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Aetiology of pneumonia in children

Research presented

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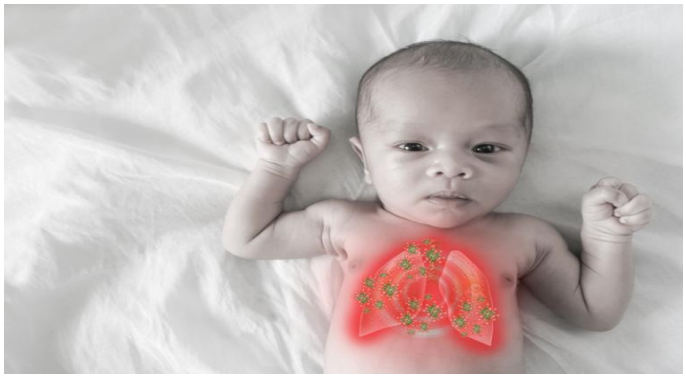

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بسم الله الرحمن الرحيم

[يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ ۚ وَاللَّهُ بِمَا تَعْمَلُونَ خَبِيرٌ]

صدق الله العظيم

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Content

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Aetiology of pneumonia in children

Abstract

Globally, pneumonia is a major cause of morbidity and mortality in children.. Although the majority of deaths attributed to pneumonia in children are mostly in the developing world, the burden of disease is substantial, and there are significant healthcare-associated costs related to pneumonia in the developed world. The objectives of this review are to determine the etiology, diagnosis and the treatment of pneumonia in children. Induced sputum and blood obtained within 24 hr of admission were examined via PCR, immunofluorescence and culture to detect 17 bacteria/viruses. A designated radiologist read the chest radiographs.

Viruses were isolated from lung or nasopharyngeal aspirates from children for whom viral cultures were done. It seems that, although viruses may initiate infection, death from pneumonia in children in developing countries is often due to *H. influenzae*, *S. pneumoniae*, or both. Antibiotic therapy would prevent many of these deaths. There is an urgent need for vaccines, effective in children less than 6 months old, that protect against all strains of *H. influenzae*, and *S pneumoniae.*

Keywords : *pneumococcus*, pneumonia , Treatment , Diagnosis

1.Introduction

1.1 pneumonia

Pneumonia is a common disease across all economic strata, especially in children less than 5-years-old. While in developed countries its incidence is about 0.05 episodes/ child/year, in developing countries it is 0.22 episodes/ child/year and remains a common cause for unscheduled health care visits and hospitalisation[1,3]. Although childhood deaths from pneumonia have reduced

significantly, pneumonia continues to afflict young children, especially from low- and middle-income countries (LMIC)[2]. Furthermore, severe pneumonia may result in long term complications like bronchiectasis which persist to adulthood and present as Chronic Obstructive Lung Disease[4,5]. Reduction in mortality and morbidity is dependent on timely and accurate treatment of these infections[6]. Therefore, being aware of the aetiology of pneumonia is crucial for successful management of the disease and planning of preventive measures such as immunisation hence impacting overall health of the young.The symptoms and signs of pneumonia in children were explained in Figure 1.

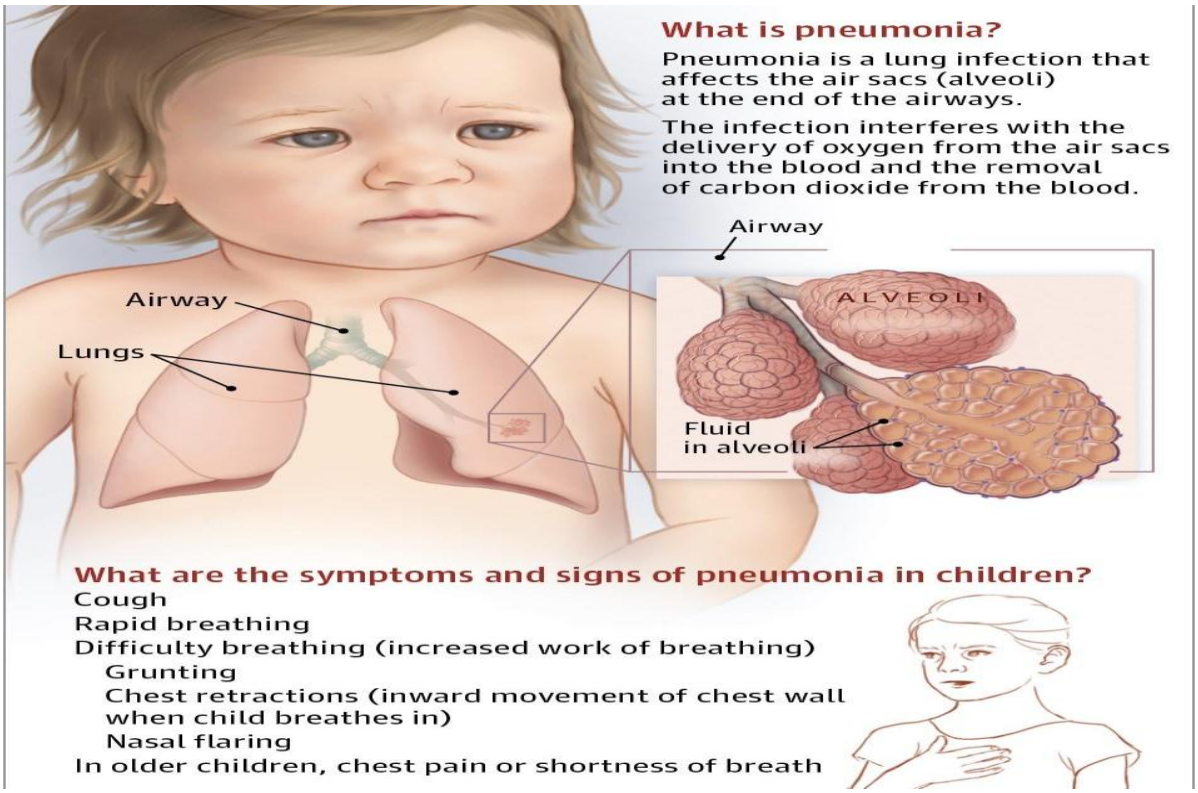

Figure 1: The symptoms and signs of pneumonia in children.

1.2 Pathophysiology

Pneumonia is an invasion of the lower respiratory tract, below the larynx by pathogens either by inhalation, aspiration, respiratory epithelium invasion, or hematogenous spread.[7] There are barriers to infection that include anatomical

structures (nasal hairs, turbinates, epiglottis, cilia), and humoral and cellular immunity.[7] Once these barriers are breached, infection, either by fomite/droplet spread (mostly viruses) or nasopharyngeal colonization (mostly bacterial), results in inflammation and injury or death of surrounding epithelium and alveoli. This is ultimately accompanied by a migration of inflammatory cells to the site of infection, causing an exudative process, which in turn impairs oxygenation [8] . In the majority of cases, the microbe is not identified, and the most common cause is of viral etiology Figure 2.

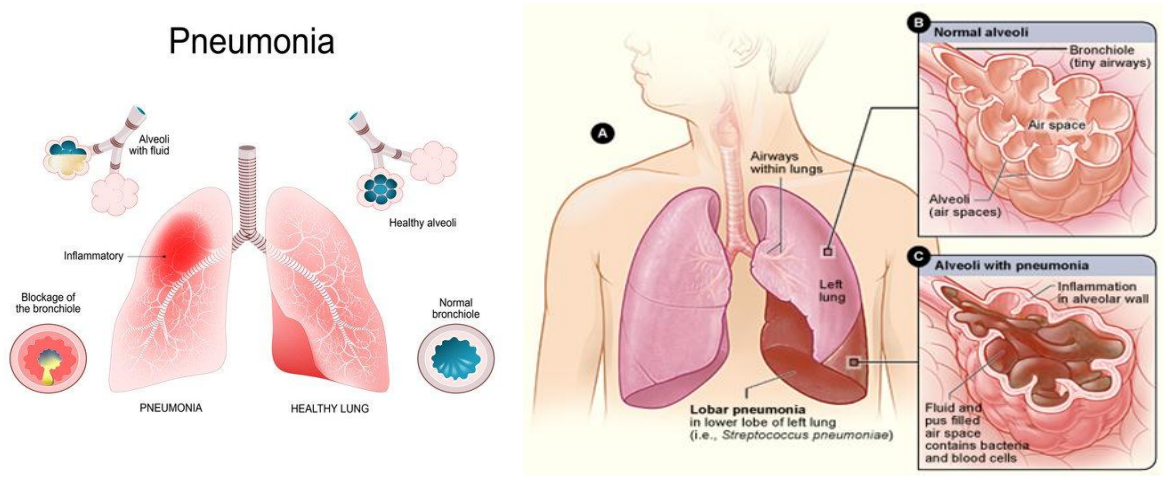

Figure 2 : pathophysiology of pneumonia

There are four stages of lobar pneumonia.

- The first stage occurs within 24 hours and is characterized by alveolar edema and vascular congestion. Both bacteria and neutrophils are present[7] .
- Red hepatization is the second stage, and it has the consistency of the liver. The stage is characterized by neutrophils, red blood cells, and desquamated epithelial cells. Fibrin deposits in the alveoli are common.[7]

- The third of the gray hepatization stage occurs 2-3 days later, and the lung appears dark brown. There is an accumulation of hemosiderin and hemolysis of red cells.[7] [8]
- The fourth stage is the resolution stage, where the cellular infiltrates are resorbed, and the pulmonary architecture is restored. If the healing is not ideal, then it may lead to parapneumonic effusions and pleural adhesions.[8]

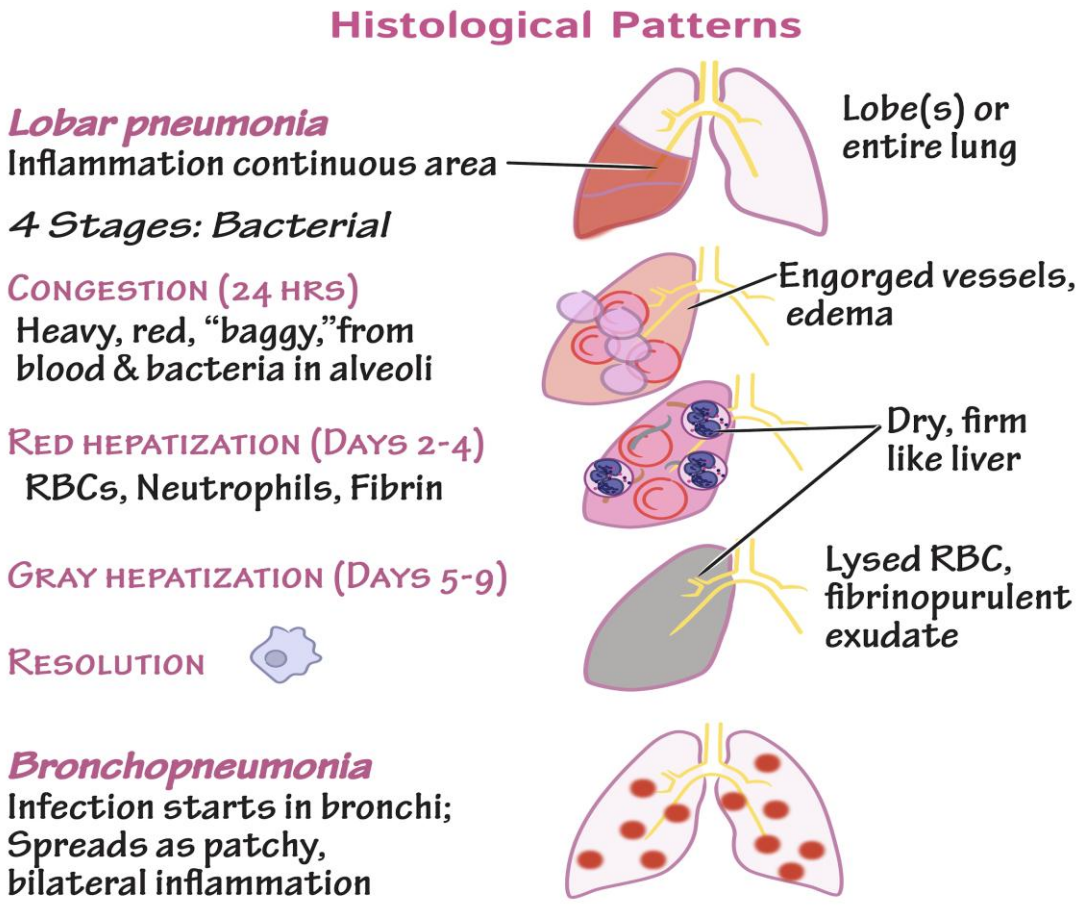

Figure 3 : Histological pattern of pneumonia

In bronchopneumonia, there is often patch consolidation of one or more lobes. The neutrophilic infiltrate is chiefly around the center of the bronchi.

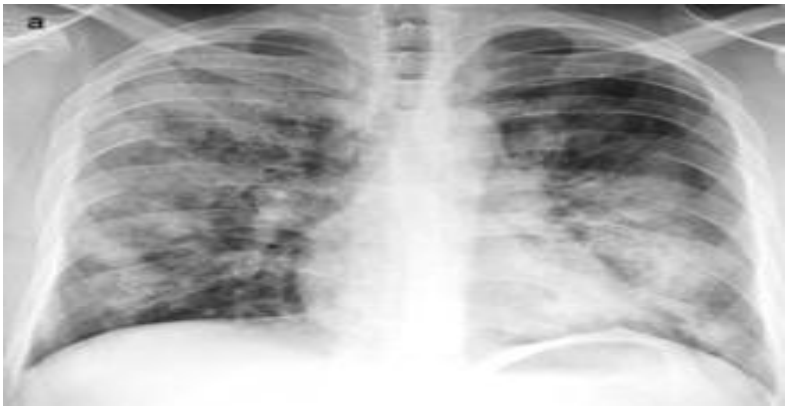

Figure 4 : CXR of Bronchopneumonia showing consolidation in lobes

1.3 Aetiology of pneumonia

1. Bacterial pneumonia

Pneumonia that is caused by a bacterial infection commonly affects one lobe (or section) of the lung. Bacterial pneumonia can affect children of any age, and can develop very quickly. It is most likely to be associated with a very high fever and a cough that is productive of sputum (phlegm), although children tend to swallow sputum rather than cough it up.[9] . The type of bacteria found varies with age, but the most common type of bacteria responsible for bacterial pneumonia in children is Streptococcus pneumoniae (or pneumococcus), with toddlers being the most at risk. However, with the introduction of vaccines that protect against pneumococcus (Prevenar, and more recently Prevenar 13) into the childhood immunisation schedule, the number of cases of pneumococcal pneumonia has dropped [9] [10]. A penicillin-based antibiotic is the standard treatment that doctors use for bacterial pneumonia.

2. Viral pneumonia

Pneumonia that is caused by a virus is probably the most common type of pneumonia affecting children of any age, although it tends to affect infants and preschool-aged children most frequently.[10]

Viruses tend not to confine themselves to a single lobe of the lungs, but have a more widespread, patchy effect. Symptoms can be more variable than with bacterial pneumonia, in terms of whether the illness comes on quickly or gradually, and whether or not there is an associated fever.[10] [11]

Antibiotics will not help viral pneumonia. Usually children with viral pneumonia will get better by themselves over a period of time that can range from days to weeks. Most children will have a cough that lasts for some weeks after the infection.

3. Mycoplasma pneumonia

The organism known as Mycoplasma pneumoniae is one of the most common causes of pneumonia in school-aged children and young adults. It is rarely seen in infants and young children. It usually occurs in epidemics among confined groups, such as families and boarding schools.[11]

Classically, Mycoplasma pneumonia develops gradually, with symptoms such as a sore throat, cold, low-grade fever and a general feeling of being unwell. Over the course of the infection, the cough tends to become worse and your child may develop shortness of breath. Your doctor can confirm the diagnosis with a chest X-ray and a blood test.[11]

Treatment usually involves antibiotics such as clarithromycin or roxithromycin

1.4 community acquired pneumonia

Community-acquired pneumonia is a common and potentially serious infection that afflicts children throughout the world; it is fundamentally different in children and in adults. The annual incidence of pneumonia in children younger than 5 years of age is 34 to 40 cases per 1000 in Europe and North America, higher than at any other time of life, except perhaps in adults older than 75 or 80 years of age.1-4 In the developing world, pneumonia is not only more common than it is in Europe and North America5-7; it is also more severe and is the largest killer of children.[12] [13]

Definitions of pneumonia vary widely. Some require only the presence of infiltrates on a chest radiograph,[14] whereas others require only certain respiratory symptoms or signs.[15] The World Health Organization has defined pneumonia solely on the basis of clinical findings obtained by visual inspection and timing of the respiratory rate.[16] Definitions are a particular problem in the case of small infants, since pneumonia and bronchiolitis are both common in this age group, and the features of these two diseases often overlap. Many studies, particularly those in the developing world, use the term "acute lower respiratory tract illness" and make no attempt to differentiate pneumonia from bronchiolitis[17] .For the purposes of this review, and particularly with respect to recommendations for treatment, pneumonia will be defined as the presence of fever, acute respiratory symptoms, or both, plus evidence of parenchymal infiltrates on chest radiography. Even this definition overlaps somewhat with that of bronchiolitis and leaves some room for disagreement among clinicians [18] .

1.5 Hospital Acquired Pneumonia

Nosocomial pneumonia is a common hospital-acquired infection in children, and is often fatal.occurring at or beyond 48 hours after admission to hospital that was not present nor incubating at the time of admission.[18]

NP is the leading cause of fatal nosocomial infection.

NP occurs as a complication of altered pulmonary or systemic antimicrobial defenses, resulting in invasion of the lower respiratory tract by a pathogenic organism. Causative organisms may derive either from the child's own flora (endogenous) or an environmental source (exogenous). Endogenous infection often occurs via subclinical aspiration of both oropharyngeal and gastric secretions or hematogeno [18] . The incidence of NP varies from 16 to 29% of hospitalized pediatric patients.[19] . Children in pediatric intensive care units (PICUs) have a higher incidence of NP than those in general wards.[20, 21].

The severity of the underlying illness and use of invasive modalities of care are important risk factors for Np [22] . diagnosis In hospitalised patients who develop respiratory symptoms and fever, one should consider the diagnosis. The likelihood increases when upon investigation symptoms are found of respiratory insufficiency, purulent secretions, newly developed infiltrate on the chest X-Ray, and increasing leucocyte count. If pneumonia is suspected material from sputum or tracheal aspirates are sent to the microbiology department for cultures. In case of pleural effusion, thoracentesis is performed for examination of pleural fluid. In suspected ventilator-associated pneumonia it has been suggested that bronchoscopy or bronchoalveolar lavage is necessary because of the risks of incorrect clinical diagnoses.[18,20]

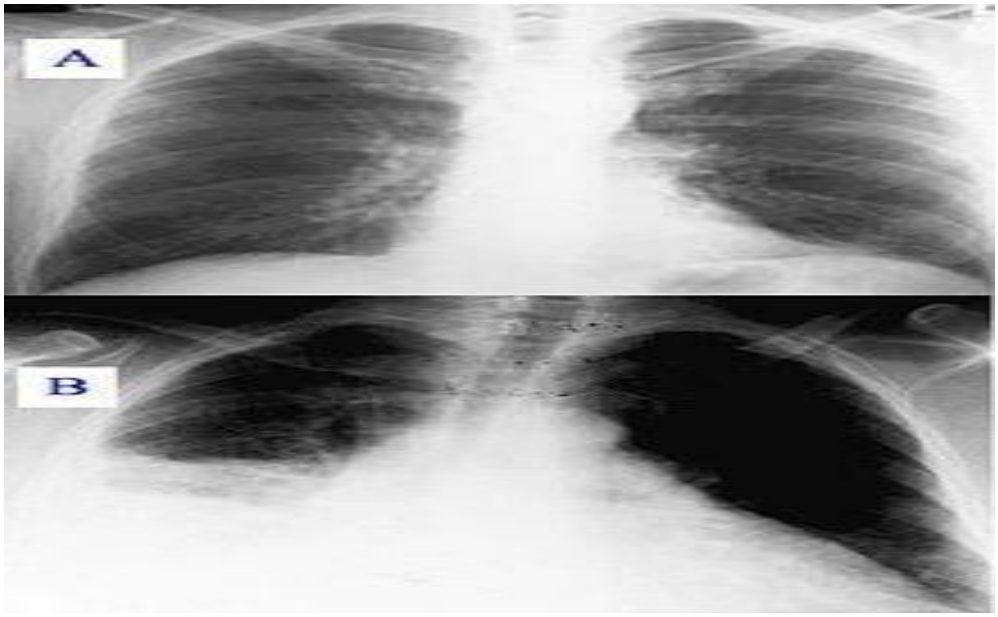

Figure 5 : Pneumonia as seen on chest x-ray. A: Normal chest x-ray.
B: Abnormal chest x-ray with shadowing from pneumonia in the right lung (left side of image).

The treatment Usually initial therapy is empirical.[3] If sufficient reason to suspect influenza, one might consider oseltamivir. In case of legionellosis, erythromycin or fluoroquinolone.[18]
A third generation cephalosporin (ceftazidime) + carbapenems (imipenem) + beta lactam & beta lactamase inhibitors (piperacillin/tazobactam) [18].

2.pneumonia in children and COVID -19

There is ample evidence that COVID-19 is less serious in children than in adult (5–10). Lu et al. found the main symptoms in 171 children with COVID-19 to be cough (48.5%), pharyngitis (46.2%), fever (41.5%), diarrhea (8.8%), and vomiting (6.4%); only 2.3% of cases experienced desaturation upon hospitalization, while 15.8% of cases were asymptomatic [23] .Olfactory and gustatory anomalies characteristic of adult COVID-19 cases are rare in pediatric populations [24,25]
The underlying cause of the lower incidence and pathogenicity of SARS-CoV-2 infection in children remains unclear at present. Although this lower incidence and morbidity was attributed to a reduced exposure and the presence of risk factors during the initial phase of the pandemic, it is now clear that biological factors that intervene in the pathogenesis of the infection and in the immune response may play a protective role in children against the more aggressive clinical manifestations seen in adults [26].
respiratory management dominates the clinical picture of hospitalized COVID-19 patients. In some case series, deterioration of the clinical picture wherein dyspnea, cyanosis, and the onset of acute respiratory distress syndrome (ARDS) emerged approximately 8–10 days after the onset of SARS-CoV-2 infection, which could rapidly progress to multiple organ failure and death [27] . In a pediatric series of children with COVID-19, 30.8% presented shortness of breath that required oxygen supplementation and 23.1% were transferred to intensive care unit (ICU) for organ dysfunction [41] In another case series of 41

children hospitalized for COVID-19, 11 of these presented lung lesions compatible with a picture of interstitial pneumonia [27] . Furthermore, in one of the largest published pediatric series that studied 585 children with SARS-CoV2 infection, 8% required ICU admission and 4% needed mechanical ventilation [29].

Although the clinical picture in pediatric populations is more complex, the severity of infection can be clinically classified as follows: asymptomatic, mild, moderate, severe, or critical [30, 31]

(Table 1). This classification makes the idea that even pediatric patients can experience severe manifestations of the pathology, which must be addressed as early as possible to limit disease progression.

Table 1: Classification of COVID-19 in children.

Classification	Clinical Features
Asymptomatic	positively on RT - PCR buffer to SARS cov-2 or positive serology in absence of any symptom of illness
Mild	symptom are mild and mainly affect the upper airway (Nasal obstruction ,sneezing) sometime associated with fever ,cough and gastrointestinal Symptom
Moderate	symptoms are more critical fever and cough (mainly dry) are almost always present and are associated with breathing difficulties . It's characterized radiologically by lung anomalies complication with interstitial pneumonia
Severe	it characterized by presence of hypoxemia (SPo2 <92%) with sign of Respiratory distress (tachypnea, grunting ,wing flap ,sags) cyanosis

	,neurological sign and symptom ,refusal to eat , and sign of dehydration
critical	disease progression with onset of Respiratory failure requiring mechanical ventilation , sign of shock or multi- organ failure

3. Diagnosis of pneumonia

Laboratory evaluation in children suspected of having pneumonia should ideally start with non-invasive, rapid bedside testing including nasopharyngeal swab assays for influenza, respiratory syncytial virus, and human metapneumovirus when available and appropriate. This can help minimize unnecessary imaging and antibiotic treatment in children with influenza or bronchiolitis. Children who present with severe disease and appear toxic should have complete blood count (CBC), electrolytes, renal/hepatic function testing, and blood cultures performed.[32] These tests are generally not required in children who present with mild disease. Inflammatory markers do not help distinguish between viral and bacterial pneumonia in the pediatric population.[32,33]] However, these tests may be obtained to trend disease progression and serve as prognostic indicators. Children who have been in areas endemic to TB, or have exposure history, and present with signs and symptoms suspicious for pneumonia should have sputum samples or gastric aspirates collected for culture.

Sputum gram stain and culture are not productive as the samples are often contaminated by oral flora. Blood cultures can be done but are often negative. Today, serology is being used to determine the presence of mycoplasma, legionella, and chlamydia species. PCR is becoming available in most hospitals, but still, the results take 24-48 hours.

There are no clear guidelines for the routine use of chest x-ray in the pediatric population.[32] Although the chest x-ray can be helpful in diagnosis and confirmation of pneumonia,[34] it carries with it risks, including radiation exposure, healthcare-associated costs, and false-negative results, increasing the use of unwarranted antibiotics. Imaging should be restricted to children who appear toxic, those with the recurrent or prolonged course of illness despite treatment, infants age 0 to 3 months with a fever, suspected foreign body aspiration, or congenital lung malformation. Imaging can also be considered in children younger than 5 years old, who present with fever, leukocytosis, and no identifiable source of infection.[34] Imaging may also be useful in those with acute worsening of upper respiratory infections or to rule out underlying mass in children who have "round pneumonia." [35,36] .

4.Treatment of pneumonia

Treatment should be targeted to a specific pathogen that is suspected based on information obtained from history and physical exam. Supportive and symptomatic management is key and includes supplemental oxygen for hypoxia, antipyretics for fever, and fluids for dehydration. This is especially important for non-infectious pneumonitis and viral pneumonia for which antibiotics are not indicated.[37.38]. Cough suppressants are not recommended. If bacterial pneumonia is suspected, treat empirically with antibiotics, keeping in mind significant history and bacterial pathogens that are common to specific age groups.

- Neonates should receive ampicillin plus an aminoglycoside or third-generation cephalosporin[37 , 39], however, not ceftriaxone, as it can displace bound bilirubin and lead to kernicterus.
- Atypical pneumonia is common in infants 1 to 3 months old, and this group should have additional antibiotic coverage with erythromycin or clarithromycin.[37,39].

- For infants and children over 3 months old, S. pneumoniae is the most common, for which the drug of choice is high-dose oral amoxicillin [37,39] or another beta-lactam antibiotic.
- In children older than 5 years old, atypical agents have a more important role, and macrolide antibiotics are usually first-line therapy.[37].
- Special attention should be given to children with chronic illnesses, as these might alter choices for antibiotics[37].
- Children with sickle cell anemia will need cefotaxime, macrolide, vancomycin if severely ill.
- Children with cystic fibrosis will require piperacillin or ceftazidime plus tobramycin. Treat fulminant viral pneumonia as indicated, depending on the virus identified
- For Varicella, use acyclovir and for the respiratory syncytial virus (RSV), use ribavirin for high-risk patients.
- Patients with HIV should be treated with sulfamethoxazole/trimethoprim and prednisone, and for Cytomegalovirus, ganciclovir and gamma globulin are the preferred agents. If methicillin-resistant Staphylococcus aureus (MRSA) is suspected, clindamycin or vancomycin may be given.

It is important to have a high index of suspicion for complications, especially in patients returning for repeat evaluation.

- For patients sent home with symptomatic or supportive management for suspected viral pneumonia, consider a secondary bacterial infection or other diagnoses upon re-evaluation.[40]
- Children with uncomplicated bacterial infections who fail to respond to treatment within 72 hours should be assessed for complications, including pneumothorax, empyema, or pleural effusion.[41] Other systemic complications of pneumonia include sepsis, dehydration, arthritis, meningitis, and hemolytic uremic syndrome.

- Neonates and infants younger than 90 days old should be hospitalized for treatment, in addition to children who are immunocompromised or have other underlying chronic diseases like sickle cell anemia or cystic fibrosis.[37]
- Children with social factors that preclude access to care, have failed outpatient therapy, or present with presumed tuberculosis, should also be hospitalized.[42]
- Admission is often required for patients with respiratory distress and low oxygenation. In most cases, the presence of a parapneumonic effusion requires admission
- Children with severe respiratory distress may require chest therapy, CPAP, or even mechanical ventilation. A large pleural effusion requires drainage for diagnostic and therapeutic purposes.

It is essential to ensure that clear discharge instructions and return precautions are given to parents or caregivers of children being discharged home in addition to close pediatrician follow-up.

5.Conclusion

This study used an expanded diagnostic armamentarium to define the broad spectrum of pathogens that cause pneumonia in hospitalized children. The data confirm the importance of *S.pneumoniae* and the frequent occurrence of bacterial and viral coinfections in children with pneumonia. These findings will facilitate age-appropriate antibiotic selection and future evaluation of the clinical effectiveness of the pneumococcal conjugate vaccine as well as other candidate vaccines.However, detection of bacterial pathogens like *S.pneumoniae* and *H. influenzae* by LA of various body fluids has been quite helpful in identifying bacterial agents in a substantial number of cases.

Even though all the cases had a duration of respiratory symptoms < 5 days, most of them had used one or the other antibiotic before coming to the hospital.

It is difficult to estimate the influence of use of antibiotics on the isolation/detection of various bacterial pathogens in our patients. However, detection *of H. influenzae* and *S. pneumoniae* by latex agglutination is not influenced by the use of antibiotics, may very well correlate with the aetiology and therefore is a considerably more sensitive test than blood culture in childhood pneumonia. *Haemophilus influenzae*, believed to be the commonest cause of pneumonia from 3 months to 5 years of age. *Klebsiella* was isolated with a percentage ranging from 23 to 25 per cent from birth to 2 years and was not isolated beyond 2 years. *Klebsiella* is believed to cause pneumonia in debilitated or immunosuppressed patients, but frequently occurs as a secondary invader.a higher percentage of isolation of RSV in the present study suggests that RSV is an important etiological organism causing pneumonia in under five children even in developing countries where the aetiology of pneumonia is mostly believed to be bacterial in origin.

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