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An Upsurge of Gram Negative Bacteria in Community Acquired Pneumonia: An Alarming Trend!

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Abstract

Introduction: Community acquired pneumonia (CAP) is a significant cause of morbidity and mortality in adults. While gram positive and atypical organisms are the common etiological agents of CAP, gram negative bacteria (GNB) are emerging as a significant etiological risk.

Aim: The purpose of the present study was to evaluate the incidence of CAP due to gram negative bacteria along with assessment of risk factors and patient's clinical profile.

Methods: 119 patients, hospitalized and diagnosed with CAP on the basis of ATS guideline, over a period of one year from July 2015 to May 2016 were studied prospectively. Each patient's clinical profile and blood investigations were correlated with the growth of a particular organism in sputum culture.

Results: Growth of bacterial organisms in sputum culture was positive in 78 patients (65.5%) and negative in 41 patients (34.4%). Though *Streptococcus pneumoniae* was the predominant causative organism of CAP in 35.2% cases (n=42), GNB had an equivalent incidence collectively (30.2%) seen in 36 out of 119 patients. Among GNB, *Klebsiella* species was the most common organism isolated followed by *Pseudomonas aeruginosa* (27.7%), *E.coli* (13.9%), *Acinetobacter* (11.08%), *Haemophilus influenza* (8.3%) and *Moraxella catarrhalis* (2.8%) in the descending order of incidence. 50-60 year age group was most commonly affected; males (69.7%) outnumbered females (30.3%). Yellow sputum (p=0.02), SPO₂ <88% (p<0.05), systolic blood pressure <106mmHg (p<0.05) and total leukocyte count >10,000/mm³ (p=0.009) had significant correlation with the growth of GNB in sputum. Smoking, alcoholism and other co morbidities had no significant correlation with the growth of organism in sputum culture.

Conclusion: Gram negative bacteria are emerging as an important etiological risk for CAP. Providing timely and adequate coverage for GNB, while covering the common etiological organisms of CAP, seems to be the need of the hour.

Keywords: Bacteria; Community acquired pneumonia

Introduction

Community Acquired Pneumonia (CAP) is defined as inflammation and consolidation of lung tissue due to an infectious agent which develops outside the hospital. A clinical definition of pneumonia is two or more of the following symptoms/physical findings: productive cough, purulent sputum, dyspnoea or tachypnea (respiratory rate >20 breaths/min), rigors or chills, pleuritic chest pain in conjunction with a new opacity on chest radiograph [1].

CAP is a common and potentially serious illness. It is the main cause of morbidity and mortality, which particularly targets elderly patients and those with co-morbid conditions. Because of the lack of epidemiological surveys, a clear population-based statistics on the condition is not available so far. In the United States, CAP occurs in 4 million adults and is the eighth leading cause of mortality there [1].

In India, the situation is no different from the rest of the world. No proper field surveys have been conducted in India so far to generate concrete data for epidemiology of CAP [2]. The epidemiology

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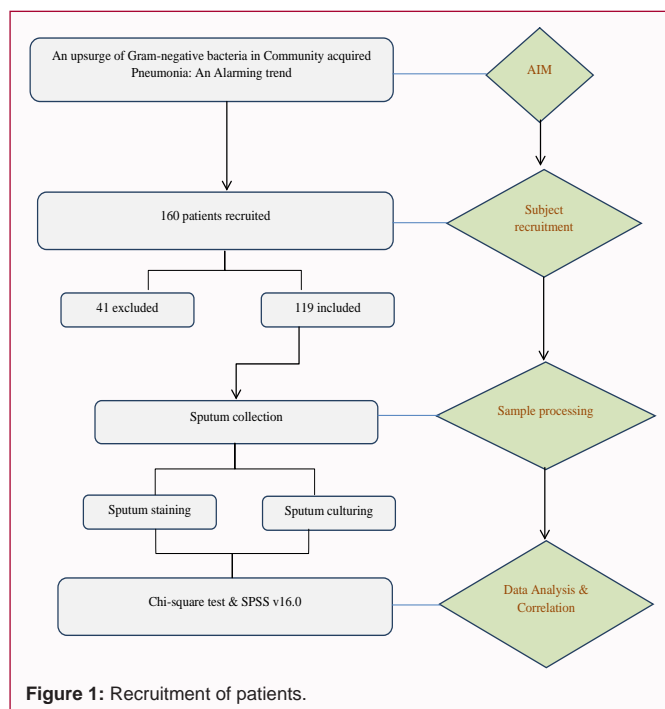


Figure 1: Recruitment of patients.

of pneumonia has changed in the recent years. This is partly due to changes in population at risk and in part to the discovery of new microbial agents that cause pneumonia such as *S. pneumoniae*, *H. influenzae* and *S. aureus* [1].

Till now, gram positive organisms have been considered as the main causative organisms responsible for CAP. In the present study, we observed the emergence of gram negative bacteria to be significant and an equivalent cause for CAP. Emergence of Gram Negative Bacilli as causative organism for CAP is a new territory and may be alarming for the physicians.

Materials and Methods

Sample selection

A prospective, community based study, was conducted at Subharti Medical College, Meerut, Uttar Pradesh after approval from Institutional Ethical committee. Patients admitted in the Department of Respiratory Medicine, fulfilling the criteria of CAP on the basis of American Thoracic Society Guidelines were studied from July 2015 to May 2016.

Inclusion criteria:

- Patients fulfilling the criteria of CAP on the basis of ATS guideline.

- All patients more than 18 years of age.

Exclusion criteria:

- Any patient hospitalized in the previous 7 days.
- Immuno-compromised or severe immune suppression status.

- Other alternative diagnosis emerging during the hospital stay.

Detailed history and thorough clinical examination was done in all patients. Chest X ray of all patients were reviewed. Patients were

also evaluated with complete blood counts, kidney function test and liver function test.

Early morning deep coughed sputum sample was collected from all participants according to standard guideline [2]. Within 24 hours of admission, patients were asked to collect sputum in a sterile wide mouthed container with a screw cap after rinsing the mouth twice with water and antiseptic solution so as to avoid oral contamination of the sample collected. Sputum was transported to the department of Microbiology within 2 hours of collection.

Self-induced sputum sample were sent to Microbiology lab for:

1. Gram's staining.
2. Ziehl Neelsen staining for acid fast bacilli.
3. Aerobic pyogenic culture.

After Gram's staining, Bartlett grading was done and cultures reported after quantitative growth measurement. MacConkey's, Blood agar and chocolate agar media were used. Biochemical tests were used for identifying the colonies.

Data analysis

The collected data were tabulated and analyzed by using the statistical package SPSS (Statistical Package for Social Sciences) version 16.0 for Windows. Chi square tests of significance were carried out to test the differences between proportions. Association between variables was considered statistically significant if p-value was < 0.05.

Results

At the end of the study period, 160 patients were recruited initially. Out of these, 41 patients were excluded from the study as 16 patients were diagnosed to be suffering with tuberculosis while 25 patients refused to enrol in the study. Excluding these patients, data of 119 patients was analysed (Figure 1).

In the study group of 119 patients, 83 patients (69.7%) were males and 36 (30.3%) were females. Patients' included in the study belonged to a wide range of age from 21 years to 92 years. The mean age of the study group was 44.45 years (Table 1,2).

Significant bacterial growth (>10⁵CFU/ml) was observed in sputum aerobic culture of 78 patients out of which Gram Positive Bacterial (GPB) growth was observed in 42 (35.3%) patients, while

Table 1: Sex distribution.

Gender	No. of patients	GNB infection
Male	83	25
Female	36	9

Table 2: No. of patients according to GNB infection in sputum according to the age group.

Age group (Years)	No. of patients
21-30	3
31-40	2
41-50	3
51-60	13
61-70	6
71-80	8
>81	1

Table 3: History of smoking in patients infected with Gram negative bacterial infection.

History of smoking	No. of patients
Yes	19
No	17

Table 4: GNB organism isolated from the sputum samples.

Organism	n=36	Percentage (%)
<i>Klebsiella</i> sps.	13	36.1
<i>Pseudomonas aeruginosa</i>	10	27.7
<i>Escherichia coli</i>	5	13.8
<i>Acinetobacter</i> sps	4	11.1
<i>Haemophilus influenza</i>	3	8.3
<i>Moraxella catarrhalis</i>	1	2.7

Table 5: Correlation of colour of sputum with presence of gram negative bacteria in sputum.

Colour of sputum	No. of patients	p- value
Green	9	Ns
Grey	5	Ns
White	10	Ns
Yellow	14	0.02

*ns= not significant.

Table 6: Correlation of SBP with gram negative infection in sputum.

Systolic blood pressure (SBP)	No. of patients	p- value
More than 106	20	ns
Less than 106	16	<0.05

*ns= not significant.

sputum culture of 36 (30.3%) patients revealed growth of Gram negative bacteria. Polymicrobial growth was not seen in any culture. No growth was present in sputum culture of 41 (34.4%) patients (Table 3.4).

Out of the total 36 patients who had gram negative bacterial infection 25 were male and 9 were female. The maximum number of cases were that of *Klebsiella* species (13), followed by *Pseudomonas* (10). Furthermore, *E.coli* constituted 5 of the 36 patients followed by *Acinetobacter* (4), *H. influenza* (3) and *Moraxella catarrhalis* (1) (Table 5.6).

In all 36 (30.3%) patients with GNB infection, 14 patients had yellow coloured sputum followed by white (10), green (8) and grey (4) colour sputum. Presence of yellow sputum also had significant correlation with gram negative growth (p=0.020).

A positive correlation was found with low systolic blood pressure and growth of Gram negative bacilli in sputum. 20 (55.5%) patients had SBP>106mmHg and 16 (44.44%) patients had SBP< 106(p<0.05). Patients presenting with SPO₂<88% were 23 out of 36 (68.8%). This had a significant correlation with GNB growth in sputum (p<0.05) (Table 7.8).

In our study, 27 (75%) patients had high total leukocyte count (on an average 15000/cumm) ranging from 4800-42500/cumm at the time of admission and were found to be infected with Gram negative bacilli. This association was found to be statistically significant (p =0.009). The rest of the patients (n=9) had a TLC of less than 12000/cumm. Smoking, alcoholism and other co-morbidities had no significant correlation with the organism growth in sputum culture.

Table 7: Correlation of TLC with Gram negative infection in sputum.

Total leukocyte count	No. of patients	p- value
More than 10000/cumm	27	0.009
More than 10000/cumm	9	ns

*ns= not significant.

Table 8: Correlation of saturation with gram negative infection in sputum.

Saturation of O ₂	No. of patients	p- value
More than 88%	13	ns
Less than 88%	23	<0.05

*ns= not significant.

We also observed that 23 patients who were found to be infected with gram negative organisms had presented with a saturation <88% at the time of admission. This parameter also had significant correlation.

Discussion

Community-acquired pneumonia (CAP) remains a major cause of morbidity and mortality worldwide. A causative agent is identified in 30% to 40% of cases [3]. The initial antibiotic therapy plays a critical role in the outcome of pneumonia. The Infectious Diseases Society of America (IDSA) pneumonia guidelines recommend gram staining and culture of expectorated sputum for inpatients with CAP [4]. This has been recommended as to permit judicious use of antibiotics and to limit drug resistance pattern which is a rapidly increasing burden. In the present study, almost 30% of cases which yielded positive growth for causative organism among sputum samples were Gram Negative Bacilli in nature. This is a growing problem which needs to be considered.

The role of GNB responsible for community acquired pneumonia has been a subject of continuing 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 our study, 30.2% patients were found to have gram negative infection. A similar study done in 2016 done by Jitendranath A et al reported an incidence of 50% gram negative bacterial infection among sputum samples [7]. Another study conducted by Shah BA et al in 2010 also showed a rising trend of GNB infection with a percentage of around 65% [8]. Similar to our study this also showed a higher no of CAP in age more than 40 years and patient presenting with tachycardia (92%), pleuritic chest pain (75%) and sputum production (65%), and leucocytosis (43%).

Our study also showed that the presence of GNB was associated Systolic blood pressure less than 106 which was found to be statistically significant. In a similar study done by Espa et al to determine the severity of CAP, which included parameters like systolic blood pressure < 90 amongst other parameters were found to be significant in diagnosing severe CAP [9]. Hence, patients with gram negative bacterial infection present with a severe infection and may need immediate attention.

In our study patients presenting with yellow coloured sputum were later found to have gram negative infection and this finding was also statistically significant. Another study conducted by Altiner A. et al showed that presence of yellow or green coloured sputum was significantly correlated with the presence of bacterial infection but does not specify any particular organism [10].

In concordance with the SEPSIS guidelines, patients presenting with leucocytosis or leucopenia and hypotension were found to have

poorer general condition. In our study patients who had hypotension and high TLC >10000/cumm were found to have gram negative bacterial infection [11]. This parameter was found to be statistically significant. Also patients who presented with a low saturation <88% at room air, on further work up showed gram negative infection and this entity was also found to be statistically significant. However, this parameter has not been included in any previous studies and can be considered in future studies.

In our study we ruled out all structural lung diseases and found that smoking, alcoholism and other co-morbidities did not have any significant correlation with the development of CAP. Although 10 out of 36 patients had hyperglycaemia at the time of admission but none of them were diagnosed with Diabetes mellitus. Hence, none of the patients were immunosuppressed. Risk factors for enteric gram-negative organisms are as follows: recent antibiotic therapy, underlying cardiopulmonary disease, residence in a nursing home, and multiple medical comorbidities [12,13]. These were ruled out as well for our study.

This high incidence may be because Gram-negative bacteria may easily colonize the tracheobronchial tree in the presence of any alterations or damage of the respiratory epithelium like that in case of preceding viral illness. Also, the injudicious use of antibiotics by physicians for an upper respiratory infection and the easy availability of over the counter antibiotics self-prescribed by patients render the respiratory tract predisposed to opportunistic organisms. In view of the potential continuum of bronchitis and pneumonia, 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 [7].

Limitations of the Study

Comparative analysis of the patients presenting with gram positive and gram negative infection was not done which would have been helpful in terms of differentiating the presenting as well as corresponding parameters of these two categories. This comparison may be important in future and might help to differentiate and help in appropriate antibiotic administration even as the patient presents in the emergency.

Tests for atypical pathogens viral as well as Legionella could not be done at the time of our study. Proper antibiotic history could not be elicited due to non-availability of any documents.

Conclusion

The most common isolated gram negative bacteria's were *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. The presence of GNB in sputum was found to be significantly correlated with low saturation (<88%), high total leukocyte count (>10000/cumm), a low

systolic blood pressure (<106) and a yellow colour sputum. Our study shows an increasing trend of gram negative bacilli as an important etiological agent of community acquired pneumonia. An appropriate and timely addition of appropriate antibiotic to cover these organisms as well may help in decreasing the morbidity as well as severity of the infection.

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