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Clinico-Bacteriological Profile and Prognostic Factors of Hospital Acquired Pneumonia in Central Kerala

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ABSTRACT

Background. Hospital Acquired Pneumonia (HAP) is the second most common hospital acquired infection and a leading cause of mortality in spite of latest diagnostic and management modalities. HAP is defined as pneumonia occurring 48 hours after hospital admission which was not incubating at the time of admission. Early onset HAP occurs within first two to four days of admission and late HAP occurs five or more days after admission.
Method. This was a hospital based longitudinal study. Fifty patients admitted in our tertiary hospital who developed HAP were included in study based on ATS/IDSA 2016 HAP guidelines and an attempt was made to study clinical and bacteriological profile as well as outcome of these patients with factors affecting the outcome. Statistical analysis included descriptive statistics, chi-square test and Fisher exact test using SPSS statistical software version 23.
Result. Male gender and age group more than sixty were found more predisposed to HAP. However both did not carry any significant association with outcome. Overall mortality in the study was 44%. Significant association with outcome was found with diabetic status, prior intravenous antibiotics use, bilateral infiltrates in chest X ray, prolonged hospital stay and septic shock. Contrary to expectations, no significant association was found between mechanical ventilation and outcome. Most common organism isolated was *K.pneumoniae*.
Conclusion. Assessing risk factors help us in prognosticating HAP. Surveillance of HAP and knowing the suspect organism is of paramount importance in deciding empirical therapy for HAP patients and antibiotics should always be used judiciously.

Keywords: Hospital Acquired Pneumonia, hospital acquired infections, antibiotics, *K. pneumoniae*, outcome

INTRODUCTION

Hospital acquired pneumonia (HAP) is the inflammation of lung parenchyma caused by an infectious agent acquired from hospital. HAP is the second common hospital acquired infection and the leading cause of mortality all over the world, which is reported as 38% to 70% in various studies. [1] Hospital Acquired Pneumonia is defined as pneumonia occurring 48 hours or more after hospital admission, which was not incubating at the time of admission. Early- onset hospital acquired pneumonia (HAP) is defined as pneumonia occurring within the first 2- 4 days of hospitalization. Late- onset HAP occurs 5 days or more after hospital admission. [2] Hospital acquired pneumonia results in serious complications in approximately 50% of patients especially in the intensive care unit. The impact of pneumonia on health care is significant in terms of morbidity, cost, and likely patient mortality. Studies have estimated that one third to half of hospital acquired pneumonia deaths are the direct result of infection. [3]

Incidence of hospital acquired pneumonia varies among different studies depending on the definition, type of hospital or ICU, population studied and level of exposure. HAP, although not a reportable

infection is thought to occur at a rate of 5-10 cases per hospital admission. [4] Lack of consensus regarding the most appropriate method to diagnose hospital acquired pneumonia also partly explains why incidence rates widely vary from one study to another. There are no much studies which describe the outcome of hospital acquired pneumonia in this part of the country. So such a study would help us to know about the organism involved and hence by formulate preventive strategy for further hospital acquired infections. This study will also shine light on possible risk factors that predict a downhill course in disease and which subset of patients require close monitoring for improvement.

MATERIALS AND METHODS

Objectives of study: The objectives of this study were to study the clinical and bacteriological profile of hospital acquired pneumonia and to study the factors affecting outcome of the same.

Study area: The study was a hospital based longitudinal descriptive study conducted in MES Medical College Hospital, Perinthalmanna, Malappuram, Kerala.

Study period: Study period was taken as one year

Working definition: Hospital acquired pneumonia was diagnosed based on the ATS/IDSA 2016 guidelines in the presence of both of below

1. Radiographic criteria – new or progressive infiltrates in chest X-Ray
2. Clinical criteria – At least two of the three clinical features (a. fever > 38 degree, b. leukocytosis or leucopenia with purulent secretions, c. decreased oxygenation) [4]

Study population:

Inclusion criteria: All the people more than fifteen years of age admitted in medicine, surgery or pulmonology ward satisfying the above working definition anytime after 48 hours of hospitalization were included in this study after availing an informed consent.

Exclusion criteria: The people excluded from study were 1) pregnant women, 2) those with psychiatric illness, 3) severely immunocompromised patients and 4) those who did not give consent to be a part of study.

Sample size: After applying the above inclusion and exclusion criteria 62 patients were interviewed during the period of study of which 50 were included in the final analysis. Twelve patients did not give consent. Significant sample size calculated and statistically validated was 46 for this study.

Data collection technique and tools: Study was initiated after getting consent from scientific committee and ethical committee of the institute. Patients were introduced to study after getting an informed consent. They were evaluated by face to face interview sessions based on a statistically validated proforma that was giving emphasis to meticulous history, clinical investigations and relevant investigations. All relevant data from the medical records and bedside flow charts of the patients, including laboratory, radiology and microbiologic information were collected on admission and at onset of pneumonia and patients were followed up till discharge or death. Ethical conduct was maintained during data collection and throughout the research process. Strict confidentiality of information was maintained.

Statistical Methods:

The data were collected, coded and entered into Microsoft Excel sheet. The whole data were rechecked and analyzed using statistical software Statistical Package for Social Sciences (SPSS version 23). Baseline characteristics of the study subjects were explained in terms of frequency, percentage, mean and standard deviation. Association between HAP and various risk factors was analysed using Pearson's chi square test. Fisher's exact test was used when expected count was less than 5. The level of significance was estimated with 95% confidence intervals and p value <0.05.

RESULTS

The age of study population ranged from 15 to 88 years with a mean age of 66.76 and majority of the subjects, 35 out of 50 were in age group of 61-80 years. Eighty four percent of study population was males and most common symptom present was cough with expectoration in 48 out of 50 (96%). Forty seven had breathlessness, forty five had fever, fifteen had chest pain and four had hemoptysis. In the study population of fifty, thirty six (72%) patients had underlying chronic obstructive pulmonary disease, thirty two (64%) had diabetes, twenty five (50%) had hypertension, thirteen (26%) old pulmonary tuberculosis, eleven (22%) ischemic heart disease, six (12%) bronchiectasis, four (8%) bronchial asthma and one person each had chronic liver disease and hypothyroidism. Nine patients (18%) had early onset hospital acquired pneumonia (HAP) and the rest forty one (82%) had late onset HAP. Thirty six of the fifty patients were from medical departments and the remaining 28% from surgical side. Thirty three patients (66%) gave history of prior intravenous antibiotics administration in past three months.

Coming to the course in hospital, fourteen patients (28%) stayed for 6-10 days in hospital, sixteen patients (32%) stayed for 11-15 days, and ten patients (20%) each stayed for 16-20 and 21-25 days respectively. Mean duration of hospital stay of my study population was 14.7 days. C reactive protein elevation was seen in 66% (33 out of 50) of subjects. In the study group twenty two patients (44%) had new infiltrates in chest X-Ray in two lobes, fifteen patients (30%) had a single lobe involvement as per X-Ray and thirteen (26%) had involvement of three lobes. Twenty two patients had bilateral lung involvement which accounted to 44% of the study population.

Ten patients (20%) had to undergo invasive mechanical ventilation. Twenty three patients (46%) developed sepsis over the course of illness and fourteen (28%) went in for septic shock. After treatment twenty eight patients (56%) recovered and twenty two (44%) succumbed to illness despite intensive care. Now moving on to the most important statistics regarding the bacterial profile of hospital acquired pneumonia (HAP) in this part of the country. Thirty eight percentage of sputum isolated *Klebsiella pneumoniae* (*K. pneumoniae*), followed by *Acinetobactor baumannii* (*A. baumannii*) in 28%, *Methicillin* resistant *Staphylococcus Aureus* (MRSA) in 16%, *Pseudomonas aeruginosa* (*Ps.aeruginosa*) in 10%, *Escherichia coli* (*E.coli*) in 4% and *citrobacter* species in 4%. Organisms isolated from sputum culture of early onset HAP subjects were *K. pneumoniae* (44%), *Ps.aeruginosa* (22%), *E.coli* (11%) and those associated with late onset were *K.pneumoniae* (36%), MRSA (19.5%), *A. baumannii* (29%) followed by *Ps.aeruginosa* (7%), *E.coli* (2%) and *Citrobacter spp*.(4%). 78% of study population showed no growth in blood culture. Eight (16%) were positive for MRSA, two showed *A. baumannii* and one was positive for *K.pneumoniae*. The sensitivity pattern of these microorganisms to commonly available broad spectrum antibiotics which are used for empirical therapy is consolidated in table 1. This table will help in initiating empirical antibiotics in suspected HAP patients in central Kerala.

Table 1: Sensitivity pattern of different microorganisms to antibiotics

Antibiotic	K.pneumoniae	Ps.aeruginosa	A.baumannii	E.coli	MRSA	Citrobacter
Ampicillin	R	R	R	R	R	R
Amoxicillin Clavulanic acid	R	R	R	R	R	R
Cefuroxime	R	R	R	R	R	R
Cefotaxime	R	R	R	R	R	R
Cefepime	R	S	R	R	R	R
Cefoperazone-sulbactam	S	S	R	R	R	R
Cotrimoxazole	R	R	S	R	R	R
Gentamicin	R	R	R	R	R	S
Amikacin	S	S	R	S	R	S
Piperacillin-tazobactam	S	S	R	S	R	S
Ciprofloxacin	S	S	R	R	R	S
Levofloxacin	S	S	R	S	S	S
Meropenem	S	S	S	S	R	S
Imipenem	S	S	S	S	R	S
Polymyxin B	S	S	S	S	R	S
Colistin	S	S	S	S	R	S

S – Sensitive R – Resistant

All MSRA patients were sensitive to linezolid and vancomycin. 87.5% were sensitive to cloxacillin, 75% to levofloxacin, 62.5% to tetracycline, 62.5% to teicoplanin and 12.5% to erythromycin.

An attempt was made to assess factors that affect outcome of HAP. Among the history part, only diabetes mellitus and prior intravenous antibiotics administration was found to have statistically significant correlation with outcome of the same. The positive correlation is brought down in table 2 below.

Table 2: Important variables in history and outcome of HAP

Diabetes Mellitus	Outcome		Total	Fischer exact test (P value)
	Recovered	Expired		
Yes	14 (43.75%)	18 (56.25%)	32	5.414 (<0.001)**
No	14 (77.78%)	4 (22.22%)	18	
Total	28 (56%)	22 (44%)	50	
Prior intravenous antibiotic use	Outcome		Total	Fischer exact test (P value)
	Recovered	Expired		
Yes	11 (33.33%)	22 (66.67%)	33	20.23 (<0.001)**
No	17 (100%)	0 (0%)	17	
Total	28 (56%)	22 (44%)	50	

**Statistically significant

No significant difference was noted in age, sex, onset of illness or other premorbidities. Duration of hospital stay was significantly associated with outcome in HAP. 90% of patients with less than ten days of hospital stay survived where as 90% of patients with more than 21 days hospital stay succumbed to illness. No significance was noted in blood investigations including C reactive protein with outcome of HAP. However bilateral infiltrates in chest X-Ray showed a statistically significant correlation with outcome of HAP which is shown in table 3 below

Table 3: Association between bilateral infiltrates in Chest X-Ray and outcome of HAP

Bilateral infiltrates	Outcome		Total	Fischer exact test (P value)
	Recovered	Expired		
Present	5 (22.73%)	17 (77.27%)	22	17.651 (<0.001)**
Absent	23 (82.14%)	5 (17.86%)	28	
Total	28 (56%)	22 (44%)	50	

**Statistically significant

The course of illness was assessed in hospital after giving optimum treatment and intensive and aggressive care. Ten patients had to be intubated and mechanically ventilated during the course of illness however that did not produce any significant difference in the outcome. Twenty three patients went to sepsis and multiple organ damage and fourteen went into septic shock, which had significant effect on outcome. Association with complications and outcome of HAP is given below in table 4.

Table 4: Association between complications and outcome of HAP

Invasive mechanical ventilation	Outcome		Total	Fischer exact test (P value)
	Recovered	Expired		
Yes	3 (30%)	7 (70%)	10	8.030 (0.09)
No	25 (62.5%)	15 (37.5%)	40	
Total	28 (56%)	22 (44%)	50	
Sepsis	Outcome		Total	Chi square test (P value)
	Recovered	Expired		
Present	7 (30.44%)	16 (69.56%)	23	11.298 (<0.001)**
Absent	21 (77.77%)	6 (22.23%)	27	
Total	28 (56%)	22 (44%)	50	
Septic shock	Outcome		Total	Chi square test (P value)
	Recovered	Expired		
Present	2 (14.3%)	12 (85.7%)	14	13.732 (<0.001)**
Absent	26 (72.22%)	10 (27.78%)	36	
Total	28 (56%)	22 (44%)	50	

**Statistically significant

Association between organisms isolated from sputum culture in patients with HAP and outcome was not statistically significant with a P value of 0.983. Thirty nine patients (78%) of HAP did not have any growth in blood culture, of which thirteen patients (33.3%) recovered. One patient had *K.pneumoniae* grown in blood culture and two grew *A. baumannii* and all three expired. Out of eight patients with positive blood culture with MRSA, six expired and only two recovered. So HAP with organism growing in blood, or in other words HAP with bacteremia had very high mortality rate according to this study.

DISCUSSION

Majority of cases of hospital acquired pneumonia occurred in the age group above 60 years. Out of the 50 cases of hospital acquired pneumonia 1 case occurred in the age group under 40 years,12 cases under the age group of 60 ,35 cases were above 60 years and 2 cases above 80 years . Predominance of HAP above the age of 60 years has also been reported in multiple similar studies. [5,6] In this study no association was found between age and outcome (p =0.123). In this study males where predominantly affected with HAP which was not a chance observation as proven by Sopena N et al in a multi-centric study previously. [7] In the present study no difference in mortality was noticed with early onset or late onset HAP where as late onset HAP is considered to have higher mortality worldwide. [8] Diabetes if present was a strong risk factor for mortality associated with HAP according to the present study. Epidemiological studies on outcome of HAP and diabetes have shown conflicting results but generally show a positive correlation between the presence of diabetes and increasing mortality. [9] Prior antibiotic use was found to be the single most important factor affecting outcome of HAP in many of the prior studies along with this one. [10] C reactive protein was not detected to be significant enough tool to diagnose or predict outcome of HAP in this study as in many others. [11] A better alternative will be pro-calcitonin, however cost and limited availability restricts its use. Bilateral involvement of infiltrates is associated with high mortality in hospital acquired pneumonia. In the present study those with bilateral involvement in chest-x-ray 5 cases recovered (22.7%) and 17 cases (77.2%) expired and the association was found to be highly significant statistically which was similar to the classical study done by Wunderink RG et al where they compared radiological diagnosis of autopsy proven ventilator associated pneumonias. [12] In this study out of the 10 cases stayed in hospital for 16-20 days, 3 cases (30%) recovered and 7 cases (70%) expired. Those who stayed more than 20 days 100 % expired which implies that the association between total duration of hospital stay and mortality was found to be highly significant statistically ($p<0.001$) similar to a recent study in United States of America. [13]

Mortality rate in this study was 44% which is consistent with the HAP mortality rates worldwide which range from 37% to 47.3%. [14] In this study, 10 patients who underwent invasive mechanical ventilation following severe pneumonia 7 (70%) expired and only 3(30%) recovered and the association was not statistically significant ($p=0.09$). There is significant disparity in opinion regarding efficacy of mechanical ventilation in improving outcome of HAP. Esperatti M reported poor outcome in patients who underwent invasive ventilation. [15] Whereas Alotair et al study reported an improvement in patients who required mechanical ventilation following severe pneumonia. [16] So this part it would be better to leave it to the discretion of treating doctor and his experience with ventilator dynamics. Early intubation and aggressive therapy may be the choice of a few, where as a guarded approach may be selected by the rest. In a financially restricted population a guarded approach may be deemed appropriate. In our study, out of the 23 cases that developed sepsis 16 cases (69.56%) expired and 7 cases

(30.43%) recovered and out of the 14 cases that went into septic shock 2 cases (14.2%) recovered and 12 cases (85.7%) expired. There is no difference of opinion regarding sepsis and septic shock in the two above mentioned international studies by Esperatti and Alotair. Hence special precautions and aggressive treatment must be done in those with sepsis or septic shock as they are universally recognized predictors of increased mortality.

K. pneumoniae was the predominant pathogen isolated in this study. It was closely followed by *A. baumannii*. Other significant culprit bacteria were *MRSA*, *Ps.aeruginosa*, *E.coli*, and *Citrobacter*. Blood culture showed significant growth mainly in late HAP and majority of the culture isolated MRSA. K.pneumoniae and MRSA were the commonest organisms causing HAP according to the microbial prediction of ATS/IDSA 2005 and in a review article done by Chao-Hsien Lee et al in 2008. [17] The frequency of specific multidrug resistant (MDR) pathogens causing HAP may vary by hospital, patient population, exposure to antibiotics and type of intensive care unit. The most common pathogens isolated from sputum culture and sensitivity in our study associated with early onset HAP were *K.pneumoniae* (44%) followed by *Ps.aeruginosa* (22%) , *E.coli*(11%) and those associated with late onset were *K.pneumoniae* (36%), *MRSA* (19.5%), *A. baumannii* (29%) followed by *Ps.aeruginosa* (7%), *E.coli*(2%) and *Citrobacter spp*.(2%) . The theory put forth decades prior that patients with early onset HAP who received antibiotics recently or had an admission to a health care facility are at risk for colonization and infection with MDR pathogens is a fact which was proven again in this study. [18] All the cases with bacteremia caused by *A. baumannii* and *K.pneumoniae* expired and 75% of those infected with MRSA expired and 25% recovered. So having MDR pathogens in sputum is something, whereas having the same in blood escalates the danger much more. Bacteremia is a major cause of mortality which shows the importance of timely blood cultures and following up the results. [19] Early aggressive treatment with the right empirical antibiotics may restrict systemic dissemination of the bacteria and hence presumptive empirical treatment is of paramount importance. So knowledge about pathogenic flora around the hospital we work along with their sensitivity pattern is essential to deal HAP successfully.

CONCLUSION

The clinical profile of HAP in this part of Kerala is similar to other parts of world. HAP was found to be more common in elderly, especially those with diabetes and who received prior antibiotic injections in near past. Prolonged hospital stay, sepsis, septic shock and bacteremia were associated with high mortality. Late onset HAP was more common than early onset HAP. Most common organism isolated from sputum was *K.pneumoniae* followed by *A. baumannii*. MRSA was the most common growth in blood culture. MRSA was grown in blood culture mainly in late HAPs. C reactive protein was found to have no role in outcome of HAP; but chest X-Ray was of immense help as bilateral new infiltrates were associated with poorer outcome and need more care. Overall mortality rate in the study population was 44%. Surveillance of HAP and prompt recognition of the above mentioned factors may provide valuable guidance for empirical antimicrobial followed by pathogen specific treatment and may even predict the outcome in patients with HAP.

Recommendations:

Use antibiotics judiciously. Prior careless antibiotic use was associated with re-infection with drug resistant strains and thus more severe infections. Similar studies can be conducted in different areas to know the main microbiological flora producing HAP and their sensitivity pattern as that will help in planning empirical antibiotic treatment. Special care must be given for diabetic and other immunocompromised patients as outcome was grave in their case.

Ensure fluid therapy and supportive care to avoid hypotension as septic shock was proven to cause a downhill course of illness. Frequent disinfection of hospital wards, intensive care units and frequent hand washing of care providers must be done to prevent hospital acquired infections as they are associated with very high mortality and prevention is always better than cure.

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