Community-Acquired Pneumonia: Bacteriological Profile and Microbiological Investigations

Common Etiologies of CAP

Community-acquired pneumonia is a disease of varied etiologies. Each case varies with many causative agents implicated. This has been attributed to regional differences in the prevalence of microorganisms. Nevertheless there are several common etiologies leading to CAP in community as well as hospital settings.

Common causative agents of pneumonia in ambulatory patients are Streptococcus pneumoniae, Mycoplasma pneumoniae, Haemophilus influenzae, Chlamydia pneumoniae and respiratory viruses (influenza A and B, adenovirus, respiratory syncytial virus and parainfluenza). Common causes of pneumonia in hospital settings are S. pneumoniae, M. pneumoniae, C. pneumoniae, Legionella spp. aspiration respiratory viruses (influenza A and B, adenovirus, respiratory syncytial virus and parainfluenza).


New and Emerging Etiologies of CAP

Literature Review

Fang et al. conducted a prospective, multicenter study in 359 cases to evaluate the new and emerging causes of CAP. It was found that the common causative agents of CAP are S. pneumoniae (15.3%), H. influenzae (10.9%), Legionella spp. (6.7%) and C. pneumoniae (6.1%). Mortality was the highest for S. aureus (50%) and the lowest for C. pneumoniae (4.5%). Mortality was not seen with M. pneumoniae. Pneumonia due to aerobic Gram-negative organisms was uncommon, even though empirical therapy with combination of broad-spectrum antibiotics was often used in this subgroup. The study concluded that empiric antibiotic prescriptions must be influenced by the realization that C. pneumoniae and Legionella spp. are common etiologies for CAP.

The emerging etiologies for CAP were also examined in a 12-month prospective study, which evaluated the microbiological yield with a new diagnostic polymerase chain reaction (PCR) platform along with conventional methods.

The microbiological tests used were as follows:
- Culture of samples of blood, sputum, and nasopharyngeal secretion.
- Analysis of sputum samples by real-time quantitative PCR for S. pneumoniae, H. influenzae, and Moraxella catarrhalis.
- Analysis of nasopharyngeal secretions by PCR.
- Serological testing for M. pneumoniae, C. pneumoniae, and viruses common in the respiratory tract.
- Detection of pneumococcal and L pneumophila antigens by urine antigen assays.

It was possible to establish microbial etiology in about 67% (n=124) of patients. A microbiological agent was identified in 89% of the patients with complete sampling. S. pneumoniae [70 patients (38%)] and respiratory virus [53 patients (29%)] were the most frequently detected pathogens. Forty-three (35%) patients out of 124, were detected with two or more pathogens.

Bacteriological Profile of CAP

The bacteriological profile of CAP is not the same across various countries. It also varies within the same country with time due to differences in the frequency of use of antibiotics, environmental pollution, awareness of the disease and life expectancy.

The most common causative pathogen in Europe, the United States, the United Kingdom, Iraq, Delhi, and Mumbai is S. pneumoniae, whereas in Singapore, it is K. pneumoniae.

Indian Data

In the Indian scenario, studies on bacteriological etiology are a few and far between, and are mostly confined to limited geographical areas. Etiological agents of CAP are different in different geographical areas, for example, S. pneumoniae predominates as etiological agent of CAP in Shimla and Delhi whereas, P. aeruginosa was found to be the most common etiological agent in blood culture-positive CAP in Ludhiana.

Bansal et al. conducted a study to identify the clinical and bacteriological profile in Shimla. Etiology was identified in about 75% of patients. It was found that S. pneumoniae, S. aureus, K. pneumoniae, M. pneumoniae, E. coli and other Gram-negative bacteria were the most frequently isolated pathogens.

A prospective study including patients with CAP assessed the etiologic agents causing CAP in Mumbai. Sputum culture, BACTEC blood culture and urine culture for pneumococcal antigen were done. The organisms isolated included S. pneumoniae, C. pneumoniae, H. influenzae, M. catarrhalis, M. pneumoniae, L. pneumophila, P. aeruginosa, Staphylococcus and S. typhi.

- S. pneumoniae was isolated in 22% (leading cause of CAP)
- Atypical organisms were identified in 19% of patients
- Mycobacterium tuberculosis was isolated in 7% of patients

A study by Shah et al. showed that factors that can predict mortality in a patient of CAP at the time of admission are:
- Patients above 65 years of age
- History of chronic obstructive pulmonary disorder
- Smoking
- Hypotension and altered sensorium
- Respiratory failure
- Staphylococcal pneumonia

The overall rate of identification of causative pathogens in CAP was just about 29%, which underlines the difficulty of challenges faced by physicians while prescribing empiric antibiotic therapy. In hospitalized patients, Staphylococcus aureus was the major causative organism identified followed by Pseudomonas, and Klebsiella.

Key Observations

- Patients with severe CAP have a distinct epidemiology and...
a different distribution of etiologic pathogens than patients with other forms of pneumonia.

- The likely pathogens can be assessed on the basis of the presence of comorbidity or advanced age.
- Enterobacteriaceae, *S. aureus*, *P. aeruginosa* should be suspected in critically ill patients.
- Although an etiologic diagnosis is optimal in the management of CAP, it is difficult to identify the responsible pathogens in 50% of patients even when extensive diagnostic tests are performed.

**Tests to Determine Etiology of CAP**

Blood cultures, sputum Gram-stain and culture are the most common tests used to identify the etiology of CAP. In addition to this, serological tests are also performed. These procedures do have their advantages and limitations. For example, blood cultures are rarely positive, but if positive, then it is indicative of severe disease. Similarly, collection of sputum is difficult in children, cannot differentiate pathogen from commensal and is of no value if sent after starting antibiotics, as it will detect colonizers. In cases where it can be obtained, an adequate sputum sample is defined as >25 polymorphs and <10 squamous epithelial cells/μl.12

**Limitations of Common Investigations**

- **Gram-Stain and Culture**: Microbe identification is possible in 50% of patients only and depends on quality of sputum sample. Invasive procedures are not justified. Culture sensitivity and specificity need correlation with smear.
- **Blood cultures give poor results**
- **Serology requires rising titre; it is expensive and not easily available**
- **Viral cultures are not useful; viral antigens are better**

**Serologic Tests**

Serologic tests help in identifying causative pathogens. The Immunoglobulin M (IgM) antibodies against mycoplasma rise 1 week after infection and remain positive for 6 months to 1 year after infection. This accounts for poor sensitivity and specificity. Other tests for diagnosing mycoplasma include cold agglutinins (sensitivity 50%, poor specificity) and elevated reticulocyte count.13

The IgM antibodies to *Chlamydia* take 3 weeks to become detectable accounting for poor sensitivity.12

The urine pneumococcal antigen detection test is fairly sensitive and specific in adults. However, it has poor specificity in children due to nasopharyngeal carriage of pneumococci.15,14

Antibody tests for viruses have poor sensitivity/specificity. Antigen detection tests for viruses in respiratory secretions have reasonably good sensitivity and specificity, but are not currently available. Multiplex PCR on respiratory secretions for viruses has limited sensitivity and specificity.10

**Spectrum of Pneumococcal Disease**

Pneumococcal disease can be classified as noninvasive or invasive disease. The noninvasive disease is contiguous, whereas invasive disease spreads via blood. Pneumonia, otitis media and sinusitis are classical presentations of the noninvasive disease while invasive disease is characterized by sepsis, meningitis, bacteremic pneumonia and arthritis.

The incidence of nasopharyngeal carriage of pneumococci is higher in children than in adults. The nasopharynx is also the anatomical site of origin and a sanctuary for drug-resistant *S. pneumoniae* (DRSP). It is estimated that up to 60% of individuals in the community carry *S. pneumoniae*.

**Drug-Resistant *S. pneumoniae***

Drug-resistant *S. pneumoniae* can be penicillin-resistant *S. pneumoniae* and penicillin non-susceptible *S. pneumoniae*, macrolide-resistant *S. pneumoniae* and multidrug-resistant *S. pneumoniae*.16

**Risks of Penicillin Resistance in Pneumococci**

A multivariate analysis of risk factors of penicillin resistance in pneumococci was evaluated in a prospective study. It was observed that the risk of penicillin resistance in pneumococci depended on the class and the duration of antimicrobial agents to which the patient was exposed. Consumption of alcohol, use of (3-lactamase with 3 months, noninvasive disease and adults aged above 65 years are the contributing risk factors for penicillin resistance in pneumococci. According to a multivariate analysis by Vanderkooi et al. the risk factors for infection with penicillin-resistant pneumococci as compared to penicillin-susceptible pneumococci were:17

- Age of occurrence of infection [odds ratio (OR), 1.28; p<0.001]
- Absence of chronic organ system disease (OR, 1.72; p=0.03)
- Previous use of penicillin (OR, 2.47; p=0.006), trimethoprim-sulfamethoxazole (TMP-SMX; OR, 5.97; p<0.001), and azithromycin (OR, 2.78; p=0.05)

**Macrolide-Resistant *S. pneumoniae***

It was observed in a prospective, population-based surveillance study that an increased risk of macrolide failure was due to macrolide resistance irrespective of underlying mechanism of resistance. This finding implies that for the treatment of bacteremic pneumonia, high macrolide blood levels are essential.18

**Fluoroquinolone Resistance in *Streptococcus pneumoniae***

The emergence of fluoroquinolone-resistant pneumococci is demonstrated in various studies and there have been published reports of treatment failures due to infection with fluoroquinolone-resistant strains.19

**Does Resistance Matter in the Indian Setting?**

In India, resistance to b-lactams is very low. The MICs of penicillin <8 mg/mL do not adversely affect outcome. In penicillin-resistant *S. pneumoniae* (PRSP), the second-generation cephalosporins are not useful in this regard. Resistance to macrolides is low in India and further studies are required to quantify the same.

**Recommendations**

- All the microbiological investigations are not recommended for outpatients
- These investigations may be done for inpatients
- Microbiological investigations are indicated in
  - Immunocompromised
  - Non-responding pneumonia
- Severe pneumonia

References


