# Bacterial Etiology and Antibiotic Resistance Pattern of Adult Pneumonia in South Asia: A Review

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A thesis submitted to the Department of Department of Mathematics and Natural Sciences in partial fulfillment of the requirements for the degree of B.Sc. (Microbiology)

Department of Mathematics and Natural Sciences
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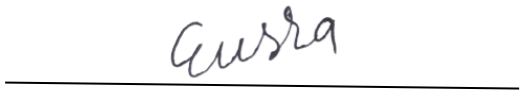
**Declaration**

It is hereby declared that

1. The thesis submitted is our own original work while completing a degree at BRAC University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. We have acknowledged all main sources of help.

**Student's Full Name & Signature:**



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**Abstract**

This article reviews literature focused on Community Acquired Pneumonia (CAP), Hospital Acquired Pneumonia (HAP) and Ventilator Associated Pneumonia (VAP) in adults published over the years of 2004 to 2021. The review was performed to identify the etiological agents of adult pneumonia and antibiotic resistant pattern in the South Asian region with the intention of determining the local etiology of pneumonia in order to make proper choices regarding empirical antibiotic treatment. Among 27 studies included, 17 were conducted in India, 4 in Bangladesh, 4 in Pakistan and 2 in Nepal. A total of 11 studies presented antibiotic resistance data along with etiology. Gram-positive organisms were more prevalent in CAP than HAP, according to information on the causative organism. However, in both HAP and CAP cases, gram-negative organisms outnumbered gram-positive organisms. Each CAP study carried out in India, Nepal, and Bangladesh revealed that *Streptococcus pneumoniae* was the most frequent causal agent. Moreover, *Klebsiella pneumoniae* was the most frequent bacteria observed to cause HAP and VAP. There was a considerably greater level of resistance to third-generation antibiotics among the major causative agents in cases of VAP compared to CAP. To combat the expanding concern of antibiotic resistance, more comprehensive research on CAP, HAP, and VAP is required in South Asia.

**Acknowledgment:**

It is by the grace of The Almighty that we have been able to complete this research, so at first, He should be thanked for granting us the strength, good health and opportunity to work on this thesis.

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Finally, we would like to express our gratitude to our parents for their unwavering support and commitment to our happiness, future, and education.

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**List of Tables**

**List of Acronyms**

ATS……..…….….American Thoracic Society

BAL……...…Bronchoalveolar Lavage

BTS……..……..….British Thoracic Society

CAP……...……..…….Community Acquired Pneumonia

CDC……..….Centre for Disease Control and Prevention

ETA……..……..…Endotracheal Aspirate

HAP……..….Hospital Acquired Pneumonia

IDSA…….……..……Infectious Diseases Society of America

PCR……...…….Polymerase Chain Reaction

TA……..……....Tracheal Aspirate

TBL……..…….Tracheobronchial Lavage

VAP……....….Ventilator Associated Pneumonia

WHO……..……....World Health Organization

## CHAPTER 1
## Introduction

Our evolving interactions with the microbial planet contribute to the constant development of new challenges in treating pneumonia in the elderly population. In this disease, the air sacs of one or both lungs could become clogged with fluid or pus (purulent material), which would result in a cough with pus or phlegm, a fever, chills, and breathing difficulties (*Pneumonia - Symptoms and Causes*, 2023). Pneumonia is classified generally as either community- or hospital-acquired. Community-acquired pneumonia (CAP), as defined by the Infectious Diseases Society of America (IDSA), is an acute infection of the pulmonary tissue accompanied by the presence of an acute infiltrate on a chest radiograph or auscultatory findings consistent with pneumonia in a patient who did not get the illness from a healthcare system or within the first 48 hours after being hospitalized (Metlay et al., 2019). On a global scale, CAP significantly contributes to morbidity and mortality. According to reports, CAP kills between 1.6 and 10.6 per 1,000 adults per year in Europe and an estimated 1,000,000 adults annually in Asia (Assefa et al., 2022). According to the 2016 IDSA guidelines, hospital-acquired pneumonia (HAP) is defined as pneumonia occurring 48 hours or more after admission to the hospital but unrelated to mechanical ventilation, whereas ventilator-associated pneumonia (VAP) is defined as pneumonia occurring more than 48 hours after endotracheal intubation (*Hospital-Acquired and Ventilator-Associated Pneumonia (HAP/VAP)*, 2016) The American Thoracic Society (ATS) reports the incidence of HAP between 5 and 10 cases per 1,000 hospital admissions, whereas the incidence of VAP rises by six to twenty times for patients who are on mechanical ventilation. ("Guidelines for the Management of Adults with Hospital-Acquired, Ventilator-Associated, and Healthcare-Associated Pneumonia," 2005) However, South Asian countries lack the same level of documentation regarding the incidence of HAP and VAP in adults as developed countries do. It is important to understand the local etiology to make appropriate selections regarding empirical antibiotic treatment since variations in etiology may lead to an unsatisfactory response to medication chosen to treat infections prevalent in western research.

In this review, articles on pneumonia were analyzed based on both HAP (Hospital-Acquired Pneumonia), VAP (Ventilator-Associated Pneumonia) and CAP (Community-Acquired Pneumonia) in adults, with a focus on bacterial etiology and antibiotic resistance patterns. According to this study, CAP and HAP have significantly different etiological bacteria. *Streptococcus pneumoniae* is the most common causative microorganism in CAP. *Klebsiella pneumoniae*, on the other hand, is the most common microorganism in HAP.

According to the WHO (World Health Organization), vaccines have the potential to help limit the spread of antibiotic resistance (*Antibiotic Resistance*, 2016). In addition, the CDC (Centre for Disease Control and Prevention) suggests a 15-valent or 20-valent pneumococcal conjugate vaccine for all adults aged 65 years and older (*Pneumococcal Disease and Antibiotic Resistance* |

*CDC*, 2022). However, reports claim a lower trend in prescribing and uptake of the pneumococcal vaccine even in a population with comorbidities (Para et al., 2018).

The "Winter Fever," as pneumonia was once known, could be traced back to 460 BC, as explained by the Greek physician Hippocrates, when this disease was only regarded as a symptom of other diseases rather than as its own infection until the 19th century. Although we've come a long way with the help of vaccines and antibiotics, we still need to get out of the woods in the fight against pneumonia, especially with antibiotic resistance lurking around the corner. Furthermore, the predominant part of the available disease burden data and epidemiological studies on pneumonia is based on western and developed countries and solely focused on the child population. Even though the rate of child mortality due to pneumonia has reduced threefold over the last three decades, the mortality rates among the other age groups have largely remained unchanged. In accordance with the growing concern about antibiotic resistance organisms, a review regarding the etiology of CAP, HAP, and VAP and the resistance pattern among the adults of the South Asian region appears to be fairly necessary.

## CHAPTER 2
## Methodology

The study design choice of potential studies was maintained open in order to broaden the target result analysis aspect and the review study was confined to original English-language articles on adult pneumonia from the South Asia region. One database Pubmed was searched to associate articles using the keywords “adult” and/or “adult pneumonia” and/or “south asia”. Additionally, references from similar review articles located in database findings and related articles discovered through random search were reviewed.

1882 studies found from the database (PubMed) was screened together with 298 publications from reviews of studies obtained from the databases and other sources. Primary screening was done in order to exclude duplicate studies obtained from a total 2180 database sources and 189 number of articles were removed. Then screening was done on the basis of the countries and studies obtained from South Asian countries (India, Pakistan, Afghanistan, Nepal, Bangladesh, Myanmar, Bhutan) were only selected. Studies were screened later on the basis of the eligibility which was done following the predetermined exclusion and inclusion criteria. This screening was based on abstracts and titles where factors including age, sample type, diagnostics method, etiology and antibiotic resistant pattern were concentrated to select the articles. Inclusion and exclusion criteria were documented earlier; those were also stringently followed while screening.

Inclusion criteria which were paid attention to select the articles-

1. Study describing bacterial etiologies of pneumonia including Community Acquired Pneumonia (CAP), Healthcare-Associated Pneumonia (HAP) and Ventilator-Associated Pneumonia (VAP) along with antibiotic resistance of the causing pathogens.

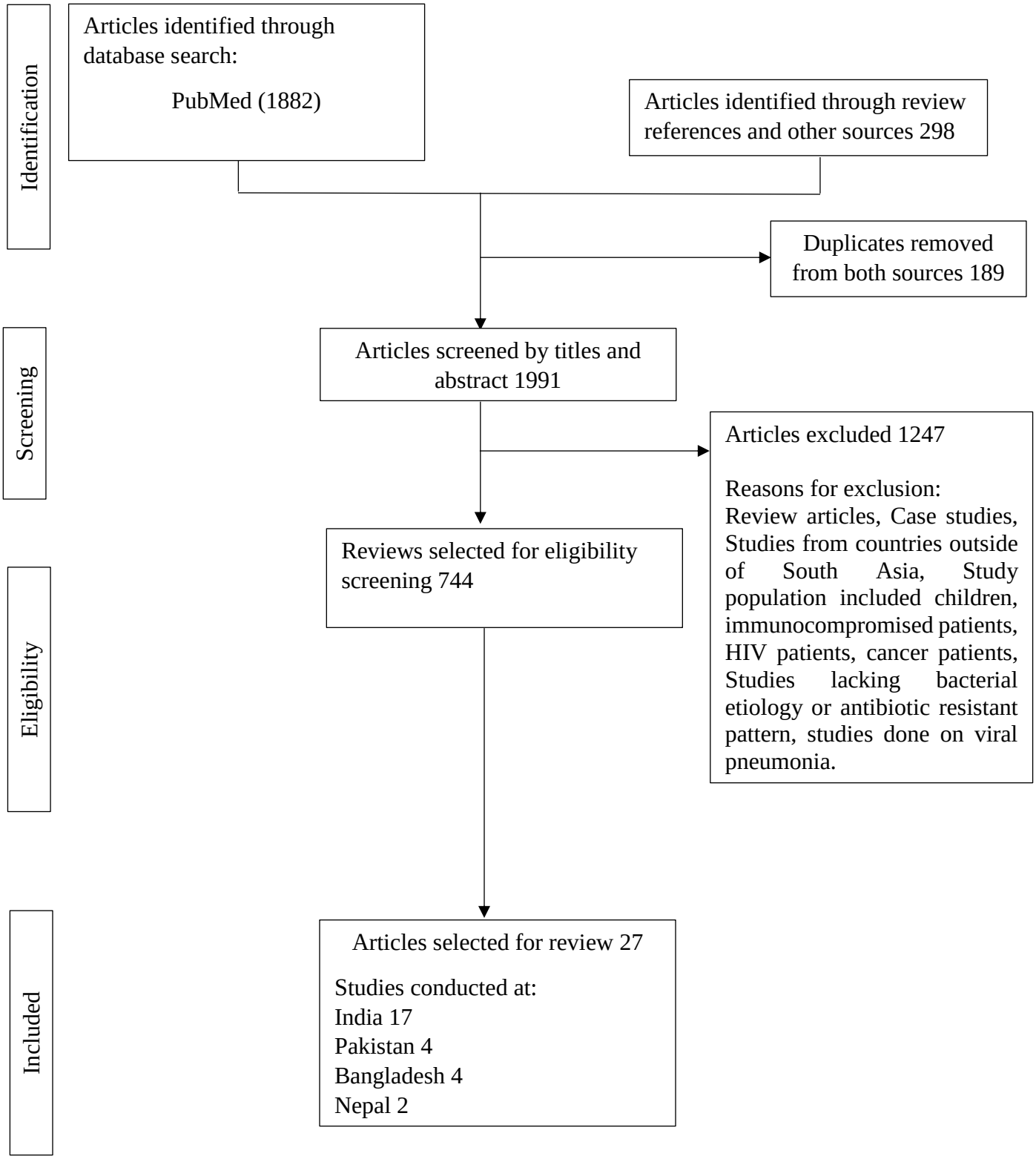
2. Studies with adults more than 18 years of old
3. All the studies publishing from South Asian countries
4. Study must mention the diagnosis of patient as “Pneumonia”

Exclusion criterias which were followed to eliminate the articles-

1. Study done on children
2. Study not relevant to our study
3. Study with no bacterial etiology
4. Review papers, case study articles
5. Study done on immunocompromised patients (HIV, autoimmune disease, cancer)
6. Study not based on South Asian countries
7. Study done on viral pneumonia

Lastly, data were extracted from the selected ‘n’ studies where case definition, specimen type, etiology, antibiotic resistance pattern, diagnostics methods, age group were meticulously maintained. Further, any disagreements among the reviewers while assessing the data were resolved unanimously.

## 2.1 PRISMA


Identification
Articles identified through database search:
PubMed (1882)
Articles identified through review references and other sources 298
Duplicates removed from both sources 189
Screening
Articles screened by titles and abstract 1991
Articles excluded 1247
Reasons for exclusion:
Review articles, Case studies, Studies from countries outside of South Asia, Study population included children, immunocompromised patients, HIV patients, cancer patients, Studies lacking bacterial etiology or antibiotic resistant pattern, studies done on viral pneumonia.
Eligibility
Reviews selected for eligibility screening 744
Included
Articles selected for review 27
Studies conducted at:
India 17
Pakistan 4
Bangladesh 4
Nepal 2

## 2.2 Study characteristics

A total of 3631 patients with CAP, HAP and VAP were reported in the 27 publications over the years of 2004 and 2020, and have been included in this review. Of these, 2437 patients have been studied for CAP and 1194 patients for both HAP and/or VAP. Three studies defined the case of Pneumonia according to the CDC, one according to the American Thoracic Society and British Thoracic Society (BTS) and most studies were defined based on the symptoms. Case confirmation of Pneumonia incorporated radiography (in five studies); culture confirmed (in six studies). One study focused on patients with and without diabetes who had been diagnosed with CAP.

The majority of the records have been collected from India. Limited data was collected from Bangladesh, Nepal and Pakistan while other South Asian countries including Sri Lanka, Bhutan, Myanmar lacked relevant research.

**Table 1: Study Characteristics**

| First Author | Publication Year | Region | Study Design | Number of patients | Age | Type of sample | Diagnostics used for the etiology detection |
|---|---|---|---|---|---|---|---|
| Bairy and Bhat | 2010 | India | Retrospective | 129 | >18 and above | Sputum and blood | Culture Confirmation |
| Dhar *et al* | 2018 | India | Prospective | 200 | | Sputum, endotracheal aspirate, bronchoalveolar lavage | Culture confirmation, VITEK 2 |
| Nusrat *et al* | 2020 | Bangladesh | Cross sectional | 105 | 16-92 years | Endotracheal aspirate | MALDI-TOF MS |
| Agarwal *et al* | 2018 | India | Prospective | 186 | 12-96 years | Endotracheal aspirate, tracheal tube aspirate, and bronchoalveolar lavage. | Culture confirmation, VITEK 2 |
| Kumari *et al* | 2021 | India | Prospective | 187 | 19-89 years | Endotracheal aspirate | Culture confirmation, MALDI-TOF MS |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Bhadade *et al* | 2017 | India | prospective observational cohort | 104 | 18-90 years | Sputum and tracheal aspirate | Culture confirmation. |
| Kalita *et al.* | 2021 | India | Cross-sectional | 574 | >18 years | Sputum and bronchoalveolar lavage | Culture confirmation, VersaTREK system |
| Khan *et al* | 2009 | Pakistan | | | | Tracheal aspirate | Culture confirmation |
| Ishtiaq *et al* | 2021 | Pakistan | Cross sectional | 39 | | Endotracheal aspirates (ETAs) and tracheobronchial lavage (TBL) samples | Culture confirmation |
| Menon *et al* | 2013 | India | Prospective | 145 | 18-90 | Sputum | Culture confirmation |
| Saibal *et al* | 2012 | Bangladesh | Prospective observational | 90 | 18-90 years | Sputum | Culture confirmation |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Shah *et al* | 2010 | India | | 100 | 15-80 years | Sputum and blood | Culture confirmation |
| Zubairi *et al* | 2012 | Pakistan | descriptive study | 124 | 16-90 years | Sputum, blood | Culture confirmation, PCR |
| Iqbal *et al* | 2019 | Pakistan | Retrospective observational | 509 | | Sputum, blood, pleural fluid bronchoalveolar lavage | Culture confirmation |
| Akhter *et al* | 2014 | Bangladesh | cross sectional study | 105 | 18-81 years | Sputum and blood | Culture confirmation, PCR |
| Para *et al* | 2018 | India | | 225 | 18-93 years | blood, sputum, urinary antigen | Culture confirmation, PCR |
| Abdullah *et al* | 2012 | India | Prospective study | 50 | 66-88 years | Sputum | Culture confirmation |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Prasad and Bhat | 2017 | India | cross-sectional study | 165 | >16 years | Sputum | Culture confirmation |
| Dongol *et al* | 2021 | Nepal | prospective observational cohort study | 438 | 18-95 years | tracheal aspirates (TA), bronchoalveolar lavage (BAL), sputum and blood samples | Vitek 2 |
| Parajuli *et al* | 2017 | Nepal | prospective study | 72 | 35-60 years | bronchoalveolar lavage fluid and endotracheal aspirate | Culture confirmation |
| Khurana *et al* | 2017 | India | prospective | 5154 | 5-78 | BAL | Culture confirmation |
| Bansal *et al* | 2004 | India | Prospective study | 70 | 17-93 years | Sputum | Culture confirmation |
| Acharya *et al* | 2014 | India | cross sectional study | 100 | 14-70 years | Sputum | Culture confirmation |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Mathai *et al* | 2014 | India | prospective observational study | 95 | | Endotracheal aspirate | Culture confirmation |
| Jain *et al* | 2014 | India | prospective study | 120 | 15-85 | Sputum and blood culture | Culture confirmation |
| Kejriwal *et al* | 2015 | India | cross sectional study | 60 | >14 years old | Sputum | Culture confirmation |
| Mallick *et al* | 2015 | Bangladesh | Prospective cohort study | 50 | Above 18 | TA | Culture confirmation |

# CHAPTER 3
# Result

## 3.1 Bacterial etiology of CAP, HAP and VAP

### 3.1.1 CAP (Community Acquired Pneumonia) Etiology

***Streptococcus pneumoniae***

The bacterium with the highest prevalence in the CAP (Community Acquired Pneumonia) is *Streptococcus pneumoniae*. CAP was found in 10 studies in India, predominantly diagnosed in sputum and blood among 1025 patients. The pathogen was shown to be most prevalent around 2015, 2011–2012, and 2000–2001, with percentages of 56%, 36.40%, and 35.80%, respectively (Bansal et al., 2004; Jain et al., 2014; Kejriwal et al., 2015). On the other hand, the pathogen was only found in the smallest amounts in the years 1998–2000 (1%), 2015–2016 (9.06%), and roughly 2017 (13.33%) (Kalita et al., 2021; Shah et al., 2010). In Pakistan, however, the pathogen was found to be most prevalent (18%) in a study conducted between 2011 and 2016, and least prevalent (7%) in a study conducted between 2007 and 2008 (Iqbal et al., 2020; Zubairi et al., 2012) According to a study in Bangladesh 2011-2012 study, the pathogen was detected at a rate of 19.05%, whereas the prevalence was 20.90% in 2009 (Akter et al., 2014; Saibal et al., 2013).

***Klebsiella pneumoniae***

As a CAP organism, *Klebsiella pneumoniae* is second most prevalent. The pathogen was detected in seven research conducted in India. According to a study, the pathogen was identified in sputum most commonly (31.8%) between 2011 and 2012 also in substantial amounts (29.09%) around 2017 (Jain et al., 2014; Prasad & Bhat, 2017). However, the pathogen was detected in low concentrations in India in the prior years 2008-2010 (6%) and around 2014 (13%) (Abdullah et al., 2012; Acharya et al., 2014). In addition, a study carried out in Pakistan between 2011 and 2016 found a significant level (14%) of the pathogen (Iqbal et al., 2020). The pathogen was also discovered in large amounts (19.10%) among diabetic patients in Bangladesh in 2009 (Saibal et al., 2013). Nevertheless, *Klebsiella pneumoniae* was not found in Nepal.

***Staphylococcus aureus***

In the years 2000 and 2001, the organism was detected to be most prevalent (17%) in a study carried out in India (Bansal et al., 2004). In contrast, it was found in low concentrations (2%, 3.30%, and 4.90%) in studies conducted in the later years 2008-2010, around 2015 and 2016 (Abdullah et al., 2012; Kalita et al., 2021; Kejriwal et al., 2015). In a study conducted in Pakistan in the years between 2011 and 2016, *Staphylococcus aureus* was detected at a high prevalence of 20% (Iqbal et al., 2020). On the other hand, in Bangladesh, in a study conducted in 2011–2012, the organism was found in sputum at a low concentration of 2.86% (Akter et al., 2014). However, the pathogen was not also found in Nepal.

**Table 2: Etiological agents of Community Acquired Pneumonia**

| **Study** | **Period** | **Study type** | **Sample size** | **Age** | **Etiology** |
|---|---|---|---|---|---|
| Kalita *et al* | May 1, 2015, and October 30, 2016 | Cross-sectional | **574** | >18 years | *Klebsiella pneumoniae* (15.51%), *Streptococcus pneumoniae* (9.06%), *Staphylococcus aureus* (4.90%), *Moraxella spp*. (1.92%), *Staphylococcus* group (nonaureus) (0.35%), *Acinetobacter spp.* (0.35%) |
| Menon *et al* | January 2009-December 2009 | Prospective | **145** | 18-90 years | *Streptococcus pneumoniae* (32.41%), *Alpha hemolytic streptococci* (6.21%), *Pseudomonas aeruginosa* (8.97%), *Klebsiella pneumoniae* (20%), *Escherichia coli* (6.21%), *Beta hemolytic Streptococci* (1.38%), Atypical coli (0.69%) |

| | | | | | |
|---|---|---|---|---|---|
| Saibal *et al* | February 2009-November 2009 | Prospective observational | **90** | 18-90 years | **Diabetic-**<br>*Streptococcus pneumoniae* (0.0%),<br>*Klebsiella pneumoniae* (19.1%),<br>*Staphylococcus aureus* (4.3%),<br>*Escherichia coli* (4.3%),<br>*Pseudomonas aeruginosa* (4.3%),<br>More than one bacteria (14.9%),<br>*Acinetobacter* (2.1%);<br>**Non-diabetic-**<br>*Streptococcus pneumoniae* (20.9%),<br>*Klebsiella pneumoniae* (4.7%),<br>*Staphylococcus aureus* (2.3%),<br>*Escherichia coli* (0.0%),<br>*Pseudomonas aeruginosa* (0.0%),<br>More than one bacteria (0.0%),<br>*Acinetobacter* (0.0%) |
| Shah *et al* | December 1998-December 2000 | | **100** | 15-80 years | **From sputum culture**<br>*Pseudomonas aeruginosa* (9%),<br>*Staphylococcus aureus* (6%),<br>*E. coli* (5%),<br>*Klebsiella* (3%),<br>*Streptococcus pneumoniae* (1%),<br>*Streptococcus pyogenes* (1%),<br>*Acinetobacter* (1%)<br>**From blood culture**<br>*Pseudomonas aeruginosa* (3%)<br>*Staphylococcus aureus* (2%)<br>*Klebsiella* (1%) |

| | | | | | |
|---|---|---|---|---|---|
| Zubairi *et al* | February 2007 to March 2008 | Descriptive study | **124** | 16-90 years | *Mycoplasma pneumoniae* (17%),<br>*Chlamydia pneumoniae* (12%),<br>*Streptococcus pneumoniae* (7%),<br>*Haemophilus influenzae* (1.6%),<br>*Klebsiella pneumoniae* (1.6%)<br>*Staphylococcus aureus* (0.8%). |
| Iqbal *et al* | January 2011-December 2016 | Retrospective observational | **509** | mean age was 63.6± 16.5 years. | *Staphylococcus aureus* (20%),<br>Methicillin Resistant *Staphylococcus aureus* (3%),<br>*Moraxella catarrhalis* (5%),<br>*Stenotrophomas maltophilia* (4%),<br>*Escherichia coli* (12%),<br>*Haemophilus influenzae* (6%),<br>*Klebsiella pneumoniae* (14%),<br>*Pseudomonas aeruginosa (*18%),<br>*Streptococcus pneumoniae* (18%) |
| Akhter *et al* | July 1, 2011 to June 30, 2012. | cross sectional study | **105** | 18-81 years | **From sputum culture:**<br>*Streptococcus pneumoniae* (20%),<br>*Staphylococcus aureus* (3%),<br>*Klebsiella pneumoniae* (13.33%),<br>*Pseudomonas aeruginosa* (5.71%),<br>*Escherichia coli* (2%),<br>*Haemophilus influenzae* (9%),<br>*Acinetobacter baumanii* (1%) |

| | | | | | |
|---|---|---|---|---|---|
| Para *et al* | November 1 2013-October 31 2015 | | **225** | 18-93 years | *Streptococcus pneumoniae* (30.5%), *Legionella pneumophila* (17.5%), *Mycoplasma pneumoniae* (7.2%), *Chlamydia pneumoniae* (5.5%), *Mycobacterium tuberculosis* (4.8%), *Klebsiella pneumoniae* (4.8%), Methicillin-resistant *S. aureus* (MRSA) (3.5%), *Pseudomonas aeruginosa* (3.1%), Methicillin-sensitive *S. aureus* (1.7), *Acinetobacter baumannii* (0.8%), Multiple pathogens (4%) |
| Abdullah *et al* | December 2008 and June 2010. | Prospective study | **50** | 66-88 years | *Streptococcus pneumoniae* (16%), *Klebsiella pneumoniae* (6%), *Pseudomonas* (4%), *Haemophilus influenzae* (4%), *Staphylococcus aureus* (2%), *Escherichia coli* (2%) |
| Prasad and Bhat | | cross-sectional study | **165** | >16 years | *Klebsiella pneumoniae* (29.09%), *Haemophilus influenzae* (4.8%), *Pseudomonas* spp. (18.18%), *Streptococcus pneumoniae* (13.33%). |

| | | | | | |
|---|---|---|---|---|---|
| Bansal *et al* | March 2000 to February 2001 | Prospective study | **70** | 17-93 years | *Streptococcus pneumoniae* (35.8%),<br>*Klebsiella pneumoniae* (22.6%),<br>*Staphylococcus aureus* (17%),<br>*Mycoplasma pneumoniae* (15%),<br>*E. coli* (11.3%),<br>*β–haemolytic Streptococci* (7.5%),<br>Other Gram- negative bacilli (9.4%) |
| Acharya *et al* | | cross sectional study | **100** | 14-70 years | *Streptococcus pneumoniae* (31%),<br>*Pseudomonas aeruginosa* (15%),<br>*Klebsiella pneumoniae* (13%),<br>*Staphylococcus aureus* (8%),<br>*Moraxella catarrhalis* (8%),<br>*E. coli* (8%),<br>*Acinetobacter* (8%),<br>*Haemophilus influenzae* (5%),<br>*Citrobacter* (3%),<br>*Enterococci* (3%). |

| | | | | | |
|---|---|---|---|---|---|
| Jain *et al* | September 2011- October 2012 | prospective study | **120** | 15 to 85 years | **Sputum culture**<br>*Streptococcus pneumoniae* (36.4%),<br>*Klebsiella pneumoniae* (31.8%),<br>*Staphylococcus aureus* (20.4%),<br>*Haemophilus influenzae* (4.5%),<br>*Pseudomonas* (2.3%),<br>*Acinetobacter* (2.3%),<br>*E. coli* (2.3%)<br><br>**Blood culture**<br>*Streptococcus pneumoniae* (36.4%),<br>*Klebsiella pneumoniae* (18.2%),<br>*Staphylococcus aureus* (18.2%),<br>*Haemophilus influenzae* (9.1%),<br>*Enterobacter* (9.1%),<br>*Citrobacter* (9.1%) |
| Kejriwal *et al* | over a period of 2 years | cross sectional study | **60** | >14 years | *Streptococcus pneumoniae* (56%),<br>*Pseudomonas* (11.1%),<br>*E. coli* (5%) *Acinetobacter* (5%),<br>*Staphylococcus aureus* (3.3%),<br>*Klebsiella* (1.3%),<br>Mixed infections (16.7%). |

### 3.1.2 HAP (Hospital Associated Pneumonia) and VAP (Ventilator Associated Pneumonia) Etiology

#### *Klebsiella pneumoniae*

*Klebsiella pneumoniae* was detected at its highest level around 2017 in a study conducted in India in both HAP (17.30%) and VAP (49%) patients (Bhadade et al., 2017). However, in a study of VAP patients from 2010 to 2015, the organism was detected at the lowest rate (13%)(Khurana et al., 2017). In the following years (2015–2016), also in a study of India, *Klebsiella pneumoniae* was found to have the lowest concentration (8.5%) (Dhar et al., 2018). In contrast, in a study of Bangladeshi VAP patients conducted between 2012 and 2014, the organism prevalence was high at both early (15.38%) and late (16.67%) onset (Mallick et al., 2015). Pathogens were found in only 24% of VAP patients in a Pakistani study in 2007 (Khan et al., 2009); however, the pathogens were not detected in Nepal.

#### *Staphylococcus aureus*

In a study conducted around 2017 in India, *Staphylococcus aureus* was detected in the highest amount in both HAP (43.40%) and VAP (9.43%) patients (Bhadade et al., 2017). On the other hand, previous studies carried out in the following years (2010–2011) and 2010–2015 revealed a low prevalence of the organism (5% and 3%, respectively) (Khurana et al., 2017; Mathai et al., 2015). Both in Bangladesh and Nepal, the prevalence of the organism was significantly low. In a study conducted between 2017 and 2018, the prevalence in Bangladesh was 2.20% in VAP patients (Nusrat et al., 2020). Similarly, among HAP and VAP patients in Nepal, the percentage of the pathogen was 3.80% according to a study conducted in 2016–2018 (Dongol et al., 2021). Nevertheless, *Staphylococcus aureus* was not detected in Pakistan.

#### *Streptococcus pneumonia*

The prevalence of *Streptococcus pneumoniae* was comparatively low and was only detected in India. In a study conducted around 2017, the prevalence was 13.04% in HAP patients and 1.80% in VAP patients (Bhadade et al., 2017).

#### *Acinetobacter baumannii*

A noteworthy identification is that *Acinetobacter baumannii* was detected in VAP patients in India, Pakistan, and Bangladesh. In India, 54% of the organism was detected in a study conducted between 2010 and 2015, and another significant amount (44.60%) was found in a study conducted between 2016 and 2017 (Agarwal et al., 2018; Khurana et al., 2017). In Pakistan, a study conducted in 2017–2018 detected a prevalence of 42.40% (Ishtiaq et al., 2021). Furthermore, in a study conducted between 2012 and 2014 in Bangladesh, *Acinetobacter baumannii* was found at a high prevalence (66.67%) in late-onset infections (Mallick et al., 2015).

**Table 3: Etiological agents of HAP and VAP**

| Study | Period | Study type | Sample size | Age | Type | Etiology |
|---|---|---|---|---|---|---|
| Bairy *et al* | January 2005-December 2007 | Retrospective | **129** | Above 18 | HAP | **Early onset:**<br>*Pseudomonas aeruginosa* (39.2%),<br>MRSA (9%),<br>*Acinetobacter* spp. (8%),<br>*Klebsiella pneumoniae* (13.6%)<br>**Late onset:**<br>MRSA (30.7%),<br>*Acinetobacter* spp. (28%),<br>*Pseudomonas aeruginosa* (15.1%) |
| Mahendra *et al* | August 2015-February 2016 | Prospective | **200** | | VAP | *Acinetobacter* (14.5%).<br>*Klebsiella* (8.5%),<br>*Streptococcus* (7.5%) |
| Nusrat *et al* | July 2017-June 2018 | Cross-sectional | **105** | 16-92 years | VAP | *Acinetobacter* spp. (43.2%),<br>*Klebsiella* spp. (20%),<br>*Pseudomonas* spp. (18.9%),<br>*E. coli* (8.9%),<br>CoN *Staphylococcus* (2.2%),<br>*Staphylococcus aureus* (2.2%),<br>Mixed growth (7.8%) |

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|---|---|---|---|---|---|---|
| Agarwal *et al* | August 2016-April 2017 | prospective observational | **186** | 12-96 years | VAP | *Acinetobacter baumannii* (44.6%), *Pseudomonas aeruginosa* (16.7%), *Klebsiella pneumoniae* (17.2%), *Escherichia coli* (8.6%), *Enterobacter aeruginosa* (3.7%), *Staphylococcus* species (2.6%), Others (6.5%) |
| Kumari *et al* | June 2019-May 2020 | Prospective | **187**(VAP), **244**(VAP, Non-VAP) | Non-VAP 19-82 years, VAP 19-89 years | VAP | *Acinetobacter baumannii* (29.4%) *Pseudomonas aeruginosa* (24.1%), *Klebsiella pneumoniae* (24.1%) *Staphylococcus aureus* (7.5%) **Early-onset VAP** *Klebsiella pneumoniae* (36.4%), *Acinetobacter baumannii* (20.5%), *S. aureus* (20.5%), **Late-onset VAP** *Acinetobacter baumannii* (32.2%), *Pseudomonas aeruginosa* (29.4%), *Klebsiella pneumoniae* (20.3%) *E. coli* (5.6%) |
| Khan *et al* | June 2007-November 2007 | | | | VAP | *Acinetobacter* spp. (76%), *Pseudomonas aeruginosa* (43%), *Klebsiella pneumoniae* (24%) |
| Ishtiaq *et al* | July 2017 - June 2018 | Cross sectional | **39** | | VAP | *Acinetobacter baumannii* (42.4%). |

| | | | | | | |
|---|---|---|---|---|---|---|
| Dongol *et al* | April 2016 and March 2018 | prospective observational cohort study | **438** | 18-95 years | HAP, VAP | *Acinetobacter* spp (31.8%), *Klebsiella* spp (32.7%), *Pseudomonas* spp (12.7%), *E. coli* (10%), *Enterobacter* spp (4.5%), Coagulase negative *Staphylococcus* (CoNS) (6.4%), *Streptococcus aureus*(3.8%) |
| Parajuli *et al* | January 2014-March 2015 | prospective study | **72** | 35-60 years | VAP | *Acinetobacter* spp (43.0%), *Klebsiella* spp (25.0%), *Escherichia coli* (13.8%), *Pseudomonas aeruginosa* (8.3%), *Burkholderia cepacia* (6.9%), *Citrobacter freundii* (2.8%), *Staphylococcus aureus* (0.0%), Coagulase-negative *Staphylococci* (0.0%) |
| Khurana *et al* | January 2010 to July 2015 | Prospective | | | VAP | *Acinetobacter baumannii* (54%), *Pseudomonas aeruginosa* (21%), *Klebsiella pneumoniae* (13%), *E. coli* (3%), *Staphylococcus aureus* (3%), *Stenotrophomona, S. maltophilia* (2%), *Burkholderia cepacia* (1%), *Providencia* spp. (0.7%), *Candida* spp. (0.7%) |

| | | | | | | |
|---|---|---|---|---|---|---|
| Mathai *et al* | October 1, 2010-September 30, 2011 | Prospective observational study | **95** | Mean age 55.49 ± 17.45 years | VAP | *Candida* (5%),<br>*Staphylococcus aureus* (5%),<br>*E. coli* (8%),<br>*Klebsiella* (16%),<br>*Pseudomonas* (13%),<br>*Acinetobacter* (53%) |
| Mallick *et al* | July 2012 - June 2014 | Prospective cohort study | **50** | >18 years | VAP | **Early onset-**<br>*Acinetobacter baumannii* (38.46%),<br>*Pseudomonas aeruginosa* (42.31%),<br>*Klebsiella pneumoniae* (15.38%),<br>MRSA (3.85%),<br>*E. coli* (3.85%);<br>**Late onset-**<br>*Acinetobacter baumannii* (66.67%),<br>*Pseudomonas aeruginosa* (20.83%),<br>*Klebsiella pneumoniae* (16.67%),<br>MRSA (12.5%),<br>*E. coli* (12.5%) |

### 3.2 Antibiotic resistance pattern of CAP, HAP and VAP

#### 3.2.1 Antibiotic resistance pattern (CAP)

**Resistance pattern of *Streptococcus pneumoniae***

An Indian study conducted between 2015 and 2016 found no resistance to Vancomycin and low resistance to Linezolid (3.50%) (Kalita et al., 2021). Resistance to Moxifloxacin and Ofloxacin was also low, at 15.80% and 19.30%, respectively (Kalita et al., 2021). In the same study, the organism showed high resistance to Co-trimoxazole (75.40%) (Kalita et al., 2021). In another study of India carried out around 2017, the organism had low resistance against Amoxyclav (20%) and Levofloxacin (20%) (Prasad & Bhat, 2017). Low resistance against Amoxyclav (5%) and Ampicillin (15%) was also found in Bangladesh in a study conducted from 2011 to 2012 (Akter et al., 2014).

**Resistance pattern of *Klebsiella pneumoniae***

*Klebsiella pneumoniae* found to be non-resistant to Meropenem and Ertapenem in two studies conducted in Bangladesh (2011-2012) and India (2015-2016) (Akter et al., 2014; Kalita et al., 2021). In the study of Bangladesh (2011-2012) the pathogen also showed low resistance against Ceftriaxone (7.15%) and Amoxyclav (14.28%) (Akter et al., 2014). However *Klebsiella pneumonia* was found in high resistant tendency in the same study against Clarithromycin (57.14%) (Akter et al., 2014). Moreover, the pathogen was found in high resistant tendency against Co-trimoxazole (66.70%), Chloramphenicol (69.60%), Cefazolin (58.80%) and Cefuroxine (57.80%) in India (2015-2016)(Kalita et al., 2021). However, the organism exhibited low resistance against Piperacillin-Tazobactam (39.50%) and Carbapenem (16.60%) in an Indian study conducted around 2017 (Prasad & Bhat, 2017).

**Resistance pattern of *Staphylococcus aureus***

In an Indian study conducted in 2015-2016, the pathogen exhibited low resistance against all the tested antibiotics and had no resistance against Vancomycin and Tiecoplanin (Kalita et al., 2021).

#### 3.2.2 Antibiotic resistance pattern (HAP, VAP)

**Resistance pattern of *Klebsiella pneumoniae***

In different studies in India on HAP and VAP patients, *Klebsiella pneumoniae* exhibited complete resistance against Cefazolin, Amoxicillin, Amoxicillin + Clavulanic acid and Ceftazidime (Bhadade et al., 2017; Kumari et al., 2021). Also, in Pakistan, in a study conducted in 2007 on VAP patients, the pathogen showed complete resistance to Ampicillin, Co-trimoxazole, Cefixime, Ceftriaxone, and Cefuroxime (Khan et al., 2009). On the other hand, in the same study, the organism was non-resistant to Amikacin, Meropenem, and Piperacillin-Tazobactam (Khan et al., 2009). Also, in an Indian study carried out between 2005 and 2007 *Klebsiella pneumoniae* showed high resistance to Ampicillin (83.33%) (Bairy & Bhat, 2010). In an Indian study carried out around 2017 on HAP and VAP patients, the pathogen showed high resistance to Cefepime (98.70%),

Methicillin (96.20%), Vancomycin (91%), Ceftriazone (85.90%), Ciprofloxacin (84.60%), and Amikacin (82.10%) (Prasad & Bhat, 2017). Nevertheless, in India and Bangladesh, *Klebsiella pneumoniae* showed low-resistant (25%) and non-resistant properties to Colistin (Agarwal et al., 2018; Kumari et al., 2021; Nusrat et al., 2020). In an Indian study conducted between 2019 and 2020, the pathogen was found to be highly resistant to Ciprofloxacin (96.10%), Ceftriaxone (93.80%), Cefoxitin (93.80%), Levofloxacin (92.20%), Piperacillin-Tazobactam (92.20%), Aztreonam (90%), and Tobramycin (88.20%)(Kumari et al., 2021). In the prior years (2015–2016), the organism was detected to be highly resistant to Linezolid (94%), Azithromycin (88%), and Cefoperazone (82%) (Dhar et al., 2018). In the same study, the pathogen was found to have low resistance against Imipenem (17%) (Dhar et al., 2018). In addition, in the studies conducted between 2005 and 2007 in Pakistan, the organism exhibited low resistance to Ofloxacin (11%), and in India, it showed low resistance to Amikacin (16.67%) (Khan et al., 2009).

**Resistance pattern of *Streptococcus pneumoniae***

*Streptococcus pneumoniae* was highly resistant to Amikacin (73%) in a study conducted in India between the year 2005 and 2007, however low resistance to Ceftazidime (13%) and Cefoperazone (13%) (Dhar et al., 2018). In addition the pathogen was non-resistant to Ciprofloxacin and exhibited 20% resistance to Amoxicillin + Clavulanic acid, Methicillin, Vancomycin, Amikacin and Piperacillin-Tazobactam in another study carried out in India around 2017 (Prasad & Bhat, 2017).

**Resistance pattern of *Staphylococcus aureus***

In Bangladesh in a study carried out in 2017 and 2018, *Staphylococcus aureus* was completely resistant to Azithromycin, Ciprofloxacin and Levofloxacin (Nusrat et al., 2020). However, in the same study, the pathogen was not resistant to Amoxyclav, Amikacin, Ceftazidime, Gentamicin and Vancomycin (Nusrat et al., 2020). In another study of India, the organism was highly resistant to Cefepime (88.90%) and Ceftazidime (72.20%) and showed low resistance to Methicillin (16.70%) and Ciprofloxacin (16.70%) (Bhadade et al., 2017).

**Resistance pattern of *Acinetobacter baumannii***

In India in a study conducted on VAP patients A*cinetobacter baumannii* exhibited complete resistance to Linezolid, Ceftazidime, Piperacillin and Azithromycin (Dhar et al., 2018). Further the organism was detected to be highly resistant to Amikacin (93%), Levofloxacin (93%) and Cefoperazone (93%) in the same study (Dhar et al., 2018). On the other hand, in two different studies the pathogen was found to be non-resistant to both Colistin and Tigecycline and low resistant (2.40%) to Colistin (Agarwal et al., 2018; Kumari et al., 2021). However, in a study carried out in 2019 to 2020 in India A*cinetobacter baumannii* was highly resistant to Ceftriaxone (96.70%), Levofloxacin (95.60%), Ciprofloxacin (90.20%), Gentamycin (88%), Imipenem (85.90%) and Amikacin (84.80%) (Kumari et al., 2021).

## Table 4: Antibiotic Resistance pattern

| Studies | Year | Antibiotics | Organisms | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | ***Acinetobacter spp.*** | ***Pseudomonas*** | ***Klebsiella pneumoniae*** | ***Streptococcus pneumoniae*** | ***Staphylococcus aureus*** | ***Acinetobacter baumanii*** | ***Pseudomonas aeruginosa*** | ***Staphylococcus species*** |
| Bairy *et al* | 2010 | Amikacin | 80.00% | 28.95% | 16.67% | - | | | | |
| | | Ampicillin | 90% | | 83.33% | - | | | | |
| | | Amoxicillin plus Clavulanic acid | 100% | | 44.44% | - | | | | |
| | | Cefoperazone | 90% | 60.53% | 55.56% | - | | | | |
| | | Cefotaxime | 100% | | 61.11% | | | | | |
| | | Ciprofloxacin | 90% | | 50% | | | | | |
| | | Ceftazidime | 100% | 15.79% | 55.56% | | | | | |
| | | Gentamicin | 100% | 50% | | | | | | |
| | | Imipenem | 100% | | 22.22% | | | | | |
| | | Netilmicin | 30% | 26.31% | 38.80% | | | | | |
| | | Ofloxacin | 50% | 39.47% | 33.30% | | | | | |
| | | Piperacillin | 90% | 36.84% | | | | | | |
| | | Tobramycin | 100% | 39.47% | | | | | | |
| Mahendra *et al* | 2018 | Linezolid | | 100% | 94% | 26% | | 100% | | |
| | | Amikacin | | 33% | 53% | 73% | | 93% | | |
| | | Ceftazidime | | 33% | 47% | 13% | | 100% | | |
| | | Imipenem | | | 17% | | | 28.00% | | |
| | | Piperacillin | | 44% | 52% | | | 100.00% | | |
| | | Azithromycin | | 100% | 88% | 26% | | 100.00% | | |
| | | Levofloxacin | | 77% | 70% | | | 93.00% | | |
| | | Cefoperazone | | 88% | 82% | 13% | | 93.00% | | |
| Nusrat *et al* | 2020 | Amoxyclav | 82.90% | 17.70% | 75% | | 0 | | | |
| | | Amikacin | 70.70% | 52.90% | 50% | | 0 | | | |
| | | Azithromycin | 73.20% | 72.20% | 66.70% | | 100% | | | |
| | | Ceftazidime | 80.50% | 61.10% | 58.00% | | 0 | | | |
| | | Ceftriaxone | 87.80% | 72.20% | 83.30% | | 50% | | | |
| | | Colistin | 19.50% | 0 | 0 | | | | | |
| | | Ciprofloxacin | 82.90% | 88.80% | 87.50% | | 100% | | | |

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|---|---|---|---|---|---|---|---|---|---|---|
| | | Gentamicin | 92.70% | 61.10% | 54.20% | | 0 | | | |
| | | Imipenem | 56.10% | 33.30% | 54.20% | | | | | |
| | | Piperacillin-Tazobactum | 73.20% | 23.50% | 11.11% | | | | | |
| | | Levofloxacin | | | | | 100% | | | |
| | | Vancomycin | | | | | 0 | | | |
| | | Oxacillin | | | | | 50% | | | |
| Agarwa *et al* | 2018 | Collistin | | | 25% | | | 2.40% | 16% | 100% |
| Kumari *et al* | 2021 | Ampicillin | | | | | | | | |
| | | Amoxy-clavulanic acid | | | | | | | 91.80% | |
| | | Amikacin | | | 78.40% | | | 84.80% | 48.90% | |
| | | Tobramycin | | | 88.20% | | | 80.40% | 75.60% | |
| | | Gentamycin | | | 80.40% | | | 88% | 82.20% | |
| | | Ciprofloxacin | | | 96.10% | | | 90.20% | 46.70% | |
| | | Levofloxacin | | | 92.20% | | | 95.60% | 91.40% | |
| | | Aztreonam | | | 90% | | | | 50% | |
| | | Ceftriaxone | | | 93.80% | | | 96.70% | | |
| | | Cefoxitin | | | 93.80% | | | | | |
| | | Cefazolin | | | 100% | | | | | |
| | | Ceftazidime | | | | | | | 62.10% | |
| | | Piperacillin-tazobactam | | | 92.20% | | | 66.30% | 53.30% | |
| | | Imipenem | | | 66.70% | | | 85.90% | 57.80% | |
| | | Meropenem | | | 70.60% | | | 65.20% | 48.90% | |
| | | Ertapenem | | | 56% | | | | | |
| | | Colistin | | | 0 | | | 0 | 0 | |
| | | Tigecycline | | | 0 | | | 0 | 0 | |

| Studies | Year | Antibiotics | Organisms | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | ***Acinetobacter spp.*** | ***Pseudomonas*** | ***Klebsiella pneumoniae*** | ***Streptococcus pneumoniae*** | ***Staphylococcus aureus*** | ***Acinetobacter baumanii*** | ***Pseudomonas aeruginosa*** | ***Staphylococcus species*** |
| Bhadade *et al* | 2017 | Amoxicillin | 93.30% | | 100% | 40% | 50% | | 100% | |
| | | Amoxicillin + clavulanic acid | 86.70% | | 100% | 20% | 27.80% | | 94.70% | |
| | | Methicillin | 80% | | 96.20% | 20% | 16.70% | | 94.70% | |
| | | Vancomycin | 73.30% | | 91% | 20% | 22.20% | | 89.50% | |
| | | Meropenem | 66.70% | | 56.40% | 40% | 33.30% | | 52.60% | |
| | | Imipenem | 46.70% | | 44.90% | 40% | 38.90% | | 50% | |
| | | Ceftriaxone | 86.70% | | 85.90% | 40% | 44.40% | | 84.20% | |
| | | Ceftazidime | 100% | | 100% | 40% | 72.20% | | 92.10% | |
| | | Cefepime | 100% | | 98.70% | 80% | 88.90% | | 97.40% | |
| | | Amikacin | 60% | | 82.10% | 20% | 33.30% | | 84.20% | |
| | | Ciprofloxacin | 73.30% | | 84.60% | 0% | 16.70% | | 92.10% | |
| | | Piperacillin + tazobactam | 46.70% | | 39.70% | 20% | 27.80% | | 44.70% | |
| Kalita *et al* | 2021 | ESBL | | | 40.20% | | | | | |
| | | Oxacillin | | | | 54.40% | | | | |
| | | Erythromycin | | | | 52.60% | 13.20% | | | |
| | | Azithromycin | | | | 52.60% | 10.50% | | | |
| | | Clarithromycin | | | | 50.90% | | | | |
| | | Co-trimoxazole | 100% | | 66.70% | 75.40% | 5.30% | | | |
| | | Clindamycin | | | | 40.40% | 10.50% | | | |
| | | Doxycyline | 100% | | 38.20% | 42.10% | 2.60% | | | |
| | | Ciprofloxacin | 0 | | 39.20% | | 10.50% | | | |
| | | Levofloxacin | 0 | | 36.30% | 21.10% | 5.30% | | | |
| | | Moxifloxacin | 0 | | 29.40% | 15.80% | 7.90% | | | |
| | | Ofloxacin | | | | 19.30% | | | | |
| | | Vancomycin | | | | 0 | 0 | | | |
| | | Linezolid | | | | 3.50% | | | | |
| | | Chloramphenicol | | | 69.60% | 68.40% | 13.20% | | | |

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|---|---|---|---|---|---|---|---|---|---|---|
| | | Amoxyclav | | | 46.10% | | | | | |
| | | Cefazolin | | | 58.80% | | | | | |
| | | Gentamicin | 50% | | 50% | | 26.30% | | | |
| | | Tobramycin | 50% | | 47.10% | | | | | |
| | | Amikacin | 0 | | 40.20% | | | | | |
| | | Piperacillin-Tazobactam | 50% | | 40.20% | | | | | |
| | | Ticarcillin - clavulanic acid | 50% | | 43.10% | | | | | |
| | | Cefuroxime (oral) | | | 57.80% | | | | | |
| | | Cefotaxime | 0 | | 42.10% | | | | | |
| | | Ceftriaxone | 0 | | 40.20% | | | | | |
| | | Cefepime | 0 | | 36.40% | | | | | |
| | | Cefoxitin | | | 55.90% | | | | | |
| | | Meropenem | 0 | | 0 | | | | | |
| | | Ertapenem | | | 0 | | | | | |
| | | Azteronam | | | 43.10% | | | | | |
| | | Tetracycline | 100% | | 50% | | 13.20% | | | |
| | | Minocycline | | | 43.10% | | | | | |
| | | Penicillin 10U | | | | | | | | |
| | | Tiecoplanin | | | | | 0 | | | |
| | | Cefixime | | | | | | | | |
| | | Cefuroxime | | | | | | | | |
| | | Ceftazidime | 0 | | 41.18% | | | | | |
| | | Ampicillin-sublactam | 100% | | | | | | | |
| | | Imipenem | 0 | | | | | | | |
| Khan *et al* | 2009 | Ampicillin/sulbactam | 72% | | | | | | | |
| | | Aztreonam | | | 100% | | | | 40% | |
| | | Amikacin | 78% | | 0 | | | | 44% | |
| | | Ceftazidime | 89% | | | | | | 44% | |
| | | Gentamicin | 92% | | 78% | | | | 60% | |

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|---|---|---|---|---|---|---|---|---|---|---|
| | | Cefepime | 73% | | | | | | 50% | |
| | | Polymyxin | 0 | | | | | | 0 | |
| | | Meropenem | 85% | | 0 | | | | 25% | |
| | | Tazobactam/piperacillin | 65% | | 0 | | | | 6% | |
| | | Ofloxacin | | | 11% | | | | 62% | |
| | | Amoxicillin/clavulanic acid | | | 33% | | | | | |
| | | Ampicillin | | | 100% | | | | | |
| | | Co-trimoxazole | 87% | | 100% | | | | | |
| | | Cefixime | | | 100% | | | | | |
| | | Ceftriaxone | 96% | | 100% | | | | | |
| | | Cefuroxime | | | 100% | | | | | |
| | | Tetracycline | 48% | | | | | | | |
| Ilshtiaq *et al* | 2021 | Piperacillin | | | | | | | | |
| | | Ampicillin-sublactum | | | | | | | | |
| | | Ceftriaxone | | | | | | | | |
| | | Gentamycin | | | | | | | | |
| | | Tetracycline | | | | | | | | |
| | | Ciprofloxacin | | | | | | | | |
| | | Trimethoprim-Sulfamethoxazole | | | | | | | | |
| | | Imipenem | | | | | | | | |
| Akhter *et al* | 2014 | Meropenem | 0% | 0% | 0% | | | | | |
| | | Ceftriaxone | 100% | 83.34% | 7.15% | | | | | |
| | | Clarithromycin | 100% | 100% | 57.14% | | | | | |
| | | Amoxyclav | 0% | 100% | 14.28% | 5% | | | | |
| | | Ciprofloxacin | 0% | 50% | 42.85% | | | | | |
| | | Cefixime | 100% | 83.34% | 50% | | | | | |
| | | Amikacin | 0% | 16.66% | 28.57% | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|
| | | Gentamicin | 0% | 66.67% | 35.71% | | | | | |
| | | Ampicillin | | | | 15% | | | | |
| Prasad and Bh | 2017 | Amoxyclav | | | | 20% | | | | |
| | | Levofloxacin | | | | 20% | | | | |
| | | Carbapenems | | | 16.60% | | | | | |
| | | Piperacillin-Tazobactam | | 42% | 39.50% | | | | | |
| | | Cefoperazone-sublactam | | | | | | | | |

## CHAPTER 4

## Discussion

Our review highlights the variation of bacterial etiology of adult pneumonia while focusing on the bacteria that cause HAP, VAP and CAP along with these bacteria's antibiotic resistance. According to data on the causative organism, gram-positive organisms were more common in CAP than HAP. However, gram-negative organisms predominated over gram-positive organisms in both HAP and CAP cases. *Streptococcus pneumoniae* was found to be the most common causative agent in each CAP study conducted in India, Nepal, and Bangladesh. The pathogen was observed to be the most common (56%) in 2015 in a study conducted in India (Kejriwal et al., 2015). The second bacteria found common in CAP was *Klebsiella pneumoniae,* which was found in seven studies in India and detected highest in the years 2011–12 (31.8%) and around 2017 (29.09%) (Jain et al., 2014; Prasad & Bhat, 2017). *Staphylococcus aureus*, which was identified frequently in the years 2000–2001 (17%) and 2011–2016 (20%), was the third most frequently found organism (Bansal et al., 2004; Iqbal et al., 2020). Our finding of *Streptococcus pneumoniae* being the most found causative agent of CAP correlates with other studies performed in Europe and the UK (Chalmers et al., 2017).

On the other hand, *Klebsiella pneumoniae* was the most common pathogen found responsible for HAP and VAP. In a study conducted in India, the organism was found in patients with HAP (17.30%) and VAP (49%) at its maximum level around 2017 (Bhadade et al., 2017). Second most common HAP and VAP causative organism was *Staphylococcus aureus* and was detected highest in India around the year 2017 in HAP (43.40%) and VAP (9.43%) patients (Bhadade et al., 2017). However, the findings of this organism were significantly low in Bangladesh and Nepal (Dongol et al., 2021; Nusrat et al., 2020). A notable finding in HAP and VAP cases was that *Acinetobacter baumannii* was detected in India, Bangladesh, and Pakistan. Moreover, the organism was found most abundant in India in two studies conducted in 2010 and 2015 (54%) and 2016 and 2017 (44.60%) (Agarwal et al., 2018; Khurana et al., 2017).

Being the most detected causative organism for CAP, *Streptococcus pneumoniae* was found to be zero-resistant to Vancomycin and mildly resistant to Linezolid and Amoxycillin in the two studies conducted in India (2015–2016), and Bangladesh (2011-2012), respectively (Akter et al., 2014; Kalita et al., 2021). However, the organism showed high resistance to Co-trimoxazole (75.40%) in an Indian study (Kalita et al., 2021). The second most common pathogen, Klebsiella pneumoniae found to have zero resistance towards Meropenem and Ertapenem in Bangladesh (2011-2012) and Indian (2015-2016) studies respectively (Akter et al., 2014; Kalita et al., 2021). However, the pathogen showed highest resistance against Chloramphenicol in an Indian study (2015-2016) (Kalita et al., 2021). Another highest identified causative organism of CAP, *Staphylococcus aureus,* found to be non-resistant against Vancomycin and Tiecoplanin in the same study (Kalita et al., 2021). On the other hand, *Klebsiella pneumoniae* the highest causative organism showed complete resistance against Cefazolin Amoxicillin, Amoxicillin + Clavulanic acid, Ceftazidime in different studies conducted in India on HAP and VAP patients (Bhadade et al., 2017; Kumari et al., 2021). Also found similar resistance pattern in a study conducted on VAP patients in Pakistan against Ampicillin, Co-trimoxazole, Cefixime, Ceftriaxone, and Cefuroxime (Khan et al., 2009). On the contrary, in the same study, the pathogen showed zero resistance against Amikacin, Meropenem, and Piperacillin-Tazobactam (Khan et al., 2009). The third common pathogen responsible for HAP and VAP *Staphylococcus aureus* exhibited complete resistance

towards Azithromycin, Ciprofloxacin and Levofloxacin in a Bangladeshi study conducted in 2017-2018 and was non-resistant to Amoxyclav, Amikacin, Ceftazidime, Gentamicin and Vancomycin (Nusrat et al., 2020).

According to American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) guidelines, it is recommended to perform sputum and blood cultures for the severe cases of CAP (Metlay et al., 2019). Also, in our reviewed papers, most of the studies performed sputum and blood cultures to diagnose the causative agent of pneumonia for CAP.

Although the reviewed studies included patients with comorbidities and the most observed risk factors were COPD, smoking, chest disease, and diabetes, most of the studies did not mention significant reflection upon the changes in CAP, HAP, and VAP prevalence accustomed due to the comorbidities except for a study conducted at Shimla, India (Bansal et al., 2004). Additionally, the effectiveness of adult pneumonia vaccines (PPV23 and PCV13) was not adequately investigated in this region of south Asia in patients with risk factors, which could be a potential study opportunity in the future.

# CHAPTER 5

## Limitations and Strengths

Performing this review was difficult for a number of reasons, which resulted in some data restrictions. First of all, lack of adequate studies in regions such as- Nepal, Bhutan and Sri Lanka prevented to draw a complete scenario of the bacterial pneumonia in South Asian adults. Moreover, studies included in this review incorporate results that had a lower isolation rate due to several reasons including- atypical agents causing pneumonia and use of prior antibiotic administration.

Conducting this review highlighted the insufficiency of articles containing both etiology and antibiotic resistant patterns in South Asia. In addition, data representation in the included studies mainly focused on the etiological agents than the resistance pattern. Since making reasonable conclusions about the empirical antibiotic therapy requires an understanding of the local etiology and antibiotic resistance pattern, the equal emphasis of bacterial etiology and resistant pattern of this review stands out to be a strength of this paper.

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