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A retrospective comparative study of empirical antibiotic treatment of hospital-acquired pneumonia at a tertiary care hospital in South India.

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ABSTRACT

Hospital-Acquired Pneumonia (HAP) continues to be a major cause of morbidity and mortality among hospitalised patients despite the introduction of broad spectrum antimicrobial agents, complex supportive modalities and the use of preventive measures. There is a paucity of data on HAP from India. Patients aged 18 years or older admitted to Kasturba Hospital, a tertiary care hospital in Manipal, Karnataka during the period 01/01/2005 through 31/12/2007 and diagnosed to have HAP were included in this retrospective comparative study. We identified 200 patients with HAP, who fit the inclusion and exclusion criteria during the study period. Common isolates included *Pseudomonas aeruginosa* (30%), MRSA (17%) and *Acinetobacter spp*. (15.5%). The most frequently used antibiotic regimens were Piperacillin-Tazobactam (32%), Ciprofloxacin-Amikacin (12.5%), Meropenem (11%) and Levofloxacin (10.5%).

Keywords: Retrospective study, Hospital acquired pneumonia, Tertiary care hospital

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INTRODUCTION

Hospital-acquired pneumonia (HAP) is one of the most common causes of morbidity and mortality among patients admitted to a hospital. It has been estimated that between one third to one half of all HAP deaths occur as a direct result of the infection, while the rest would not be expected to survive an episode of HAP, even with appropriate antimicrobial therapy [1]. This has raised doubts about benefits from antibiotic use in HAP patients not dying from other causes [2]. The incidence of HAP, risk factors and the antibiogram patterns vary across and within countries, and even seasonally within the same hospital [3].

There are very few published studies on the epidemiology and treatment of HAP from India. While current guidelines recommend consideration of local microbiologic data when selecting empirical treatment for hospital-acquired pneumonia, few specifics of how to do this have been offered. In this study, we report epidemiology, pathogens, sensitivity pattern and efficacy of various empirical antibiotic regimens used in the treatment of HAP in patients admitted to a tertiary care hospital in south India.

MATERIALS AND METHODS

This was a retrospective study with collection and analysis of data of hospital acquired pneumonia patients diagnosed and treated at a tertiary care hospital in south India from January 2005 through December 2007. The patients aged 18 years or above and of both sexes who were immunocompetent and not suffering from HIV infection, active tuberculosis or cystic fibrosis were included in the study. Patients undergoing active treatment for cancer or with a history of organ transplantation were not included.

HAP was diagnosed if patient had a new or persistent infiltrate on chest X-ray and two of the following:

- Sputum/blood culture positive for causative organisms
- Pyrexia – Temperature <36^{o} C or >38^{o}C
- Signs and symptoms of pneumonia (Purulent sputum in non-intubated patients or tracheal secretions in intubated patients; Increased inhaled oxygen requirement; Cough; Increased respiratory rate)
- Blood leucocytosis (>11,000 cells per dl) or leukopenia (<4000 cells per dl).

Data regarding the age and sex, signs and symptoms, clinical and laboratory investigations, antibiotic regimen used and adverse effects encountered if any was recorded. Incidences of Hospital Acquired Pneumonia in different age groups, sex-wise distribution and adverse effects of various antibiotic regimens were expressed in percentage. Overall clinical, radiological and sputum improvement for various antibiotic regimens were calculated using the Kruskal-Wallis non parametric test for K independent samples. This was followed by Post Hoc analysis with Mann-Whitney U test for 2 independent samples to compare outcomes among the various regimens. This was done using SPSS 14.0 statistical software package.

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RESULTS

200 patients admitted during the study period who met the inclusion and exclusion criteria were included in the study. The incidence of HAP was higher among the elderly with a peak incidence of 26.5% in patients aged 65 years and above. There was a clear male preponderance with 71.5% of the patients suffering from HAP being of the masculine gender.

Hospital-acquired pneumonia is classified as early onset if signs and symptoms manifest after 2 days and within 4 days of hospitalization and when pneumonia occurs after 5 days of hospitalization it is termed as late-onset HAP [4]. Of the 200 patients included in the study 125 (67.5%) of the patients had early-onset HAP while the rest had late-onset of HAP.

Pseudomonas aeruginosa (30%), Methicillin-Resistant *Staphylococcus aureus* (MRSA) (17%) and *Acinetobacter spp*. (15.5%) were the most common pathogens isolated from patients with hospital-acquired pneumonia (Fig-1). It was however observed that the causative microorganisms in late-onset HAP differ from those in early-onset pneumonia in frequency. Late-onset HAP was more likely due to MRSA (30.7%), followed by *Acinetobacter spp*. (28%) and *Pseudomonas aeruginosa* (15.1%) (Fig-2). While MRSA and *Acinetobacter spp*. accounted for 9% and 8% of cases respectively in early-onset HAP; the most common organisms in this group were *Pseudomonas aeruginosa* (39.2%) and *Klebsiella pneumoniae* (13.6%) (Fig-3).

Among the other organisms –

- The MRSA (n=23) were all sensitive to Vancomycin and Cefoperazone plus Sulbactam.
- 96% of *S.pneumoniae* (n=8) were sensitive to Ampicillin, Amoxicillin-Clavulinic acid and Cefotaxime, 76% were sensitive to Penicillin, 84% were sensitive to Erythromycin and 72% were sensitive to Ciprofloxacin.
- H.influenzae (n=4) isolated were all sensitive to Ampicillin, Amoxicillin-Clavulinic acid, Erythromycin, Ciprofloxacin and Co-trimoxazole, while 81.8 % were sensitive to Cefotaxime.

The efficacies of different antibiotic regimen were calculated based on clinical signs and symptoms, sputum/blood cultures and chest radiographs. The overall mortality associated with HAP was 23% and complete recovery was seen in 72% of the patients. 5% of the patients either worsened or showed no improvement and were lost to follow-up. It was observed that the mortality in late-onset HAP (48%) was six times higher than the corresponding outcome in early-onset HAP (8%) (Table-2).

Comparison was carried out between monotherapy regimen and combination therapy regimen using 2 independent samples Mann-Whitney test; individual regimens were compared amongst each other using Kruskal-Wallis non parametric test for K independent samples, followed by Mann-Whitney test for post hoc analysis.

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Antibiotics which where used as monotherapy were placed in one group and those used in combination were placed in another group. Mann-Whitney 2 independent samples test showed no significant difference in the outcome following empirical monotherapy or combination therapy for HAP.

The most frequently used antibiotic regimens (Piperacillin-Tazobactam, Meropenem, Ciprofloxacin plus Amikacin, Levofloxacin, Vancomycin, Vancomycin plus Ciprofloxacin) were compared (Table-6). There was no significant difference among the various regimes in terms of clinical outcome among the patients**.**

Fig 1 – Causative organisms isolated in HAP (n=129)

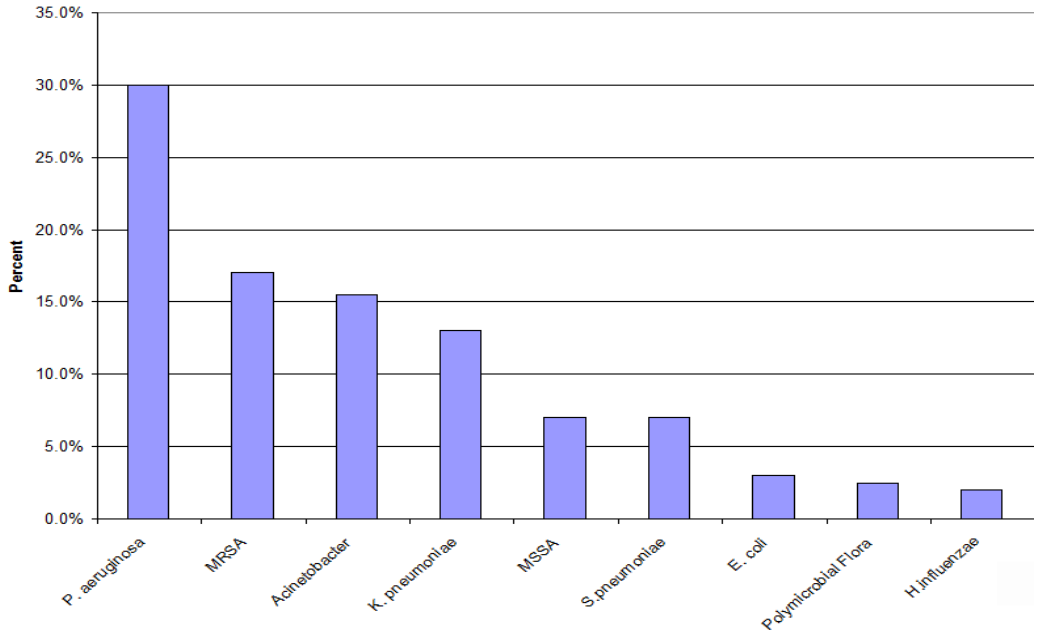

Fig 2 – Causative organisms in Early-onset HAP (n=91)

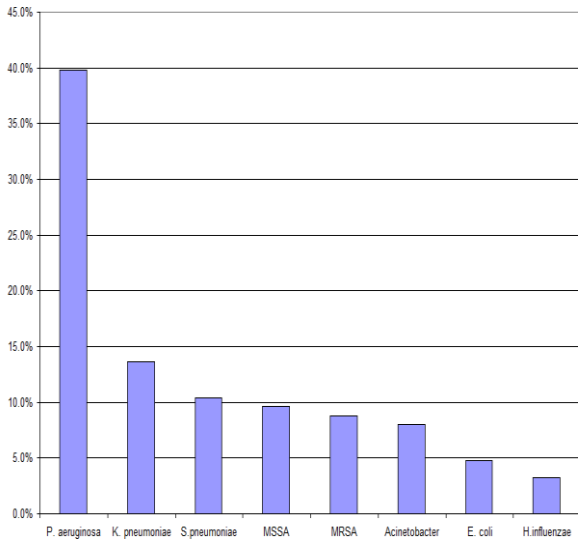

Fig 3 – Causative organisms in Late-onset HAP (n=38)

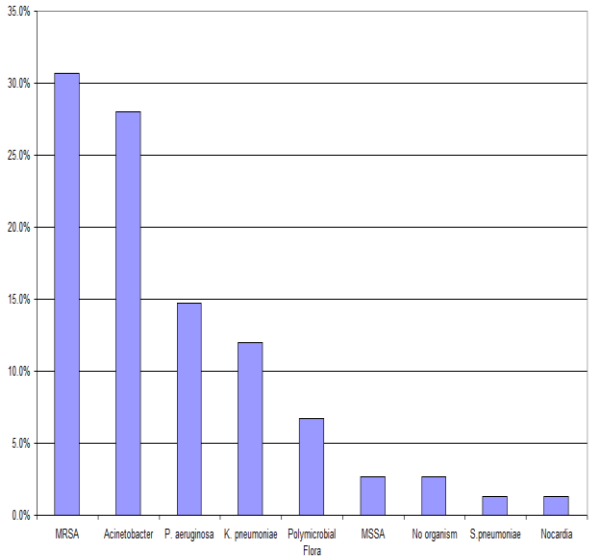

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Table 1 – Sensitivity and Resistance pattern of commonly isolated organisms in HAP

Antibiotic / Organism	Amk	Czd	Cfp	Genta	Netil	Oflox	Piper	Tobra		
Pseudomonas (n=38)	S – 27 R – 11	S – 32 R – 6	S – 15 R – 23	S – 19 R– 19	S – 28 R – 10	S – 23 R – 15	S – 24 R –14	S – 23 R – 15		
Antibiotic / Organism	**Amk**	**Czd**	**Cfp**	**Cft**	**Netil**	**Oflox**	**Cipro**	**Imp**	**Amp**	**Am - Cl**
Acinetobacter (n=20)	S – 4 R – 16	S – 0 R – 20	S – 2 R – 18	S – 0 R–20	S – 14 R – 6	S – 10 R – 10	S – 2 R - 18	S – 0 R -20	S – 2 R - 18	S – 0 R - 20
Antibiotic / Organism	**Amk**	**Czd**	**Cfp**	**Cft**	**Netil**	**Oflox**	**Cipro**	**Imp**	**Amp**	**Am - Cl**
Klebsiella (n=18)	S – 15 R – 3	S – 8 R – 10	S – 8 R – 10	S – 7 R –11	S -11 R – 7	S – 12 R – 6	S – 9 R – 9	S – 14 R – 4	S – 3 R – 15	S – 10 R – 8

(Amk = Amikacin; Amp = Ampicillin; Am-Cl – Amoxicillin plus Clavulinic acid; Cfp = Cefoperazone; Cft = Cefotaxime; Cipro = Ciprofloxacin; Czd = Ceftazidime; Genta = Gentamicin; Imp = Imipenem; Netil = Netilmicin; Oflox = Ofloxacin; Piper = Piperacillin; Tobra = Tobramycin)

Table 2 - Clinical Outcome in HAP Following Antibiotic treatment

Outcome	Overall	Early-Onset	Late-Onset
No Change	4(2%)	3(2.4%)	1(1.3%)
Improved	144 (72%)	111(88.8%)	33(44%)
Worsened	6(3%)	1(0.8%)	5(6.7%)
Expired	46(23%)	10(8%)	36(48%)
Total	200	125	75

Table 3 - Antibiotic Regimen used in HAP

Regimen	No. of Patients	Percentage
Piperacillin-Tazobactam	64	32
Ciprofloxacin plus Amikacin	25	12.5
Meropenem	22	11
Levofloxacin	21	10.5
Vancomycin plus Ciprofloxacin	17	8.5
Vancomycin	17	8.5
Ciprofloxacin plus Gentamicin	11	5.5
Cefoperazone plus Sulbactam	6	3.0
Ceftriaxone-Tazobactam	5	2.5
Ceftazidime	5	2.5
Ceftriaxone	3	1.5
Linezolid	3	1.5
Ciprofloxacin	1	0.5

DISCUSSION

Appropriate antibiotic therapy significantly reduces the mortality associated with HAP. Multiple regimens of antibiotics are available, the choice of the which is influenced by the patient's recent antibiotic therapy (if any), the resident flora in the hospital or intensive care unit, the presence of underlying diseases, available culture data, and whether the patient is at risk for MDR pathogens. The present study was undertaken to compare the efficacy of various antibiotic regimens used at Kasturba Hospital, Manipal during the period January 2005 to December 2007 in the treatment of HAP.

The preponderance of HAP among the elderly (age > 65) and in the male gender (78.5%) in our study co-relates well with findings from previous studies, which have highlighted age >70 and male gender as risk factors for development of HAP [5-8].

Causative organisms in HAP can be varied from the nasopharyngeal commensals such as *streptococci, H.influenzae* to drug resistant organisms such as MRSA, *Pseudomonas aeruginosa* and *Acinetobacter spp*. There is difference in the type of organism from hospital to hospital and also the onset of HAP [4,9,10]. In this study *Pseudomonas aeruginosa* (30%), MRSA (17%) and *Acinetobacter spp*. (15.5%) were the predominant organisms. This correlates well with data from previous studies conducted in India which have shown Pseudomonas aeruginosa (33.3% and 55%) to be the commonest isolate from HAP patients followed by Staphylococcus aureus (29% and 17.5%), Acinetobacter (13.1% and 20%) and Klebsiella pneumoniae (15.5% and 7.5%) [11,12].

With relation to onset of HAP, a review by Donald EC and Kathleen AS found that the predominant organisms in early-onset HAP are the core organisms - *Pseudomonas spp*., *E.Coli*, *Klebsiella spp*., *H. Influenzae,* and gram-positive organisms such as MSSA and *Streptococcus pneumonia* [13]. We found that *Pseudomonas aeruginosa* (39.2%) and *Klebsiella pneumoniae* (13.6%) were the most common organisms in early-onset HAP. The organisms in late-onset pneumonia differed in frequency with MRSA (30.7%) being the most common followed by *Acinetobacter spp*. (28%) and *Pseudomonas aeruginosa* (15.1%). Studies in western countries have shown that late-onset pneumonia is more likely to be due to multi drug resistant organisms with higher incidence of MRSA, *Acinetobacter* and *Legionella* among other organisms [4].

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