Burden of Pneumonia in the Community

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Introduction

Community-acquired pneumonia (CAP), a common and potentially serious respiratory illness, accounts for the single largest group of sepsis-triggering events. Community-acquired pneumonia is an acute infection of the lung parenchyma in a patient who has acquired the infection in a community, as distinguished from hospital-acquired pneumonia. Community-acquired pneumonia may be acquired by inhalation or aspiration of pulmonary pathogenic organisms into a lung segment or lobe or from secondary bacteremia from a distant source. This condition is associated with significant rates of morbidity and mortality, particularly in elderly patients and in those with coexisting comorbidities. Typical bacterial pathogens Streptococcus pneumoniae (S. pneumoniae), Haemophilus influenzae (H. influenzae), and Moraxella catarrhalis (M. catarrhalis) account for approximately 85% of these cases. While the etiology of this condition may vary by geographic region, S. pneumoniae remains the most common cause of CAP worldwide.

Microbiology of Bacterial CAP in Adults

Meta-analysis (122 clinical studies: 1966-1995) shows the following:

<table>
<thead>
<tr>
<th>Agent</th>
<th>Patients (n)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus</td>
<td>4432</td>
<td>12.3</td>
</tr>
<tr>
<td>pneumoniae</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemophilus</td>
<td>833</td>
<td>7.4</td>
</tr>
<tr>
<td>influenzae</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mycoplasma</td>
<td>507</td>
<td>1.4</td>
</tr>
<tr>
<td>pneumoniae</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staphylococcus</td>
<td>157</td>
<td>31.8</td>
</tr>
<tr>
<td>aureus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Klebsiella</td>
<td>56</td>
<td>35.7</td>
</tr>
<tr>
<td>species</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>18</td>
<td>61.1</td>
</tr>
<tr>
<td>aeruginosa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>17</td>
<td>35.3</td>
</tr>
</tbody>
</table>

The emergence of penicillin-resistant strains of the three most important implicated pathogens that also exhibit resistance to other antibiotics is a grave threat to effective management of CAP. Standard aggressive medical care, even with the introduction of potent new antimicrobials, has failed to aid in decreasing mortality due to the condition. An ideal pneumococcal vaccine that is a preventable cause of morbidity and mortality in high-risk adults has eluded immunization programs adding to the existing difficulties. The vaccination to prevent pneumococcal infections has not yet been introduced in the Universal Immunization Program (UIP) in India, even as pediatricians advocate its use.

Incidence of Community-acquired Pneumonia (Global)

In Europe, incidence of CAP ranges from 1.6 per 1,000 in Spain to 11.6 per 1,000 in Finland with the highest rate being reported in the winter months (2.21 per 1,000). Incidence rates for CAP in the United States (US) are estimated to be 2.7 per 1,000 in a large cohort. Streptococcus pneumoniae, the most commonly isolated pathogen, was responsible for 4.2 million ambulatory care visits for CAP in the US in 2006.

Reliable data on CAP incidence in other parts of the world is lacking. Few studies report incidence rates from 0.2 to 0.9 per 1,000 in the Asian-Pacific region. But these seem to be underestimated. Recently published reports state an increase of 30% in the hospital admissions due to CAP, thereby suggesting an increase in the annual incidence rates.

Among the world regions, on examining in-hospital mortality differences, the highest mortality was in Latin America (13.3%), followed by Europe (9.1%), and North America (7.3%). The excess mortality in patients surviving the initial CAP episode is reported to be as high as 50% within 5 years following hospital discharge. An increase in the overall incidence of CAP is noted with advancing age of the patient. The estimated range is from 18.2 per 1,000-person years in people aged 65-69 years to 52.3 per 1,000 years in people > 85 years of age. The overall incidence of CAP in adults over 60 and 90 years of age was 7.7 and 35.8 per 1,000, respectively. Among adults ≥ 50 years of age in the US, over 25,000 pneumococcal-related deaths were estimated to occur annually. In a large Spanish cohort, mortality rate in elderly patients was 10.3%. Mortality rates are as high as 55% in cases of severe CAP requiring ventilation.

Global Burden of Disease

The 2010 Global Burden of Disease Study demonstrated that the lower respiratory tract infections (LRTIs), including pneumonia, are the fourth most common cause of mortality globally and the second most frequent reason for years of life lost. The World Health Organization (WHO) estimated LRTIs including CAP accounted for 429.2 million episodes of illness worldwide and 94.5 million disability-adjusted life years (DALYs). About 1.6 million deaths annually are reported in adults aged over 59 years.

Prevalence of Community-acquired Pneumonia

When compared to other bacterial infections, the burden of invasive pneumococcal disease continues to be a problem worldwide, which is attributed to its changing cellular and virulence characters and complex detection methods. In 2008, the WHO reported the highest burden of pneumonia to be from Asia with the majority of the cases (43 million) from the Indian subcontinent, 21 million from China, 10 million from Pakistan, and additional high numbers in Bangladesh and Indonesia. There are reports of about 600,000 patients being hospitalized with pneumonia every year. Incidence rates of radiologically confirmed CAP in different populations vary between 1.3 and 11.6 cases per 1,000 inhabitant-years with highest rates in elderly adults (13-15 cases per 1,000 inhabitant years). Half of total hospitalization for pneumonia is seen to occur in adult patients over 65 years of age.
Prevalence of Community-acquired Pneumonia in India

Although data on the total mortality caused by ‘LRTIs’ in India is available, there are very few large studies on the incidence of CAP. In the year 2008, 35.1/100,000 population succumbed to LRTIs compared to 35.8/100,000 patients to tuberculosis and 194.9/100,000 to parasitic and infectious diseases. Therefore, LRTIs account for around 20% of the mortality due to infectious diseases in India.11

The estimation of the exact pneumococcal burden in India continues to pose a challenge, while the rates of morbidity and mortality remain high.6 The overall estimates of the annual incidence of CAP are seen to vary between 2 and 12 cases per 1,000 with the highest rates being reported in infants and the elderly.6 The mortality of CAP in India is comparable to that reported elsewhere in the world.11

The mortality rates are less than 1–5% in the outpatient setting, but may be as high as 12% in hospitalized patients.12 In a study of 150 patients hospitalized with CAP, 8% (12) patients died in the hospital, while 2.7% (4) succumbed within 30 days of discharge. In another study consisting of 72 patients with CAP over 18 months, 14% of young and 35% of elderly patients died due to fulminant sepsis or respiratory failure. Other studies from India reported a variable mortality between 3.3% and 11%.11

Among hospitalized patients, the incidence of bacteremic pneumonia is 25% with a mortality rate of 20%. The incidence of infection peaks in winter and spring.12

Indian Burden of Disease

India accounts for 23% of the global pneumonia burden and 36% of the WHO regional burden. National estimates may, however, hide significant sub-national disparities.16 Indian reports on the etiological agents of CAP are very few.11

Streptococcus pneumoniae predominates as the etiologic agent of CAP in cities such as Shimla and Delhi. A study of blood cultures in CAP revealed S. pneumoniae (35.3%) as the commonest isolate, followed by S. aureus (23.5%), Klebsiella pneumoniae (20.5%), and Haemophilus influenzae (8.8%). Another earlier study also found S. pneumoniae to be the commonest cause (35.8%), while also reporting Mycoplasma pneumoniae in 15% of the microbiologically positive cases.11

An important cause, which is often not considered in India, is Legionella pneumophila (L. pneumophila). A recent study revealed 27% of patients with CAP to be serologically positive for this organism, with about 18% demonstrating L. pneumophila antigenuria. Mycoplasma was isolated as the etiological agent in 35% patients. No large studies have specifically addressed viruses as the cause of CAP other than the pandemic influenza H1N1 virus.11

Pneumonia is also noted to be increasingly common among the elderly population and in those with comorbid conditions, such as chronic obstructive pulmonary disease (COPD), diabetes mellitus, renal failure, congestive heart failure, chronic liver disease, etc.14

Clinical Manifestations of Community-acquired Pneumonia

Clinical manifestations of CAP due to the different implicated pathogens are as detailed below.

General clinical manifestations

Streptococcus pneumoniae

The classical presentation of S. pneumoniae is that of a very abrupt onset. The acute febrile illness is frequently preceded by mild coryza or other upper respiratory tract symptoms. Pleuritic chest pain is a common symptom attributed to the infection often involving the peripheral lung and quickly spreading to the pleura. Sputum is usually yellowish or greenish in color or blood-streaked or rusty. Findings on physical examination include an ill- looking patient, fever, tachycardia, tachypnoea, cyanosis, impaired percussion note, and tubular bronchial breathing.12

Haemophilus influenzae

• The onset of symptoms is slower than that of S. pneumoniae.
• Clinical symptoms are indistinguishable from those
• Pseudomonas aeruginosa
  - Pseudomonas pneumonia may result in microabscess, alveolar hemorrhage, and necrotic areas. Bacteremia may develop in certain cases resulting in septic shock with hypotension and oliguria.12

Klebsiella pneumoniae
• Infection tends to be severe and may cause a confluent pneumonia of lobar distribution.
• Sputum is viscid and may be blood-stained.

- Cavitation and abscess formation may occur.12
  Moraxella catarrhalis
  - Causes patchy segmental bronchopneumonia in the lower lobes.
  - Cavitation and pleural effusion are rare.12
  - Anaerobic bacteria
  - Foul-smelling sputum in more than 50% of patients.
  - Patchy pneumonitis in the dependent segments.
  - Potential to progress to lung abscess and empyema.12

Risk Factors for Community-acquired Pneumonia

The knowledge of risk factors for CAP is integral to the designing of preventive measures (promoting effective vaccines, identifying and treating modifiable risk factors, etc.) with an aim to reduce CAP-related death. The risk factors for CAP can be categorized as follows:

Comorbidities and related therapies

Chronic diseases of the respiratory system such as COPD and asthma are responsible for a 2-3 fold increase in the risk of CAP both in the general and elderly population. Not only do chronic lung diseases increase the risk of outpatient pneumonia, but also increase the risk of CAP requiring hospitalization. Medications, such as inhaled drugs, corticosteroids, β-2 agonists, and anticholinergics used by these patients also represent a risk independent of the underlying respiratory disease and its severity. Oxygen therapy is associated with drying of the nasal and oropharyngeal mucosa leading to superinfected lesions, dysphagia, and a greater aspiration risk. The upper respiratory tract diagnostic and therapeutic techniques such as the nasogastric tube, bronchoscopy, gastroscopy, general anesthesia, tonsillectomy, and adenoidecтомy may produce contamination, affect natural aspiration barriers, or cause the epithelial destruction of the airways and hence, facilitate infection.4

Other comorbid conditions that are known to increase the risk of CAP include frequent colds, recurrent bacterial pneumonia, diabetes, heart failure, convulsive conditions, stroke, dementia, gastroesophageal reflux, hiatal hernia, chronic liver or renal disease, dysphagia, oral pathologies such as severe periodontitis, and cancer. Medications, namely diuretics, digoxin, amiodarone, gastric acid suppressants, corticosteroids, immunosuppressive cancer treatments, and inappropriate antibiotic prescription in the management of these conditions are also seen to be associated with an increased risk for CAP.4,9

Demographic and socioeconomic factors

Age is a significant risk factor for CAP with the highest risk in the elderly population. The risk that gender poses for CAP is unclear, while there is no evidence on any risk with differences in ethnicity for CAP. Overcrowding, low education status, poor dietary, and hygiene habits favor the development of CAP.4

Low body weight either due to malnutrition or an underlying disease is associated with an increased risk for CAP and an increased risk of death from pneumonia. However, being overweight or obese does not imply a risk for CAP.4

Lifestyle-related factors

Tobacco happens to be a major modifiable risk factor for CAP. The
risk of pneumonia increases between 50% and 400% in smokers. About 15% and 30% of CAP cases could be avoided on the elimination of smoking. The risk due to smoking is independent of the effect of chronic bronchitis, COPD, and heart failure. Ex-smokers are at similar risk for the initial 2 years following abstinence, while the impact of passive smoking, especially in the younger population, remains to be clearly elucidated as yet. Consumption of high levels of alcohol (<40–80 g/day) is yet another independent risk factor for CAP. Intake of >80 g/day of pure alcohol exerts a risk for CAP independent of smoking, chronic bronchitis, heart failure, or chronic liver disease.

Environmental factors
It is not clear whether soot, crystalline silicon, cadmium, and cotton dust that cause COPD can directly lead to CAP development. There has been no association described between occupational contact with fumes, gases, gasoline, vapors, oil, organic and inorganic fibers, hydrocarbons, or ionizing and nonionizing radiation. Metal fumes, particularly iron, is known to reversibly predispose to CAP. Construction and industrial work (carpentry, painting, etc.), exposure to dust, and sudden workplace changes in temperature represent risk factors for CAP. Living with pets, such as dogs, cats, or birds increases the risk of CAP in line with the number of pets at home and is independent of other housing conditions and comorbidity. Also, adults in close and regular contact with children with respiratory tract infections are at an increased risk for CAP.

Epidemiology of Community-acquired Pneumonia
Bacteriologic profile of CAP differs among countries and changes with time within the same country, which is attributed to factors like frequent use of antibiotics, changes in environmental pollution, increased awareness of the disease, and changes in life expectancy.

To Summarize
Lower respiratory tract infections, including pneumonia, are the fourth most common cause of mortality globally and the second most frequent reason for years of life lost. S. pneumoniae is a leading cause of bacterial pneumonia worldwide. An increase in the overall incidence of CAP is noted with advancing age of the patient, and in patients with coexisting comorbidities. The disease burden of pneumonia, particularly of S. pneumoniae in the country, highlights the necessity for the improvement of access to care and increase in coverage and equity of pneumonia preventing vaccines, particularly in older adults.

References