

Clinical and microbiological profile of health care associated pneumonia in patients with chronic renal disease referred to a tertiary care hospital- a prospective study

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Abstract

Background: Healthcare associated pneumonia (HCAP) is a public health problem in the era of home care of chronic illness including chronic renal disease. They have greater burden of comorbidities, immune suppression and impaired mobility. **Aim of the Study:** To characterise the clinical, radiological and microbiological profile of health care associated pneumonia in chronic renal disease cases including its resistance pattern and outcome in the study population. **Materials and Methods:** This prospective study was conducted among patients with chronic kidney disease (CKD) who had been treated in multiple hospitals across Odisha. They were subjected to history taking, clinical examination, laboratory and radiological investigations. Sputum or endotracheal tube culture were sent for gram stain and aerobic culture. All the categorical parameters were compared using Fisher's exact test. Continuous parameters were compared using independent t-test. All the statistical analysis was carried out using the software Stata 15.1. A p-value less than 0.05 was considered significant. **Results:** 58 patients with an underlying chronic kidney disease were included. 54 (93.1%) patients survived while 4 (6.9%) died. The mean age, total leucocyte count and serum urea levels were higher among patients who died in comparison to the survivors (p= 0.95, 0.334 and 0.386 respectively). *Klebsiella spp* (12.07%), and *Acinetobacter* (8.6%) were most commonly isolated. Multi-drug resistance (MDR) and extensive drug resistance (XDR) were encountered among these organisms. Death was more commonly associated in patients ≥ 60 yrs (p= 1), TLC ≥ 11000 cells/mm³ (p= 0.0091), serum creatinine ≥ 3 mg/dl (p= 0.329) and radiological involvement of ≥ 3 zones (p= 1). **Conclusion:** CKD is an important contributor in HCAP. Data from different institutions to corroborate our findings regarding antibiotic resistance pattern of the microbes in HCAP cases is recommended.

Keywords: HCAP, *Klebsiella spp*, *Acinetobacter*, MDR, XDR.

Introduction

Chronic kidney disease is a huge public health problem and currently awareness of treatment by dialysis and transplantation is also increasing. The essential criteria refined by Kidney Disease Improving Outcomes (KDIGO) in 2012 stipulates as follows-

- a. Evidence of chronic kidney damage
 - i- Persistent proteinuria and or abnormal urinary sediment
 - ii- Structural abnormalities (identified on imaging)
 - iii- Abnormalities in renal histology
 - iv- Low GFR (less than 60 ml /min)

v- Presence of either of these criteria for a period of at least 3 months OR Renal allograft recipient with or without low GFR.

Using this definition, the Global Burden of Kidney study 2015 has identified CKD as the most common non-communicable disease in the world and a leading cause of mortality.

The global prevalence of CKD is reported as 13.4% [1] and in India 17% respectively [2]. The expenditure on medical care is about 48.1 billion us dollars in USA. The incidence of diabetes, a major cause of CKD is on the rise as also the average life span of population. As diabetes is increasing in the developed and developing

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countries like a silent epidemic, so is CKD. Respiratory infection is an important component of uremic symptoms. The cause of pneumonia has been changing for decades in response to a multitude of such factors such as age, chronic illness, frequency of empirical antibiotic therapy and the emergence of new pathogens.

The 2005 update on the treatment of nosocomial pneumonias, the American Thoracic Society and Infectious Diseases Society of America includes health care-associated pneumonia as a separate category in a set of risks including chronic kidney disease patients on maintenance [3].

Increased population of immunosuppressed patients, device associated infections, instrumentation which are often needlessly applied, colonisation on hands of health care workers and irrational antibiotic therapy in Indian hospitals are contributory factors of the changes in epidemiology of antimicrobial resistance and increased vulnerability for nosocomial infections. However, a well-designed good study on healthcare associated pulmonary infection associated with chronic renal disease in India is infrequently reported.

Determining the regional etiology of HCAP is essential for optimising therapy outcome while minimising unnecessary broad-spectrum antimicrobial use.

The emergence of multidrug resistance among bacterial species is a worldwide public threat that is evolving at an alarming rate. Pathogens, including extended-spectrum beta-lactamase (ESBL) producing and carbapenem-resistant *Enterobacteriaceae* (CRE), methicillin-resistant *Staphylococcus aureus* (MRSA), Vancomycin-resistant *Enterococcus species* and multidrug resistant *Acinetobacterbaumanni* pose an ongoing challenge and are associated with health care associated infections [4, 5].

European centre for disease control (ECDC) and Centre for Disease control & prevention (CDC), Atlanta have defined multidrug resistant (MDR), extensive drug resistance (XDR) and pan drug resistant (PDR) bacteria among patients admitted in hospital acquired infection in ICU. Multidrug resistant bacteria are defined as acquired resistance to at least one agent in three or more antimicrobial categories. Extensively drug resistant is defined as bacterial isolate susceptible to only one or two antimicrobial categories. Pan drug resistance is defined as non-susceptibility to all agents in all antimicrobial categories. In the last decade, there has been a dramatic increase worldwide in the number of multidrug resistant Gram neg (MDRGN) bacterial pathogens.

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Compared with CAP, HCAP patients have more severe disease, higher mortality, and increased length of hospital stay and greater cost of care.

Materials and Methods

Study design: It was a prospective cohort analysis of patients with chronic kidney disease (CKD) with symptoms and/or signs of pulmonary infection who had been treated in multiple hospitals across Odisha and adjoining West Bengal.

Study area: The study was conducted at Kalinga Institute of Medical Sciences (KIMS), Bhubaneswar, a tertiary care hospital. Thus, patients from nearby areas and adjoining districts were referred for treatment.

Study period: The study was conducted between November 2016 and October 2018.

Study population: The study included patients with chronic kidney disease (CKD) admitted to the nephrology ward, intensive care unit or pulmonary ward with symptoms and/or signs of pulmonary infection who had been treated in multiple hospitals across Odisha and adjoining West Bengal. A total of 58 patients were included in the study.

Inclusion criteria: All patients of CKD with a pneumonia and fulfilling the following criteria from 2005 IDSA/ATS guidelines along with a diagnosis of pneumonia were included in the study:

1. Hospitalisation for at least 48hrs in the preceding 90 days due to kidney disease with or without associated co morbidities if any.
2. Chronic dialysis within 30 days.

Pneumonia was defined as new/progressive radiographic infiltrate at presentation plus two or more of the following:

- Temperature of > 38 degree C or < 36 degree C
- White blood cell count of more than 12000 or < 4000cells/cu mm or
- New/ worsening respiratory symptoms.

Exclusion criteria

1. Patients with tuberculosis.
2. Patients with malignancy.

Procedure: All the eligible patients were subjected to detailed history taking, systemic examination, chest X-ray and/or HRCT scan of thorax (when needed) to confirm pneumonia. Laboratory investigations including CBC, sputum Gram stain and culture, ET aspirate if on

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ventilator and serum procalcitonin were performed before any antibiotics were administered. A written informed consent was obtained from all the patients/attendants before inclusion in the study. The study was approved by the ethical committee of the institute.

Statistical methods: The data collected was clubbed in a single excel chart. All the categorical parameters were presented as frequency and percentage and compared

between the two groups using Fisher's exact test. Continuous parameters were presented as mean \pm SD and compared between the two groups using independent t-test. A p value of < 0.05 was considered as statistically significant.

All the statistical analysis was carried out using the SPSS software Stata 15.1.

Results

58 patients with an underlying chronic kidney disease were included in the study. Majority of the patients belonged to the age group > 60 years. The mean age among the patients with chronic kidney disease was 65.44 ± 12.18 years. The male to female ratio was 3.83:1 (Table 1).

Table-1: Demographic profile of the patients in the study.

Demography	Mean
Age	65.44 years (± 12.18)
<45 years	3
45-60 years	14
61-75 years	29
>75 years	12
M:F	3.83:1
Patients on hemodialysis.	27 (46.55%)
Patients on supportive therapy.	31 (53.45%)

Dyspnoea and cough (79.3% and 77.6% respectively) were the most commonly reported symptoms among the CKD patients with HCAP. Only 17 (29.3%) cases had fever (Table 2). The most common co-morbidity reports in the sub-group of patients was COPD (34.48%) followed by cardio-vascular diseases and diabetes mellitus (25.86% each). Majority of the patients (65.5%) had a illness of less than 1 week.

Table 2: Symptoms and co-morbidities and duration of illness of the patients in the present study.

Symptom	n (%)
Fever	17 (29.3%)
Cough	45 (77.6%)
Dyspnea	46 (79.3%)
Extra-pulmonary symptoms	15 (25.86%)
Co-Morbidities	
COPD	20 (34.48%)
Cardio-vascular diseases	15 (25.86%)
DM	15 (25.86%)
Neurological diseases	1 (1.7%)
Malignancy	2 (3.4%)
Others	10 (29.4%)
Duration of illness	
A. < 1 week	38 (65.5%)
B. ≥ 1 week	20 (34.5%)

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Table 3 signifies 39 (67.24%) cases had a normal total count (< 11000 cells/mm³). The mean levels of serum urea (96.61±42.91mg/dl) and creatinine (3.846±2.235mg/dl), procalcitonin 13.42(±18.63) were high.

Table 3: Total count and biochemical test of the patients in the present study.

Total count (cells/mm ³)	n (%)
< 11000	39 (67.24%)
≥11000	19 (32.75%)
Biochemical Tests	Mean
Hemoglobin	9.33mg/dl (±2.17)
S. Urea	96.61mg/dl (±42.91)
S. Creatinine	3.846/dl (±2.235)
Total bilirubin	0.916 (±1.7)
Procalcitonin	13.42 (±18.63)

Sample collection could be done from 38 (65.5%) patients and the remaining 20(34.5%) cases were diagnosed on clinical and radiological grounds. Sputum was the most commonly collected specimen (29.3%) followed by ET tube aspirate (18.97%) and blood (17.24%). Out of the 17 sputum samples collected, 8 (13.79%) reported growth of organism while 9 (15.5%) had no growth (sensitivity: 52.95%).

Among the 11 ET tube aspirate specimens, 5 (8.6%) showed growth while 6 (10.3%) did not report any growth (sensitivity: 45.45%). 5 blood culture samples reported growth (8.6%) (sensitivity: 50%) (Table 4).

Table-4: Results of samples collected (n-38)

Sample		Total (38)		Positive 18 (31.03%)		Negative 20 (34.48%)	
		ICU	Non-ICU	ICU	Non-ICU	ICU	Non-ICU
Sputum	17 (29.3%)	7	10	4	4	3	6
Et aspirate	11 (18.7%)	11		5	-	6	-
Blood	10 (17.24%)	5	5	3	2	2	3
Total	38	23	15	12	6	11	9

Klebsiella spp (12.07%) was the most common organism reported followed by *Acinetobacter spp* (8.6%). This was followed by *Pseudomonas* (5.17%) and *E. coli* (1.7%). Resistance was reported among *Klebsiella spp*, *Acinetobacter spp* and *Pseudomonas* pathogens (Table 5).

Table-5: Organisms isolated and their sensitivity pattern (n-18).

	Sensitive		MDR		XDR		PDR		Total
	ICU	Non-ICU	ICU	Non-ICU	ICU	Non-ICU	ICU	Non-ICU	
<i>E. coli</i>	1	-	-	-	-	-	-	-	1
<i>Klebsiella</i>	2	-	-	-	-	4	1	-	7
<i>Pseudomonas</i>	1	-	-	-	1	1	-	-	3
<i>Acenito-bacter</i>	2	-	3	-	-	-	-	-	5
(Fungus, pneumocystis jiroveci)	1	1	-	-	-	-	-	-	2
Total	7	1	3	-	1	5	1	-	18

Table-6: Distribution of organisms in clinical specimens (n-18).

	<i>E. coli</i>	<i>Klebsiella</i>	<i>Pseudomonas</i>	<i>Acinetobacter</i>	Others
Sputum	-	6	-	1	1
ET aspirate	1	-	2	2	-
Blood	-	1	1	2	1
Urine	-	-	-	-	-

Out of the total of 58 cases, 54 survived and 4 died. Death was commonly observed in patients with age ≥ 60 years ($p=1.0$), TLC ≥ 11000 cells/mm³ ($p=0.0091$), serum creatinine ≥ 3 mg/dl ($p=0.3292$) and radiological involvement of ≥ 3 zones ($p=1.0$) (Table 7).

Table-7: Mortality profile of the patients from the present study.

Age	Survivors	Deaths	P
<60 years	13	1	p= 1.00
≥ 60 years	41	3	
Gender			
Male	44	2	p= 0.186
Female	10	2	
TLC (cells/mm³)			
< 11000	39	0	p= 0.0091
≥ 11000	15	4	
S. creatinine (mg/dl)			
< 3	30	1	p= 0.3292
≥ 3	24	3	
Radiological involvement (zones)			
< 3	18	1	p= 1.00
≥ 3	36	3	

Discussion

The purpose of the study was to find out the etiology of health care associated pulmonary infection in CKD patients in our hospital and to elucidate their clinical, laboratory, radiological profile and further to identify microbiological etiology. A conscious and careful effort was made to find out incidence of drug resistance and outcome of therapy. Further attempt was made to find out the pattern of risk factors, incidence of healthcare pneumonia who supposedly did not show any pulmonary symptoms.

This prospective study shows that these patients had developed pulmonary infection after contact with health care system before being admitted to our hospital. They were vulnerable to subsequent pulmonary infection; the source of the infection could be ventilators,

haemodialysis, device associated or from healthcare personnel. The appropriateness of antibiotic therapy may not be effective in all cases [6].

Out of 58 cases having chronic kidney disease 27 were on haemodialysis. Haemodialysis status in our series (46.55%) may be associated with recent hospitalisation, nursing home residence that may have contributed to risk of HCAP. Two large retrospective studies showed high disease burden and mortality of pneumonia in haemodialysis patients [7, 8]. This may not be necessarily related to haemodialysis as the only illness.

Majority of the patients were elder 60 and above (70.7%). In most studies patients were older compared with CAP patients [9,10,11,12]. The gender distribution was not statistically significant. Cough, dyspnoea and

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fever were predominant pulmonary presentations and majority presented within 7 days; this was due to the severity of the presentation as evidenced by raised mean leukocyte count, procalcitonin level, renal and hepatic impairment. Bilateral lung lesions on radiography were also common features [13].

Many patients had multiple co-morbidities, majority having immunocompromised illness including COPD, diabetes mellitus and malignancy. They were having altered sensorium as extra pulmonary symptoms that could predispose them risk of aspiration. Similar observations were made by Carratala J et al [10].

Klebsiella spp, *Acinetobacter*, *Pseudomonas* and *E. coli* were notable gram-negative pathogens isolated from the clinical specimens. Pan drug resistance and extensive drug resistance were encountered among the *Klebsiella spp*, multidrug resistance among *Acinetobacter* and extensive drug resistance among *Pseudomonas* species respectively.

D'Agata EM found 0.55%-17% prevalence of infections caused by pathogens possessing extended -spectrum β -lactamases. Among the recent emergence of carbapenem - resistant *Klebsiella* species, three carbapenem hydrolysing β -lactamase variants (KPC-1—KPC-3) have been reported [14, 15, 16], these enzymes confer moderate to high level resistance to all agents in the carbapenem class.

Some of the plasmids that carry the genes responsible for carbapenem resistance also carry genes encoding extended - spectrum β lactamases, in addition many of the isolates also carry determinants of resistance to aminoglycosides and are fluroquinolone resistant [17], thus making these strains resistant to multiple classes of antimicrobial agents.

Pathogens were isolated among 18 of 38 available cases; this could be due to viral etiology which were not evaluated. The real incidence of pathogenic causes could be underestimated [18].

Acinetobacter baumannii has emerged globally as an important pathogen in hospitalised patients, causing high morbidity and mortality. It can cause pneumonia, bacteraemia, meningitis, urinary tract infections and skin and soft tissue infections. This organism accounts for around 10% of all gram-negative isolate identified in Brooklyn, New York [19].

This spread of Gram- negative bacteria resistance to carbapenems is an urgent public threat and a critical priority according to World Health Organisation [20].

The variability of MDRO prevalence may be based on geographic location and patient population.

Thus, treatment choice should be guided by local microbial epidemiology. Our studies on microbial resistance are consistent with studies by Chalmers JD [21] and Aliberti S [22] et al.

Device Associated infections such as ventilator-associated pneumonia, central line- associated blood stream infections, catheter-associated urinary tract infections and surgical-site infections account for most of the health care -associated infections that contributes to the growing antimicrobial resistance with resultant morbidity, mortality and adverse patient outcomes [23, 24, 25].

Correlation of various parameters with outcome reveals elderly age, elevated leucocytosis, creatinine levels and bilateral consolidation on radiographs associated with increased mortality. CKD disrupts the internal metabolic milieu and hence is associated with many systemic abnormalities including cardiovascular, skeletal, haemopoietic, endocrine, nervous system, and also lungs. Greater awareness, thorough evaluation of all organs is essential to provide a better quality of life for the patient.

Limitations of the study

1. Small sample size.
2. Diagnostic samples could not be collected from all patients.

Conclusion

HCAP was witnessed in 58 CKD cases with some having COPD, DM and malignancy as comorbid illnesses. Majority of patients were male, presented within a week of onset of symptoms of cough, dyspnoea, altered sensorium and also had increased leucocytes count and procalcitonin levels.

Non survivors had bilateral consolidation and increased leucocytosis. *Klebsiella spp*, *Acinetobacter* and *Pseudomonas* were important gram-negative resistant pathogens.

What the study adds to the existing knowledge?

Targeted antibiotic therapy is the key to managing such cases. Hospitals should adopt effective infection control measures to contain spread of multidrug resistance.

This study gives an insight into the epidemiology and prevalence of resistance pattern among organisms

causing HCAP in CKD patients in this part of the country.

However, further research involving a large number of patients from different institutions to corroborate the present findings regarding antibiotic resistance pattern of the microbes in HCAP cases is essential.

Contributions from authors

Dr. C. Mohan Rao: Conceived and designed the analysis, collected data.

Dr. Saswat Subhankar: Performed the analysis.

Dr. Aswini Prasad Patnaik: Contributed to the analysis.

Prof Debee Prasad Dash: Wrote the manuscript.

Findings: Nil; **Conflict of Interest:** None initiated

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