274 ($P < 0.0001$). The comparison of observations documented in the present study with other recent published studies is shown in table 3.²¹⁻²⁶

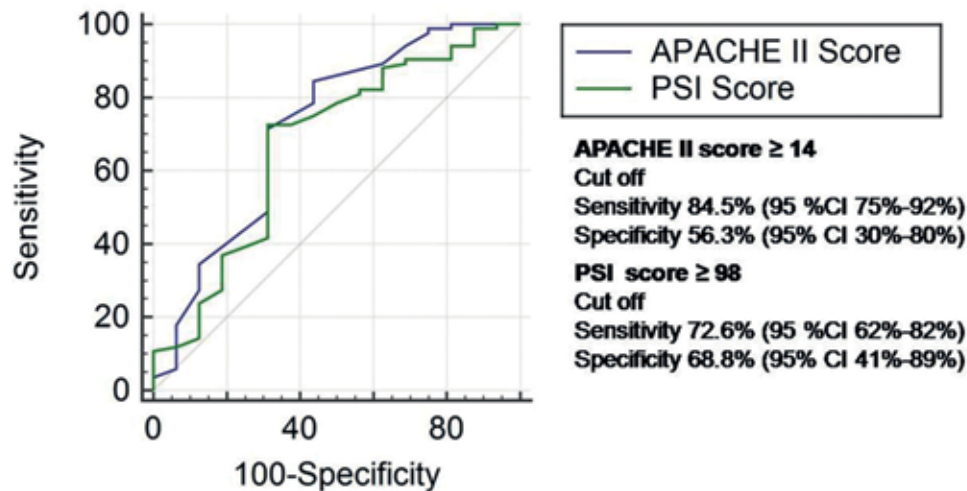


Figure 2. Comparison of performance of ROC curves of APACHE II and PSI scores in predicting mortality

Definition of abbreviations: ROC curve=Receiver-operator characteristic curve; APACHE II=Acute physiology and chronic health evaluation II; PSI=Pneumonia severity index

Table 2. Comparison of performance of APACHE II and PSI scores in predicting mortality

Variable	AUC	SE	95% CI
APACHE II score	0.718	0.0807	0.620 - 0.804
PSI Score	0.673	0.0815	0.572 - 0.763

Definition of abbreviation: APACHE II=Acute physiology and chronic health evaluation II; PSI=Pneumonia severity index; AUC=Area under the curve; SE=Standard error; CI=Confidence intervals

Discussion

Community-acquired pneumonia is an important cause of morbidity and mortality among infectious diseases in patients requiring hospitalisation, especially in the developing nations. In spite of extensive diagnostic work-up aetiology of CAP remains unknown in nearly 50% of the cases.²⁷ Aetiology of CAP is different in different parts of the world and it changes within same place with time. In India, aetiology of CAP remains changing with time and place.

Most of the patients in the present study belonged to sixth and seventh decade of life. These observations are similar to that reported from other studies in India.²¹⁻²³ However, mean age of the patients in the present study

was less than that reported from the other parts of the world.²⁴⁻²⁶ Whether this is due to differences in the immune status of the patients, effect of concomitantly present co-morbid conditions (and their duration), or virulence of the strains of aetiological organisms merits further study.

In the present study, men outnumbered women. A similar trend was evident in other published studies²¹⁻²³ from India and other world studies except for those in studies from Iceland²⁵ and Philippines²⁶ where gender distribution was found to be equal. In Tirupati and the Rayalaseema area, which is predominantly rural where the present study was carried out, traditionally, men seek and receive medical attention earlier compared to women who still are denied the basic medical facilities. Another reason for male predominance could be that as men tend to stay outdoors and in over-crowded places for work, they are at a higher risk of exposure to a wide variety of infectious agents.

Majority of the patients in the present study belonged to lower-middle class.^{14,15} Similar observations have been reported in other studies.^{3,28,29} These observations suggest that poverty, and associated over-crowding could perhaps have a bearing on occurrence of CAP. The present study had documented seasonal trends

Table 3. Comparison of present study with other studies

Variable	Study, Year (Reference)	Study, Year (Reference)	Study, Year (Reference)	Study, Year (Reference)	Study, Year (Reference)	Study, Year (Reference)	
	Dey et al 1997 (21)	Shah et al 2010 (22)	Mahendra et al 2018 (23)	Lui et al 2009 (24)	Bjarnason et al 2018 (25)	Lupisan et al 2019 (26)	Present Study
Period of study	Jan 1993–June 1994	Dec 1998–Dec 2000	March 2015–July 2015	Jan 2004–June 2005	Dec 2008–Nov 2009	May 2010–May 2012	March 2018–June 2019
Place of study	AIIMS, New Delhi	Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, India	JSS Medical College, Mysore, Karnataka, India	Hong Kong	Landspítali University Hospital in Reykjavik, Iceland	Eastern Visayas Regional Medical Center, Central Philippines	SVIMS, Tirupati, Andhra Pradesh, India
Study setting	Tertiary care teaching hospital	Tertiary care teaching hospital	Tertiary care teaching hospital	Teaching hospital	Secondary care hospital	Tertiary care teaching hospital	Tertiary care teaching hospital
Study design	Prospective	Prospective	Prospective	Prospective	Prospective	Prospective	Prospective
Study patients	72 consecutive patients admitted with CAP	100 consecutive patients admitted with CAP	100 consecutive patients admitted with CAP	1193 consecutive patients admitted with CAP	310 consecutive patients admitted with CAP	535 consecutive patients admitted with CAP	100 consecutive patients admitted with CAP
Age (years)	50.6 (range 18-80)	53.7±14.7	54.0	70.8±18.0	62.8±2.3	ND	54.4±5.7
Gender (male:female)	46:26	58:42	66:64	59:41	154:156	271:264	57:43
Aetiological confirmation	11/72 (15%)	29/100 (29%)	34/100 (34%)	468/1193 (39%)	164/310 (53%)	ND	73/100 (73%)
Common aetiological organisms	<i>Streptococcus pneumoniae</i> (n=6) <i>Klebsiella pneumoniae</i> (n=3)	<i>Pseudomonas aeruginosa</i> (n=10), <i>Staphylococcus aureus</i> (n=7), <i>Escherichia coli</i> (n=6) and <i>Klebsiella pneumoniae</i> (n=3)	<i>Klebsiella pneumoniae</i> (n=8) Influenza virus (H1N1) (n=8) <i>Pseudomonas aeruginosa</i> (n=5) <i>Streptococcus pneumoniae</i> (n=4)	Influenza virus (n=102), <i>Streptococcus pneumoniae</i> (n=101) <i>Mycoplasma pneumoniae</i> (n=78) <i>Haemophilus influenzae</i> (n=62) <i>Chlamydia pneumoniae</i> (n=55)	<i>Streptococcus pneumoniae</i> (n=61), <i>Mycoplasma pneumoniae</i> (n=36), Influenza A virus (n=27), <i>Haemophilus influenzae</i> (n=22)	<i>Hemophilus influenzae</i> (n=64), <i>Klebsiella pneumoniae</i> (n=62), <i>Streptococcus pneumoniae</i> (n=56), <i>Mycobacterium tuberculosis</i> (n=39)	Influenza A (H1N1)pdm09 (n=37), <i>Legionella pneumophila</i> (n=32), <i>Streptococcus pneumoniae</i> (n=24), <i>Mycoplasma pneumoniae</i> (n=22)
Need for mechanical ventilation	13/72	ND	40/100	ND	8/310	ND	65/100

Variable	Study, Year (Reference)	Shah <i>et al</i> 2010 (22)	Mahendra <i>et al</i> 2018 (23)	Lui <i>et al</i> 2009 (24)	Bjarnason <i>et al</i> 2018 (25)	Lupisan <i>et al</i> 2019 (26)	Present Study
Mortality	Dey <i>et al</i> 1997 (21)	19/72 (26.4%)	14/100 (14%)	78/1193 (6.5%)	9/310 (3%)	76/535 (14%)	16/100 (16%)
Predictors of mortality							
On univariate analysis		age >50 years (P=0.046), history of smoking (P=0.016), presence of COAD (P=0.039), systolic blood pressure <90mmHg (P=0.006), diastolic blood pressure <60mmHg (P<0.001), blood urea > 38 mg/dL (P=0.005) serum albumin <2.5 (P<0.001) at the time of hospitalisation and development of septic shock during hospital stay (P<0.001)	age >62 years, altered sensorium, respiratory failure, hypotension, leucocytosis, <i>Staphylococcus pneumoniae</i> and undetermined microbial aetiology	ND	ND	Shock (P<0.001), apnoea (P<0.001), cyanosis (P= 0.018), coma (P=0.022), irritability (P= 0.018), drowsiness (P<0.001), SpO ₂ <90% (P<0.001), and systolic blood pressure <90mmHg (P=0.006)	Respiratory rate (P=0.030), ESR (P=0.031), APACHE II score (P<0.001), and PSI score (P=0.016), Shock (P<0.001), ESR>76 (P=0.009), APACHE II >14 (P=0.002), PSI >98 (P=0.004) and need for IMV (P<0.001)
On multivariable analysis		ND	ND	ND	ND	Drowsiness (AOR 5.95, 95% CI 2.03–17.45) and SpO ₂ <90% (AOR 2.65, 95% CI 1.24–5.67)	Need for IMV

Definition of abbreviations: AIIMS=All India Institute of Medical Sciences; CAP=Community-acquired pneumonia; COAD=Chronic obstructive airway disease; SVIMS=Sri Venkateswara Institute of Medical Sciences; SpO₂=Arterial oxygen saturation measured by pulse oximeter; PSI=Pneumonia severity index; APACHE II=Acute physiology and chronic health evaluation II; ESR=Erythrocyte sedimentation rate; ND=Not described; AOR=Adjusted odds ratio; IMV=Invasive mechanical ventilation;

with most of the cases occurred during winter and rainy seasons with highest incidence in the month of November (n=13). While there is paucity of reliable published data regarding CAP with seasonality in India, highest incidence of viral pneumonia has been found in a study from Iceland²⁵, with two peaks during the months of February and October. Further studies are required to confirm the seasonal trends of CAP with different aetiological agents. These trends may assist in alerting health administrators and public health, so that preventive measures like vaccination and health education regarding symptomatology of the disease for early initiation of the treatment, particularly during epidemics can be considered.

In the present study, fever (97%) and respiratory complaints constituted most common presenting symptoms. Similar observation were noted in other published studies from India^{21,23,30} and other parts of the world.²⁴⁻²⁶ In the present study, co-morbid conditions were present in 45%. In other published studies, from India²³ and other countries,²⁴⁻²⁶ the co-morbid conditions ranged from 18% to 80%. These observations suggest that presence of co-morbid conditions must be taken in to consideration while planning management of patients with CAP.

Aetiological confirmation in the present study was possible in 73% which was more than that reported in other Indian studies²¹⁻²³ and studies from rest of the world²⁴⁻²⁶ which could be attributed to extensive diagnostic work-up in the present study as compared to other studies and rest of the world. The spectrum of aetiological causes of CAP are similar but with differences in different parts of the country as well as in different parts of the world. In India majority of the published studies²¹⁻²³ show bacteriological agent as the predominant agent where as viral and bacterial aetiology is evident in studies from the world.^{24,25,26,31} In the present study, viral aetiology emerged as a predominant with influenza A (H1N1)pdm09 being most common, reason for this could be the fact that RT-PCR was used as a diagnostic test. Similar pattern of viral aetiology being predominant has been reported from other parts of the world along with bacteriological agents, which can be considered as a result of advanced diagnostic modalities used in those studies.³¹

In the present study, multiple concurrent aetiological agents were evident in 31% which occurred as a result of different aetiological agents found in sputum and blood culture, RT-PCR and serology for atypical agents causing CAP and considered as a result of either initial viral infection followed by secondary bacterial infection

in those with mixed viral and bacterial aetiological agents or due to multiple concurrent bacterial infections leading to CAP in those patients. Presence of multiple concurrent aetiological agents was described in a study from Srinagar³⁰, India; however, obvious reasons were not explained. Presence of single and multiple concurrent aetiological agents were described in studies^{20,24,26} from other parts of the world and their presence was attributed to initial viral infection followed by secondary bacterial infection; or multiple concurrent infection with atypical agents.

In the present study, 65% of the patients needed mechanical ventilation. This figure is higher compared to other studies from India²¹⁻²³ and rest of the world²⁴⁻²⁶. The tertiary care teaching institute where the present study was conducted is the only government institution in Rayalaseema area of Andhra Pradesh State extending critical care and mechanical ventilatory support under the government's health insurance scheme³² to eligible beneficiaries. Therefore, it is more likely that the higher figure regarding patients requiring mechanical ventilatory support may actually reflect a referral bias.

Mortality in CAP depends on severity of illness at the time of presentation which can be assessed by PSI score and APACHE II score at the time of admission. While mortality in the present study (16%) is similar to some of the studies²¹⁻²³ from in India and rest of the world²⁴⁻²⁶, still remains high for an infectious disease. These observations suggest that there is a need for further optimisation and sustenance of the epidemiological data regarding microbiological aetiology, early efficient use of procuring appropriate specimens and subjecting them to rapid diagnostic methods and institution of appropriate antibiotic treatment.

The present hospital-based study was a single centre study. Whether these observations can be extrapolated to the community as a whole needs to be further confirmation. Due to logistic reasons, the present study was conducted over a fixed period in time. Therefore, time-trends of CAP could not be recorded.

Conclusions

Our observations suggest that CAP can present with single or multiple concurrent aetiologies. A trial of NIV can obviate the need for IMV. Need for IMV is an independent predictor of death in patients with CAP.

Acknowledgements

The authors wish to acknowledge Indian Council of Medical Research-Department of Health Research (ICMR-DHR) Virus Research and Diagnostic Laboratory (VRDL), Sri Venkateswara Institute of Medical Sciences, Tirupati for their kind help with laboratory diagnosis.

References

1. The global burden of the disease. Available at URL: http://www.who.int/topics/global_burden_of_disease/en/. Accessed on October 10, 2019.
2. Garibaldi RA. Epidemiology of community-acquired respiratory tract infections in adults. Incidence, etiology, and impact. *Am J Med* 1985;78:32–7.
3. Ramirez JA, Wiemken TL, Peyrani P, Arnold FW, Kelley R, Mattingly WA, et al; University of Louisville Pneumonia Study Group. Adults hospitalized with pneumonia in the United States: incidence, epidemiology, and mortality. *Clin Infect Dis* 2017;65:1806–12.
4. Gupta D, Agarwal R, Aggarwal AN, Singh N, Mishra N, Khilnani GC, et al for Pneumonia Guidelines Working Group. Guidelines for diagnosis and management of community- and hospital-acquired pneumonia in adults: Joint ICS/NCCP(I) recommendations. *Lung India* 2012;29:S27–62.
5. Marrie TJ, Durant H, Yates L. Community-acquired pneumonia requiring hospitalization: 5-year prospective study. *Rev Infect Dis* 1989;11:586–99.
6. Lode HM. Managing community-acquired pneumonia: a European perspective. *Respir Med* 2007;101:1864–73.
7. Bartlett JG, Mundy LM. Community-acquired pneumonia. *N Engl J Med* 1995;333:1618–24.
8. Howard LS, Sillis M, Pasteur MC, Kamath AV, Harrison BD. Microbiological profile of community-acquired pneumonia in adults over the last 20 years. *J Infect* 2005;50:107–13.
9. Al-Ghizawi GJ, Al-Sulami AA, Al-Taher SS. Profile of community- and hospital-acquired pneumonia cases admitted to Basra General Hospital, Iraq. *East Mediterr Health J* 2007;13:230–42.
10. Lee KH, Hui KP, Tan WC, Lim TK. Severe community-acquired pneumonia in Singapore. *Singapore Med J* 1996;37:374–7.
11. Bansal S, Kashyap S, Pal LS, Goel A. Clinical and bacteriological profile of community acquired pneumonia in Shimla, Himachal Pradesh. *Indian J Chest Dis Allied Sci* 2004;46:17–22.
12. Capoor MR, Nair D, Aggarwal P, Gupta B. Rapid diagnosis of community-acquired pneumonia using the BacT/Alert 3D system. *Braz J Infect Dis* 2006;10:352–6.
13. Malini A, Deepa E, Gokul B, Prasad S. Nonfermenting gram-negative bacilli infections in a tertiary care hospital in Kolar, Karnataka. *J Lab Physicians* 2009;1:62–6.
14. Kuppuswamy B. *Manual of Socioeconomic Status (Urban)*. New Delhi: Manasayan; 1981.
15. Wani RT. Socioeconomic status scales-modified Kuppuswamy and UdaiPareekh's scale updated for 2019. *J Family Med Prim Care* 2019;8:1846–9.
16. Lim WS, Baudouin SV, George RC, Hill AT, Jamieson C, Le Jeune I, et al. BTS guidelines for the management of community acquired pneumonia in adults: update 2009. *Thorax* 2009;64 (Suppl. 3):iii1–55.
17. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med* 1985;13:818–29.
18. Fine MJ, Auble TE, Yealy DM, Hanusa BH, Weissfeld LA, Singer DE, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med* 1997;336:243–50.
19. Aujesky D, Fine MJ. The pneumonia severity index: a decade after the initial derivation and validation. *Clin Infect Dis* 2008;47(Suppl. 3):S133–9.
20. Mohan A, Naik GS, Harikrishna J, Kumar DP, Rao MH, Sarma K, et al. Cleistanthuscollinus poisoning: experience at a medical intensive care unit in a tertiary care hospital in south India. *Indian J Med Res* 2016;143:793–7.
21. Dey AB, Nagarkar KM, Kumar V. Clinical presentation and predictors of outcome in adult patients with community-acquired pneumonia. *Natl Med J India* 1997;10:169–72.
22. Shah BA, Singh G, Naik MA, Dhobi GN. Bacteriological and clinical profile of community acquired pneumonia in hospitalized patients. *Lung India* 2010;27:54–7.
23. Mahendra M, Jayaraj BS, Limaye S, Chaya SK, Dhar R, Mahesh PA. Factors influencing severity of community-acquired pneumonia. *Lung India* 2018;35:284–9.
24. Lui G, Ip M, Lee N, Rainer TH, Man SY, Cockram CS, et al. Role of 'atypical pathogens' among adult hospitalized patients with community-acquired pneumonia. *Respirology* 2009;14:1098–105.
25. Bjarnason A, Westin J, Lindh M, Andersson LM, Kristinsson KG, Löve A, et al. Incidence, etiology, and outcomes of community-acquired pneumonia: a population-based study. *Open Forum Infect Dis* 2018;5:ofy010.
26. Lupisan S, Suzuki A, Macalalad N, Egos R, Sombrero L, Okamoto M, et al. Etiology and epidemiology of community-acquired pneumonia in adults requiring hospital admission: a prospective study in rural Central Philippines. *Int J Infect Dis* 2019;80:46–53.
27. Bates JH, Campbell GD, Barron AL, McCracken GA, Morgan PN, Moses EB, et al. Microbial etiology of acute pneumonia in hospitalized patients. *Chest* 1992;101:1005–12.
28. Jahanihashemi H, Babaie M, Bijani S, Bazzazan M, Bijani B. Poverty as an independent risk factor for in-hospital mortality in community-acquired pneumonia: a study in a developing country population. *Int J Clin Pract* 2018;72:e13085.
29. Loeb MB. Community-acquired pneumonia in older people: the need for a broader perspective. *J Am Geriatr Soc* 2003;51:539–43.

30. Para RA, Fomda BA, Jan RA, Shah S, Koul PA. Microbial etiology in hospitalized North Indian adults with community-acquired pneumonia. *Lung India* 2018;35:108–15.
31. Jain S, Self WH, Wunderink RG, Fakhran S, Balk R, BramleyAM, *et al*; CDC EPIC Study Team. Community-acquired pneumonia requiring hospitalization among U.S. Adults. *N Engl J Med* 2015;373:415–27.
32. Dr YSR Aarogyasri Health Care Trust. Andhra Pradesh State Government. Available at URL: <http://www.ysraarogyasri.ap.gov.in/>. Accessed on October 24, 2019.