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REVIEW ON BACTERIAL PATHOGENS ASSOCIATED WITH COMMUNITY-ACQUIRED PNEUMONIA IN CHILDREN

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Abstract

Community-acquired pneumonia is the acute infection lung tissue infection in a patient who established it in the community or within 48 hours of admission to the hospital. and accounts for a significant proportion of the acute lower respiratory infection disease burden. The treatment strategies used in the management of community-acquired pneumonia are Antibiotics, Bronchodilators. The current study aims to find out the bacterial pathogens associated with community-acquired pneumonia. This review discusses the common pathogens found in community-acquired pneumonia in children below twelve years. Various treatment strategies are also discussed in view of identifying the pathogens of community-acquired pneumonia. Depending on the pathogens and age of the patient's antibiotics were selected. The author discusses recent patents relating to the treatment of community-acquired pneumonia. Generally, *Haemophilus influenza* is the most common cause of community-acquired pneumonia in children younger than 5 years. The most common bacterial cause is *Streptococcus pneumonia*, which affects people of all ages. On clinical grounds, bacterial and viral pneumonia cannot be consistently differentiated in the majority of cases. In fact, most children with pneumonia are treated with antibiotics on a case-by-case basis.

Key words: Epidemiology, Etiology, Polymerase chain reaction, *Streptococcus pneumonia*, tachypnea.

Introduction

Community-acquired pneumonia is the acute lung tissue infection in a patient who established it in the community or within 48 hours of admission to the hospital. Streptococcus pneumonia infections are one of the most common causes of disease and death in young children under the age of five and elderly patients around the world, as well as a leading cause of hospitalization in children in the United States[1,2]. Pneumococcal disease is suspected to affect 500,000 cases of pneumonia in the United States per year[3]. Since the early 1980s, a vaccine for the 23 most common serotypes of S. pneumonia has been available. Patients with some underlying medical conditions leading to an elevated risk of pneumococcal disease and its complications should get the vaccine, according to the Advisory Committee on Immunization Practices (ACIP)[4]. Pneumovax 23 can be given to children as young as 2 years old and as old as 65 years old. According to the United Nations International Children's Emergency Fund(UNICEF), paediatric pneumonia is a significant cause of death for more than 800,000 young children worldwide each year. Pneumonia is a serious type of acute lower respiratory infection that affects the lungs only, and it accounts for a large portion of the ALRI disease burden[5]. A bacterial, viral, or fungal infection is usually the starting point. The lungs become inflamed, and the tiny air sacs within the lungs, known as alveoli, fill up with blood, limiting the capacity of the lungs to exchange gases. Breathing becomes more difficult. COVID-19, which is classified as one of the lower respiratory infections by the Global Burden of Disease, has the potential to increase all-cause pneumonia mortality by 70%, raising the annual death toll to 4.5 million people[6].

Cause of Pneumonia based on the age groups

Neonates (<3 weeks) -*Group streptococcus, Escherichia coli, other Gram-negative bacilli, Streptococcus pneumonia, Haemophilus influenza.* 3 weeks - 3 months. *pneumonia, H. influenza,* If the patient is afebrile, consider *Chlamydia trachomatis.* 4 months-4 years –*S. pneumonia, H. influenza, Mycoplasma pneumonia,* group A*Streptococcus.* ≥5 years -*M. pneumonia, S. pneumonia, Chlamydophila pneumonia, H. influenza, influenza viruses, adenovirus, other respiratory viruses, Legionella pneumonia* [7].

Two groups of pathogens cause community-acquired pneumonia

Bacteria, viruses, fungi, and parasites are among the many agents that can cause community-acquired pneumonia, but this article will focus on bacterial pneumonia and its causes. Bacteria are traditionally divided into two groups based on their aetiology: "typical" and "Atypical" species. Typical species can be cultured on standard media and identified using Gram stain, but "atypical" organisms lack these abilities. Based on their age groups frequent pathogens are classified in Table 1.

Typical agents

Typical agents such as *Streptococcus pneumonia, Haemophilus influenza, Moraxella catarrhalis, Staphylococcus aureus, Group A Streptococci, anaerobes, and gram-negative organism*

Atypical agents

Legionella, Mycoplasma, Chlamydia pneumonia, and C. psittaci are sources of atypical agents. Due to the availability of polymerase chain reaction-based detection methods, influenza and non-influenza respiratory viruses have been increasingly detected as pathogens. *Human rhinovirus, influenza virus, and Streptococcus pneumonia* were the most common pathogens in the United States. *S. Pneumonia*, *Klebsiella pneumonia, Haemophilus influenza, and Pseudomonas aeruginosa* are the most common bacteria found in Community-acquired pneumonia.

Epidemiology

CAP affects more than 5 million people in the United States per year. The prevalence of CAP varies by gender; males and African Americans, for example, are more likely than females and other Americans to have it. The total number of deaths among women, on the other hand, has been rising. In the United States and Canada, influenza and pneumonia were the eighth-most prevalent causes of death, respectively, in 2005 [8]. In developed countries, the annual incidence of community-acquired pneumonia is 36 to 40 per 1,000 children

under the age of five, and 11 to 16 per 1,000 children aged 5 to 14 [9].

Types of pneumonia

There are four types of pneumonia, according to the new classification: community-acquired (CAP), hospital-acquired (HAP), healthcare-associated (HCAP), and ventilator-associated pneumonia (VAP)

- **CAP:** Acute infection of the lungs in a patient who established it in the community or within 48 hours of admission to the hospital.
- **HAP:** Acute infection of the lungs that occurs after 48 hours of hospitalization in a non-intubated patient.
- **VAP:** A form of nosocomial lung infection that occurs 48 hours or longer after mechanical ventilation intubation.
- **HCAP:** Acute lung infection obtained from a healthcare facility such as a nursing home, dialysis unit, outpatient clinic, or a patient who has been hospitalised in the previous three months.

Pathophysiology

The lower respiratory tract is not sterile, and it is continuously exposed to bacteria from the environment. Bacterial pneumonia is caused by the invasion and dissemination of the bacteria described above into the lung parenchyma at the alveolar stage. The clinical syndrome of pneumonia is caused by the body's inflammatory reaction to it. There are several host defenses, such as mechanical defenses, that work together in the lungs to prevent microorganism proliferation. Immune cells, such as alveolar macrophages are another part of the pulmonary defense system, and they function to engulf and destroy proliferating bacteria. However, once bacteria exceed the ability of host defenses, they begin to proliferate. The inflammatory response is activated by alveolar macrophages in this situation to improve the lower respiratory tract defenses. The key cause of bacterial pneumonia's clinical presentation is an inflammatory response[9]. The constitutional symptoms are caused by cytokines, which are released in response to an inflammatory reaction; for example, IL-1 (interleukin-1) and TNF (tumour necrosis factor) cause fever. Chemokine-like IL-8 (interleukin-8) and colony-stimulating factors like G-CSF (granulocyte colony-stimulating factor) facilitate chemotaxis and neutrophil maturation, respectively, resulting in leukocytosis and purulent secretions in serological labs. These cytokines cause the alveolar-capillary membrane to leak at the site of inflammation, resulting in decreased compliance and shortness of breath. Even erythrocytes may pass through this barrier, resulting in hemoptysis [10].

Histopathology

Pathologically, Acute exudative inflammation of one or more lung lobes is known as lobar pneumonia. If left untreated, it will proceed to the four advanced stages mentioned below. The stages are congestion, Red hepatization, grey hepatization, Resolution.

- **Congestion:** As a result of an infection, high blood pressure, or cardiac insufficiency, blood vessels in the lungs constrict and blood fills the alveoli. The alveoli are tiny air sacs in the lungs that exchange carbon dioxide and oxygen.
- **Red hepatization**: The lobe becomes consolidated, strong, and liver-like at this point. Fibrin and serous exudate, bacteria, neutrophils, and macrophages can all be seen under the microscope. The capillaries are clogged, and the walls of the alveoli have thickened.
- **Grey hepatization:** Due to suppurative and exudate-filled alveoli, the lobe is still liver-like in appearance but grey in colour.
- **Resolution:** It begins to clear after a week when lymphatic drainage or a productive cough removes the exudate [11].

Laboratory investigation

This involves lab results like complete blood count with differentials, inflammatory biomarkers like ESR and C-reactive protein, blood cultures, sputum analysis or Gram staining, and/or urine antigen screening, as well as a polymerase chain reaction for nucleic acid detection of certain bacteria.

- **An atrial blood gas:** An ABG is a blood test that determines the acidity, or pH, of an artery as well as the levels of oxygen (O2)

and carbon dioxide (CO_2). The test is used to determine how well the patient's lungs perform in terms of carrying oxygen into the bloodstream and removing carbon dioxide. ABGs are usually drawn on patients in the ICU and ER, but they can be drawn on any patient on any floor, depending on their diagnosis. In the short term, it is used to reveal hypoxia and respiratory acidosis [12].

- **Pulse oximetry:** Oxygen saturation, as measured by pulse oximetry, is the percentage of oxygen in haemoglobin proteins. Oxygen saturation is a calculation of how much oxygen enters the organs. Between 95 and 100 %, oxygen saturation is considered natural. Oxygen saturation levels less than 92% When Trusted Source is abnormally poor, it may be a medical emergency that indicates severe hypoxia, and elevated CRP predicts a serious infection [13].
- **Blood cultures:** Blood cultures should be taken before administering antibiotics. Unfortunately, they are only 40 % of cases have positive reports. Wubbel L et al found only sterile blood cultures in a sample of 168 patients with known pneumonia. Blood culture of at least 1 ml of blood from a clean and prepared peripheral venous or arterial site is needed in neonates. This is because many neonatal cases of pneumonia are haematogenous in origin and others serve as a focus for secondary seeding of the bloodstream [14]. WHO criteria follow during the collection of a blood sample, the sample should be collected before the administration of antibiotics, if empirical therapy was started then the blood sample should be collected before the next dose of antibiotic.
- **Radiological Evaluation:** Despite the fact that chest radiographs are widely used to diagnose pneumonia, they are of limited use in the absence of respiratory findings, particularly in young children. Chest radiography is used mainly in children that have problems such as pleural effusions or who have not responded to antibiotic therapy [15]. When the lab and clinical aspects are supportive, a chest X-ray with the finding of pulmonary infiltrates on clear film is found the gold standard for diagnosis. The chest x-ray may reveal a consolidation or Para pneumonic effusion. The repeated chest radiograph should be obtained in children who fail to demonstrate clinical improvement and in those who have progressive symptoms or clinical deterioration within 48–72 hours after initiation of antibiotic therapy[16].

Diagnosis

Fever, cough, respiratory disturbance including tachypnea, intercostals /subcostal /suprasternal retraction, nasal flaring, grunting, and radiologic evidence of acute pulmonary infiltrates and consolidation is typically used to make the diagnosis. Different diagnosis of recurrent pneumonia is shown in table 1 [7].

Pharmacology treatment

Empirical therapy should be begun as soon as possible in all patients with bacterial pneumonia. A risk assessment is the first step of care to determine if the patient should be handled in an outpatient or inpatient environment. The risk of bacterial pneumonia is affected by cardiopulmonary conditions, age, and the severity of symptoms[17].The selection of patients, such as in-patients or out-patients based on the CURB-65 pneumonia severity score CURB- 65 stand for C=Confusion, U=Urea [BUN greater than 20 mg/dl], R=Respiration [greater than 30 per min, B=Blood pressure [BP=less than 90/60 mmHg]

Each of these risk factors is worth one point.

- Outpatient treatment is indicated with a score of 0-1.
- A cumulative score of 2 or more suggests admission to a medical ward.
- ICU admission is suggested if the cumulative score is 3 or higher.

Antibiotics

For children with uncomplicated community-acquired pneumonia, high-dose amoxicillin is used as a first-line agent because it protects against Streptococcus pneumonia. Alternatives include

second-and third-generation cephalosporin, as well as macrolide antibiotics including azithromycin. Similarly, because of the cephalosporin lower systemic absorption and pneumococcal tolerance to macrolides, they should not be used as the first-line agents [18].

A key recommendation by WHO on the treatment of pneumonia

Recommendation 1

A. Oral amoxicillin should be given to children with fast breathing pneumonia who have no chest drawing or other symptoms of risk.
- Age and weight of the children: 2Months up to 12 months, 4 kg –less than 10 kg
- Dose of Amoxicillin: 250 mg [1 tablet twice a day for 5 days]

B. Children with fast-breathing pneumonia that do not respond to amoxicillin as a first-line treatment should be referred to a facility that can offer effective second-line treatment.

Recommendation 2

A. Children age 2–59 months with chest indrawing pneumonia should be treated with oral amoxicillin: at least 40mg/kg/dose twice daily for five days.

Recommendation 3

A. As first-line therapy, children aged 2–59 months with serious pneumonia should be given parenteral ampicillin (or penicillin) and gentamicin.
- Ampicillin: 50 mg/kg, or benzylpenicillin: 50 000 units per kg IM/IV every 6 hours for at least five days
- Gentamicin: 7.5 mg/kg IM/IV once a day for at least five days

B. In children with serious pneumonia who have failed to respond to the first-line treatment, ceftriaxone may be used as a second-line treatment.

Recommendation 4

A. For HIV-infected and -exposed babies, as well as children under the age of 5, ampicillin (or penicillin if ampicillin is not available) plus gentamicin or ceftriaxone is prescribed as a first-line antibiotic regimen for chest indrawing pneumonia or serious pneumonia.

B. Ceftriaxone alone is suggested as a second-line treatment for HIV-infected and -exposed infants and children with chest indrawing pneumonia or serious pneumonia who do not respond to ampicillin or penicillin plus gentamicin.

Recommendation 5

A. For HIV-infected and -exposed infants aged 2 months to 1 year with suspected *Pneumocystis jirovecii* (previously *Pneumocystis carinii*) pneumonia (PCP), empiric cotrimoxazole therapy is recommended as an alternative treatment.

B. For HIV-infected and -exposed children over 1 year of age with chest indrawing or extreme pneumonia, empirical cotrimoxazole treatment for *Pneumocystis jirovecii* pneumonia (PCP) is not recommended [19].
- **Anti-inflammatory therapy:** Glucocorticoids can be helpful in the treatment of severe (hospitalized) community-acquired pneumonia, according to a few small studies in adults. The research design and sample size, on the other hand, restrict the ability to accurately interpret these findings [20].
- **Bronchodilators:** Bronchodilators should not be used on a daily basis. Wheezing that is often heard in patients with pneumonia is usually caused by airway inflammation, mucus plugging, or both, and does not respond to a bronchodilator. Infants and children with reactive airway disease or asthma, on the other hand, can experience bronchospasm in response to a viral infection, which contributes to bronchodilators.
- **Duration:** Shorter treatment courses, particularly for more moderate disease treated on an outpatient basis, can be just as effective as 10-day treatment courses [21].
- **Follow-up Chest x-ray:** Patients with complicated pneumonia who are experiencing worsening respiratory failure or clinical dysfunction, or who have a recurrent fever that is not responding to treatment after 48–72 hours, should have follow-up chest radiographs taken. In case of recurrent pneumonia. The Patients with persistent pneumonia affecting the same

lobe and patients with lobar collapse on initial chest radiography with fear of an anatomic defect, chest mass, or foreign body aspiration should have their chest radiographs repeated 4–6 weeks after the diagnosis of CAP.

- **Prevention:** Pneumococcalvaccine PPV23 is prescribed for the prevention of pneumococcal infections in children aged greater than 2 years and older who have serious chronic underlying disorders and are at high risk of developing pneumococcal infection complications. However, all of the data concerning the possible prevention of CAP in paediatric subjects of any age, regardless of their state of health, come from children who had received a PCV and are mainly found in epidemiological studies evaluating the impact of PCV7 on the incidence of pediatric [22]. PPV23 is indicated for pneumococcal disease prevention in children over the age who have serious chronic underlying conditions and are at high risk of developing pneumococcal infection complications. All evidence on the potential prevention of CAP in paediatric subjects of any age, regardless of their health, comes from children who have earned a PCV and is often used in epidemiological studies assessing the effect of PCV7. The first pneumococcal conjugate vaccine (PCV7) was approved by the Food and Drug Administration (FDA) in 2000. In the same year, the United States started regularly testing children for PCV7. It protected against infections caused by seven different types of pneumococcal bacteria (serotypes). PCV7 was found to be highly effective in preventing invasive pneumococcal disease in young children caused by serotypes used in the vaccine (vaccine serotypes). Two pneumococcal vaccines have been approved for use in the United States by the Food and Drug Administration[FDA].

Vaccination

PCV13 (Prevnar 13) Vaccination

All children under the age of two should receive the PCV13 vaccine. It defends against 13 of the most common pneumococcal bacteria strains. The first shot should be given at two months, followed by two more shots at four and six months. When the child is between 12 and 15 months old, a final booster shot should be given. A single shot is typically all that is needed for children older than this age. Adults aged 65 and up should also discuss and settle on PCV13 vaccination with their physician consultant.

PPSV23(Pneumovax23) Vaccination

Children over the age of two who have such medical problems, such as leukaemia or chronic cardiovascular disease, should get the PPSV23 vaccine. PPSV23 is a pneumococcal vaccine that protects against 23 different forms of pneumococcal bacteria. PPSV23 is usually given in two doses to children with these medical conditions.

Side effects: There are very few side effects. Just one in a million people are believed to have an allergic reaction to the vaccine. If a person has had an allergic reaction to some other vaccine, they should tell their doctor. When a child is sick, a vaccine may be postponed, but a doctor may be able to help to have advice on this.

Influenza vaccination

Influenza infection, also known as the flu, is one of the bacterial causes of pneumonia. The influenza vaccine does not protect all children from catching the flu, but it is the most effective way of avoiding infection. All children over the age of six months can get a flu vaccine shot once a year before the end of October, according to the CDC. Every year, a new vaccine is needed because the particular influenza viruses that are circulating in the population change over time. Vaccination is not recommended for babies under the age of six months. The only way to protect them from the flu is to ensure that everyone in their immediate vicinity has been vaccinated.

Conclusion

Community-acquired pneumonia is a leading cause of death and morbidity in developed countries. In children under the age of five, viruses

are the most frequent cause of community-acquired pneumonia. The most common bacterial cause in people of all ages is *Streptococcus pneumonia. Haemophilus influenza, Streptococcus pyogenes, Staphylococcus aureus, Moraxella catarrhalis,* and *Mycoplasma pneumonia* are some of the most common bacterial causes in children under the age of five. Other essential bacterial causes in children aged 5 years and include *Mycoplasma pneumonia* and *Chlamydophila pneumonia,* in addition to *S. pneumonia.*

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HEREDITARY DISORDERS
Cystic fibrosis Sickle cell disease
DISORDERS OF IMMUNITY
HIV/AIDS Bruton agammaglobulinemic Selective immunoglobulin G subclass deficiencies Common variable immunodeficiency syndrome Severe combined immunodeficiency syndrome Chronic granulomatous disease Hyper immunoglobulin E syndromes Leukocyte adhesion defect
DISORDERS OF CILIA
Primary ciliary dyskinesia Kartagener syndrome
ANATOMIC DISORDERS
Pulmonary sequestration Lobar emphysema Congenital cystic adenomatous malformation Gastroesophageal reflux Foreign body Tracheoesophageal fistula (H type) Bronchiectasis Aspiration (oropharyngeal incoordination Aberrant bronchus

Table 1: Different diagnoses of Recurrent pneumonia