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Research Article

Community acquired pneumonia due to gram negative bacilli and its antibiotic sensitivity pattern in a tertiary care centre

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ABSTRACT

Background: Gram negative bacteria along with *Pseudomonas* constitute a significant cause of morbidity and mortality due to pneumonia. As a result it is essential to have appropriate empirical antimicrobial treatment strategies based on the sensitivity pattern of a particular region. In cases with high likelihood of gram negative pneumonia it is essential to start appropriate empirical antibiotics as early as possible to reduce the morbidity and mortality. This study is done to know the antibiotic pattern of gram negative organisms isolated from the institute so that the study can constitute an empirical antibiotic regimen.
Methods: A retrospective study was done from January to March 2016. Patients admitted in the medicine and pulmonology department of the hospital who were diagnosed to have pneumonia symptoms. Patients with symptoms, signs and radiological features of pneumonia and sputum cultures with gram negative organisms were included in the study. Gram staining of all samples were taken and bartlet grading was done. All the sputum samples were cultured on blood agar, chocolate agar and macconkey agar. The colonies were then identified using biochemical tests. Antibiotic sensitivity was done following CLSI 2015 guidelines. We also tested for Amp C, ESBL and MBL using standard testing protocol.
Results: During the study period in 120 cases of pneumonia, there was growth of pathogenic organism. Among the GNB isolated *Klebsiella spp* was the most common organism isolated at 33.9% followed by *Pseudomonas aeruginosa* and *Escherichia coli* at 22.1%. Out of the 53 gram negative samples isolated 4 (7%) were *Amp C* positive, 10 (18.8%) were ESBL positive and there was one single case of MBL. The antibiotic sensitivity showed that all the isolates were sensitive to colisitin (100%), while *Klebsiella spp*, *Pseudomonas spp*, and *Escherichia coli* were 100% sensitive to imipenem and meropenem. Resistance pattern of all the isolates showed that the isolates exhibited high resistance to amoxycillin-clavulunate, cefuroxime and cotrimoxazole. While resistance against ceftazidime and cefipime was >40%. On the other hand, isolates showed a low level of resistance against piperacillin tazobactam and cefoperazone-sulbactam. Extremely low level of resistance was observed against imipenem and meropenem, while colistin showed no resistance among the isolates obtained in this study.
Conclusions: The study showed that gram-negative bacteria and *P. aeruginosa* form a relevant part of the microbial pattern of CAP in patients who require hospitalization, particularly those with severe CAP. Initiating antibiotics with gram negative coverage should be considered in this subgroup of patients since initiating the correct antibiotic plays a critical role in the outcome of pneumonia.

Keywords: Community acquired pneumonia, Gram negative bacilli, Pseudomonas, Colistin

INTRODUCTION

Pneumonia management is complex and the current guidelines require an initial empirical antimicrobial treatment.[1-3] This approach is based on microbial patterns derived from several large prospective epidemiological series originating from different regions. Gram negative bacteria along with *Pseudomonas* constitute a significant cause of morbidity and mortality due to pneumonia. As a result it is essential to have appropriate empirical antimicrobial treatment strategies based on the sensitivity pattern of a particular region. In cases with high likelihood of gram negative pneumonia it is essential to start appropriate empirical antibiotics as early as possible to reduce the morbidity and mortality.

The incidences of CAP in the general population have been quite variable, ranging from 0% to 9% for GNB and 0% to 5% for P aeruginosa.[4-7] On the other hand, these pathogens have repeatedly been found to bear an adverse prognostic potential.[8] Numerous anti-pseudomonal antibiotics are used currently for the treatment of bronchial infections, including ticarcillin, carbenicillin, piperacillin, tazobactam, tobramycin, gentamicin, amikacin, ciprofloxacin, ceftazidime, imipenem, cilastatin and aztreonam. However, resistance to these agents is becoming more prevalent.[9]

Given these variations and the potentially serious prognosis, it seems useful to determine which patients are at risk for these infections, thereby providing an additional target to ensure the adequacy of antimicrobial treatment and obviating the need for a general antimicrobial coverage of these pathogens in all patients. Several recent studies have reported the presence of multidrug-resistant bacteria at hospital admission in patients with severe pneumonia.[10] Nonfermenting gram-negative bacilli, including *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, are the most frequently isolated multidrug-resistant bacteria.[11] So this study is done to know the antibiotic pattern of gram negative organisms isolated from the institute so that the study can constitute an empirical antibiotic regimen.

METHODS

A retrospective study was done from January to March 2016 at Sree Gokulam Medical College and Research Foundation, Venjaramoodu, Thiruvananthapuram, Kerala, India. Patients admitted in the medicine and pulmonology department of the hospital who were diagnosed to have pneumonia symptoms.

Inclusion criteria

Patients with symptoms, signs and radiological features of pneumonia and sputum cultures with gram negative organisms were included in the study.

Exclusion criteria

- Hospitalization within the last 7 days.
- Severe immune suppression (eg, solid organ or bone marrow transplantation, neutropenia [<1000/µL], human immunodeficiency virus infection) or treatment with oral corticosteroids in daily doses of at least 20 mg/d of a prednisone equivalent for more than 2 weeks or with azathioprine sodium, cyclosporine, or cyclophosphamide.
- Other alternative diagnoses emerging during the hospital stay.

Details of history and clinical examination were collected. X-ray of all the patients were reviewed by the pulmonologist.

Sputum samples were sent to the microbiology lab for

- Gram staining.
- Culture and identification.
- Antibiotic sensitivity.

Grams staining of all samples were taken and bartlet grading was done.

All the sputum samples were cultured on blood agar, chocolate agar and macconkey agar. The colonies were then identified using biochemical tests. Antibiotic sensitivity was done following CLSI 2015 guidelines. We also tested for Amp C, ESBL and MBL using standard testing protocol.

RESULTS

During the study period in 120 cases of pneumonia there was growth of pathogenic organism. Among them 53 were found to have gram negative origin. Majority of cases were males (30) to female (23). Among the GNB isolated *Klebsiella spp* was the most common organism isolated at 33.9% followed by *Pseudomonas aeruginosa* and *Escherichia coli* at 22.1%.

Table 1: GNB organism isolated from the sputum samples.

Organism	Nos (%) Total =53
Klebsiella spp	18 (33.9%)
Pseudomonas aeruginosa	12 (22.1%)
Escherichia coli	12 (22.1%)
Acinetobacter spp	11 (20.7%)

Bacterial growth was polymicrobial in 3 cases. Out of the 53 gram negative samples isolated 4 (7%) were Amp C β-lactamases (Amp C) positive, 10 (18.8%) were extended-spectrum beta-lactamases (ESBL) positive and there was

one single case of metallo-beta-lactamase (MBL). Out of these maximum resistance mechanism were observed in *Klebsiella spp* followed by *Acinetobacter spp* and there was a single case of *E coli* showing the resistant strain.[6,8]

Table 2: Sputum culture showing polymicrobial growth.

Polymicrobial growth isolated	No of cases
Klebsiella spp+Acinetobacter spp	2
Pseudomonas spp+Acineotobacter	1
Total	3

The antibiotic sensitivity showed that all the isolates were sensitive to colisitin (100%), while *Klebsiella spp*, *Pseudomonas spp*, and *Escherichia coli* were 100% sensitive to imipenem and meropenem.

Resistance pattern of all the isolates when analysed as a group against various classes of antibiotics showed that the isolates exhibited high resistance to amoxycillin-clavulunate, cefuroxime and cotrimoxazole.

Table 3: Drug resistance type.

Drug resistance type	Nos	Organism
AmpC β-lactamases (Amp C)	4	*Klebsiella spp* (2)+*Acinetobacter spp* (2)
Extended-spectrum beta-lactamases (ESBL)	10	*E.coli* (1) + *Klebsiella spp* (6)+ *Acinetobacter spp* (3)
Metallo-beta-lactamase (MBL)	1	*Acinetobacter spp*

Table 4 : Antibiotic sensitivity pattern of gram negative bacilli isolated.

Antibiotics	Organism			
	Klebsiella spp (18) Sensitivity (%)	*Pseudomonas aeruginosa* (12) Sensitivity (%)	*E coli* (12) Sensitivity (%)	*Acinetobacter spp* (11) Sensitivity (%)
Cefuroxime	0		0	0
Amoxycillinclavulunic acid	0		0	0
Ceftazidime	44.4	41.6	50	45.4
Cefipime	44.4	50	50	45.4
Amikacin	44.4	58.3	58.3	49.7
Cotrimoxazole	16.6	0	25	27.2
Ciprofloxacin	27.7	8.3	25	27.2
Cefaperazonesulbactum	77.7	66.6	83.3	72.7
Piperacillin tazobactum	88.8	83.3	91.6	81.8
Imipenem	100	100	100	90.9
Meropenem	100	100	100	90.9
Colistin	100	100	100	100

While resistance against ceftazidime and cefipime was >40%. On the other hand, isolates showed a low level of resistance against piperacillin tazobactam, and cefoperazone-sulbactam. Extremely low level of resistance was observed against imipenem and meropenem, while colistin showed no resistance among the isolates obtained in this study.

DISCUSSION

Community-acquired pneumonia (CAP) remains a major cause of morbidity and mortality. A causative agent is identified in 30% to 40% of cases.[12] The initial antibiotic therapy plays a critical role in the outcome of pneumonia. The infectious diseases society of America pneumonia guidelines recommend gram staining and culture of expectorated sputum for inpatients with CAP.[13] The reasons for this recommendation are to permit optimal antibiotic selection directed to the causative agent; to limit injudicious antibiotic use in terms of cost; to limit inducible resistance and adverse drug reactions; to support a rational basis for change from parenteral to oral therapy and any change in therapy necessitated by an adverse drug reaction; to identify drug resistant pathogens.[13]

In this study almost 50 % of cases which yielded growth among sputum samples were Gram negative bacilli in nature. This is a growing problem which needs to be considered. The role of GNB has been subject to considerable debate. In the general population of patients with CAP, only 4 recent studies had a proportion of greater than 3% of CAP due to GNB the highest reaching 9%.[5,6] In this study, isolated GNB from 8% of the cases is in concordance with the above studies done by Lim et al and Jian et al.[5,6] In this study, the incidence of GNB was

8% and within the range expected. However, with an incidence of high percentage of *P aeruginosa* and *Acinetobacter spp.*

Possible explanations for this particularly high incidence include a higher proportion of patients with severe CAP. Gram-negative bacteria may easily colonize the tracheobronchial tree in the presence of any alterations or damage of the respiratory epithelium. A critical issue consists in the criteria for an etiological diagnosis of GNB. A definite proof for the involvement of these pathogens and to rule out whether the organism were colonizers or not, for that the study clinically correlated with clinical signs and also repeat culture.

Isolation of gram negative bacteria in the culture of any respiratory secretion cannot be taken to establish a definite etiologic diagnosis of CAP due to GNB or pseudomonas. Nevertheless, in view of the potential continuum of bronchitis and pneumonia and of the adverse prognostic potential of these pathogens, it seems to be prudent to consider any corresponding isolate in valid cultures of lower respiratory tract secretions at least as a probable underlying pathogen.[14]

Antibiotic sensitivity showed that majority of isolates were resistant to cephalosporins and aminoglycosides. This is in concordance with majority of the other studies which showed that higher drugs like piperacillin tazobactum and penems were preferred.

This study bears significant implications for the management of CAP that might influence future updates of management guidelines.

CONCLUSION

The study has showed that gram-negative bacteria and *P.aeruginosa* form a relevant part of the microbial pattern of CAP in patients who require hospitalization, particularly those with severe CAP. Initiating antibiotics with gram negative coverage should be considered in this subgroup of patients since initiating the correct antibiotic plays a critical role in the outcome of pneumonia.

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