Section A-Research paper

An Overview about Pneumonia among Children

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Abstract

Pneumonia is an acute form of respiratory infection that impacts the lungs. It is defined as an inflammation of the lung tissue due to an infectious agent. The commonly used clinical WHO operational definition is based only on clinical symptoms (cough or difficulties in breathing and tachypnea). Pneumonia is the only major infectious cause of pediatric mortality internationally. Pneumonia death is about 920 000 children under the age of 5 years in 2015, representing 16% of all pediatric mortality below 5 years old. Pneumonia influences children and families everywhere, however, is most usual in South Asia and Sub-Saharan Africa. Children can be avoided with easy interventions and treated with low-cost, low technical medication, and care .In Egypt, it was estimated that 10% of deaths in children under the age of 5 years is probably caused by pneumonia and other acute respiratory infections. The onset is gradual, with headaches, malaise, fever, not reaching a high degree of severity. Respiratory tract symptoms: Dry, hacking to productive cough with light sputum. Cough is the most common symptom of a respiratory tract infection. Pneumonia is frequently preceded by several days of symptoms of an upper respiratory tract infection, typically rhinitis and cough. In viral pneumonia, fever is usually present but temperatures are generally lower than in bacterial pneumonia.

Keywords: Pneumonia, Children

Introduction

Pneumonia was first described by Hippocrates . The first descriptions of its clinical and pathological features were made 22 centuries later in 1819 by Laennec. while Rokitansky in 1842 was the first to differentiate lobar and bronchopneumonia. **(1)**

Definition

Pneumonia is an acute form of respiratory infection that impacts the lungs. It is defined as an inflammation of the lung tissue due to an infectious agent. The commonly used clinical WHO operational definition is based only on clinical symptoms (cough or difficulties in breathing and tachypnea*).***(2)**

Pneumonia has been identified as the major "forgotten killer of children" by the United Nations Children's Fund (UNICEF) and WHO .

The World Health Organization defines pneumonia as an acute disease episode with cough combined with fast breathing with age specific cut-values for increased respiratory rate. This case definition of childhood pneumonia is widely used in poor-resource settings to guide the management of pneumonia. The definition is also commonly used as an entry criteria or endpoint in different intervention and disease burden studies **(3).**

Scott *et al.*, (4) simply defines it as an illness usually caused by infection, where the lungs become inflamed and congested, thus reducing oxygen exchange and leading to cough and breathlessness. It's the leading cause of mortality among children under five years of age, despite effective vaccines and nutritional and environmental interventions.

In adults, the definition of pneumonia relies heavily on characteristic changes on the chest radiograph. However, many children who have suggestive clinical signs of pneumonia and who respond to appropriate

antibiotics do not have any abnormalities on the chest radiograph taken at the onset of the illness; furthermore, radiological facilities are not always available in developing countries. In short, there is no single definition of pneumonia in childhood that is sensitive, specific, and can be widely implemented (**4)**

Epidemiology

Pneumonia, defined as inflammation of the lung parenchyma, is the leading infectious cause of death globally among children younger than 5 yr, accounting for an estimated 920,000 deaths each year **(5).**

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Pneumonia mortality is closely linked to poverty. More than 99% of pneumonia deaths are in low- and middle-income countries, with the highest pneumonia mortality rate occurring in poorly developed countries in Africa **(6).**

The wide spread of acute pneumonia poses a great danger to children. Pneumonia is the leading single cause of death in children worldwide. Every year, it claims the lives of approximately 1.1 million children under the age of five. It is the cause of all deaths of children under the age of five worldwide**(7)**

Etiology

Pneumonia is an inflammation of the parenchyma cells of the lungs caused by an infectious agent, either a gram-positive or gram-negative microbe. It is a major cause of morbidity and mortality worldwide, particularly in vulnerable populations such as the elderly, immunocompromised individuals, and those with underlying health conditions . This serious respiratory infection can be acquired in both community and hospital settings**(8)**

Although most cases of pneumonia are caused by microorganisms, noninfectious causes include aspiration (of food or gastric acid, foreign bodies, hydrocarbons, and lipoid substances), hypersensitivity reactions, and drug- or radiation-induced pneumonitis**. (9)**

The cause of pneumonia in an individual patient is often difficult to determine because direct sampling of lung tissue is invasive and rarely performed. Bacterial cultures of sputum or upper respiratory tract samples from children typically do not accurately reflect the cause of lower respiratory tract infection. **(10)**

Streptococcus pneumoniae (pneumococcus) is the most common bacterial pathogen in children 3 wk to 4 yr of age, whereas Mycoplasma pneumoniae and Chlamydophila pneumoniae are the most frequent bacterial pathogens in children age 5 yr and older. **(11).**

Necrotizing pneumonia (NP) is a rare complication of community-acquired pneumonia (CAP) and is characterized by catastrophic illness and a prolonged hospital stay and disease course, Streptococcus pneumoniae, Staphylococcus aureus and Mycoplasma pneumoniae are the most common pathogens reported in children with NP**(11).**

In addition to pneumococcus, other bacterial causes of pneumonia in previously healthy children in the United States include group A streptococcus and Staphylococcus aureus S. aureus pneumonia often complicates an illness caused by influenzath Asia **(12)**

Pathophysiology

The lower respiratory tract possesses a number of defense mechanisms against infection, including mucociliary clearance, macrophages and secretory immunoglobulin A, and clearing of the airways by coughing. Previously, it was believed that the lower respiratory tract was—in the absence of infection—kept sterile by these mechanisms, supported primarily by culture-based studies. **(13)**

Accumulation of inflammatory exudates leads to alveolar edema, which serves as medium for the multiplications of bacteria and spread of infection to other parts of the lungs. Collapsed or airless portion of the lung (atelectasis) and obstruction of smaller airways occurs. Children are very susceptible to pneumonia because of the short distance between upper respiratory tract and alveoli, the small diameter of the airways,

profuse mucus production, and the immaturity of the immune defense. Nasopharyngeal colonization of pneumonia causing bacteria is common in young children **(14).**

More recent conceptual models postulate that pneumonia results from disruption of a complex lower respiratory ecosystem that is the site of dynamic interactions between potential pneumonia pathogens, resident microbial communities, and host immune defenses. **(14).**

Viral pneumonia usually results from spread of infection along the airways, accompanied by direct injury of respiratory epithelium, which results in airway obstruction from swelling, abnormal secretions, and cellular debris. The small caliber of airways in young infants makes such patients particularly susceptible to severe infection. Atelectasis, interstitial edema, and hypoxemia from ventilation–perfusion mismatch often accompany airway obstruction. Viral infection of the respiratory tract can also predispose to secondary bacterial infection by disturbing normal host defense mechanisms, altering secretions, and through disruptions in the respiratory microbiota. Bacterial pneumonia most often occurs when respiratory tract organisms colonize the trachea and subsequently gain access to the lungs, but pneumonia may also result from direct seeding of lung tissue after bacteremia. **(15)**

When bacterial infection is established in the lung parenchyma, the pathologic process varies according to the invading organism. M. pneumoniae attaches to the respiratory epithelium, inhibits ciliary action, and leads to cellular destruction and an inflammatory response in the submucosa. As the infection progresses, sloughed cellular debris, inflammatory cells, and mucus cause airway obstruction, with spread of infection occurring along the bronchial tree, as is seen in viral pneumonia. S. pneumoniae produces local edema that aids in the proliferation of organisms and their spread into adjacent portions of lung, often resulting in the characteristic focal lobar involvement. Group A streptococcus lower respiratory tract infection typically results in more diffuse lung involvement with interstitial pneumonia **(16)**

The pathology includes necrosis of tracheobronchial mucosa; formation of large amounts of exudate, edema, and local hemorrhage, with extension into the interalveolar septa; and involvement of lymphatic vessels with frequent pleural involvement. S. aureus pneumonia manifests as confluent bronchopneumonia, which is often unilateral and characterized by the presence of extensive areas of hemorrhagic necrosis and irregular areas of cavitation of the lung parenchyma, resulting in pneumatoceles, empyema, and, at times, bronchopulmonary fistulas **(17)**

Findings indicate that crackles are due to explosive equalization of gas pressure between terminal bronchiole and the alveoli. Wheezes result from the oscillation of air through a narrowed airway that produces a musical sound likened to a vibrating reed while decreased breath sounds may also be heard in areas of consolidation. Virulence of the causative organism and the inflammatory response in the lungs predicts the outcome of a pulmonary infection. Insufficient inflammatory response can result in life-threatening infection, but an excessive response can lead to life-threatening inflammatory lung injury **(13)**

Recurrent pneumonia is defined as 2 or more episodes in a single year or 3 or more episodes ever, with radiographic clearing between occurrences. An underlying disorder should be considered if a child experiences recurrent pneumonia **(14).**

Clinical Manifestations

The onset is gradual, with headaches, malaise, fever, not reaching a high degree of severity. Respiratory tract symptoms: Dry, hacking to productive cough with light sputum. Cough is the most common symptom of a respiratory tract infection**(7)**

Pneumonia is frequently preceded by several days of symptoms of an upper respiratory tract infection, typically rhinitis and cough. In viral pneumonia, fever is usually present but temperatures are generally lower than in bacterial pneumonia **(17)**

Tachypnea is the most consistent clinical manifestation of pneumonia. Increased work of breathing accompanied by intercostal, subcostal, and suprasternal retractions, nasal flaring, and use of accessory muscles is common. Severe infection may be accompanied by cyanosis and lethargy, especially in infants. Auscultation of the chest may reveal crackles and wheezing, but it is often difficult to localize the source of these adventitious sounds in very young children with hyperresonant chests. It is often not possible to

distinguish viral pneumonia (especially adenovirus) clinically from disease caused by Mycoplasma and other bacterial pathogens **((7)**

Bacterial pneumonia in adults and older children typically begins suddenly with high fever, cough, and chest pain. Other symptoms that may be seen include drowsiness with intermittent periods of restlessness; rapid respirations; anxiety; and, occasionally, delirium. In many children, splinting on the affected side to minimize pleuritic pain and improve ventilation is noted; such children may lie on one side with the knees drawn up to the chest. **(16)**

Physical findings depend on the stage of pneumonia. Early in the course of illness, diminished breath sounds, scattered crackles, and rhonchi are commonly heard over the affected lung field. With the development of increasing consolidation or complications of pneumonia such as pleural effusion or empyema, dullness on percussion is noted and breath sounds may be diminished. A lag in respiratory excursion often occurs on the affected side. Abdominal distention may be prominent because of gastric dilation from swallowed air or ileus. Abdominal pain is common in lower-lobe pneumonia. The liver may seem enlarged because of downward displacement of the diaphragm secondary to hyperinflation of the lungs or superimposed congestive heart failure. **(7)**

Symptoms described in adults with pneumococcal pneumonia may be noted in older children but are rarely observed in infants and young children, in whom the clinical pattern is considerably more variable. In infants, there may be a prodrome of upper respiratory tract infection and poor feeding, leading to the abrupt onset of fever, restlessness, apprehension, and respiratory distress. These infants typically appear ill, with respiratory distress manifested as grunting; nasal flaring; retractions of the supraclavicular, intercostal, and subcostal areas; tachypnea; tachycardia; air hunger; and often cyanosis. Auscultation may be misleading, particularly in young infants, with meager findings disproportionate to the degree of tachypnea. Some infants with bacterial pneumonia may have associated gastrointestinal disturbances characterized by vomiting, anorexia, diarrhea, and abdominal distention secondary to a paralytic ileus. Rapid progression of symptoms is characteristic in the most severe cases of bacterial pneumonia. **(13)**

Previous studies indicated that some of most determinants for pneumonia include the educational status of parents, age of the mother, family child caring practice, family income, age and sex of the child, parental smoking or indoor air pollution from biomass fuel smoke, absence window in the kitchen, overcrowding, parental asthma, household history of pneumonia, malnutrition, lack exclusively breastfeeding, lack of zinc supplementation, comorbidity condition such as diarrhea, measles, acute upper respiratory infection (AURTI), previous history of asthma, and wide variation across the regions of the world (**18)**

Diagnosis

Clinical practice guidelines for community-acquired pneumonia in children older than 3 mo of age were published in 2011 by the Pediatric Infectious Diseases Society (PIDS) and the Infectious Diseases Society of America (IDSA). These evidence-based guidelines provide recommendations for diagnostic testing and treatment of previously healthy children with pneumonia in both outpatient and inpatient settings. **(19)**

Radiological investigation

- An infiltrate on chest radiograph (posteroanterior and lateral views) supports the diagnosis of pneumonia; a pleural effusion or empyema also may be identified .
- Viral pneumonia is usually characterized by hyperinflation with bilateral interstitial infiltrates and peribronchial cuffing.
- Confluent lobar consolidation is typically seen with pneumococcal pneumonia . The radiographic appearance alone does not accurately identify pneumonia etiology, and other clinical features of the illness must be considered.
- Repeat chest radiographs are not required for proof of cure for patients with uncomplicated pneumonia. Moreover, current PIDS–IDSA guidelines do not recommend that a chest radiograph be performed for children with suspected pneumonia (cough, fever, localized crackles, or decreased breath sounds) who are well enough to be managed as outpatients because imaging in this context only rarely changes management **(20)**.

Laboratory investigation

- Leukocytosis below 15x109 / l is observed in the first days of the disease in 40% of patients with coccal and 96% of atypical pneumonia, in fact, as often as with bronchitis. And only numbers above 15x109/l make it possible to exclude the viral etiology of lesions of the lower respiratory tract with a moderate probability, since such figures are possible with bronchitis (RS viral in children aged 2-3 months).
- CRP >30 mg/L and PCT >2 ng/mL are more reliable for diagnosing pneumonia. Levels of leukocytosis above 15x109/l and procalcitonin (PCT) above 2 ng/ml exclude atypical pneumonia, however, at lower levels, the differences are almost completely smoothed out **(7)**
- The definitive diagnosis of a viral infection rests on the detection of the viral genome or antigen in respiratory tract secretions. Reliable PCR assays are widely available for the rapid detection of many respiratory viruses, including RSV, parainfluenza, influenza, human metapneumovirus, adenovirus, enterovirus, and rhinovirus **(21).**
- The definitive diagnosis of a typical bacterial infection requires isolation of an organism from the blood, pleural fluid, or lung. Culture of sputum is of little value in the diagnosis of pneumonia in young children **(22).**
- Percutaneous lung aspiration is invasive and not routinely performed.
- Blood culture is positive in only 10% of children with pneumococcal pneumonia and is not recommended for nontoxic-appearing children treated as outpatients. Blood cultures are recommended for children who fail to improve or have clinical deterioration, have complicated pneumonia or require hospitalization.
- Urinary antigen tests should not be used to diagnose pneumonia caused by S. pneumoniae in children because of a high rate of false positives resulting from nasopharyngeal carriage.
- Serologic evidence, such as antistreptolysin O and anti-DNase B titers, may also be useful in the diagnosis of group A streptococcal pneumonia. . ***(23)***

Prognosis

- Typically, patients with uncomplicated community-acquired bacterial pneumonia show response to therapy, with improvement in clinical symptoms (fever, cough, tachypnea, chest pain), within 48-72 hr of initiation of antibiotics.
- General risk factors for multidrug-resistant/ extensively drug-resistant/pandrug-resistant pneumonia in ICU:

Local epidemiology
ICU with high rates of MDR pathogens[a,b]
Local prevalence not known
Individual risk factors
Structural lung disease (bronchiectasis or cystic fibrosis; for MDR BGN)
Intravenous antibiotic use within the previous 90 days prior to HAP/VAP
Hospitalization (⩾ 2 days) within the previous 90 days prior to HAP/VAP
Septic shock at the time of VAP
ARDS preceding VAP
At least 5 days of hospitalization prior to the occurrence of VAP
Acute renal replacement therapy prior to VAP onset
Individual prior microbiological data
Previous colonization with MDR pathogens
Previous infection with MDR pathogens

ARDS, acute respiratory distress syndrome; BGN, Gram-negative bacilli; HAP, hospital-acquired pneumonia; MDR, multidrug resistant; MRSA, methicillinresistant Staphylococcus aureus; VAP, ventilator-associated pneumonia.**(24)**

- A chest radiograph is the first step in determining the reason for a lack of response to initial treatment. Bronchoalveolar lavage may be indicated in children with respiratory failure; high-resolution CT scans may better identify complications or an anatomic reason for a poor response to therapy.
- Mortality from community-acquired pneumonia in developed countries is rare, and most children with pneumonia do not experience long-term pulmonary sequelae. ***(23)***

References

1. **Mackenzie, G. (2016):** The definition and classification of pneumonia. Pneumonia, 8(1), 14.
2. **Hameda A M M, Yasser T. Kassema, Hamada K. Fayedb, A. M. S. (2020).** Serum zinc levels in hospitalized children with pneumonia: a hospital-based case–control study. Egypt J Bronchol 2019, 13(730–737), Egypt J Bronchol 2019 13:730–737 © 2020 Egyptian J.
3. **Lanks, C. W., Musani, A. I., & Hsia, D. W. (2019).** C o m m u n i t y - a c q u i red P n e u m o n i a an d H o s p i t a l - a c q u i red Pn e u m o n i a. In Medical Clinics of NA (Vol. 103, Issue 3, pp. 487–501)..
4. **Scott, J. A. G., Brooks, W. A., Peiris, J. M., Holtzman, D., & Mulholland, E. K. (2008).** Pneumonia research to reduce childhood mortality in the developing world. The Journal of clinical investigation, 118(4), 1291-1300.
5. **DeAntonio, R., Yarzabal, J. P., Cruz, J. P., Schmidt, J. E., & Kleijnen, J. (2016).** Epidemiology of community-acquired pneumonia and implications for vaccination of children living in developing and newly industrialized countries: A systematic literature review. Human vaccines & immunotherapeutics, 12(9), 2422-2440.
6. **Takeuchi, N., Naito, S., Ohkusu, M., Abe, K., Shizuno, K., Takahashi, Y., ... & Ishiwada, N. (2020).** Epidemiology of hospitalised paediatric community-acquired pneumonia and bacterial pneumonia following the introduction of 13-valent pneumococcal conjugate vaccine in the national immunisation programme in Japan. Epidemiology & Infection, 148.
7. **Safarovna, G. A. (2023).** PNEUMONIA IN CHILDREN. International Scientific Research Journal, 4(1), 2776–0979.

8. **Alshammari, M.K.; Alotaibi, M.A.; AlOtaibi, A.S.; Alosaime, H.T.; Aljuaid, M.A.; Alshehri, B.M.; AlOtaibi, Y.B.; Alasmari, A.A.; Alasmari, G.A.; Mohammed, M.H**. Prevalence and Etiology of Community- and Hospital-Acquired Pneumonia in Saudi Arabia and Their Antimicrobial Susceptibility Patterns: A Systematic Review. Medicina 2023, 59, 760.
9. **Chi, H., Huang, Y. C., Liu, C. C., Chang, K. Y., Huang, Y. C., Lin, H. C., ... & Hsieh, Y. C. (2020). Characteristics** and etiology of hospitalized pediatric community-acquired pneumonia in Taiwan. Journal of the Formosan Medical Association, 119(10), 1490-1499.
10. **Rueda, Z. V., Aguilar, Y., Maya, M. A., López, L., Restrepo, A., Garcés, C., ... & Vélez, L. A. (2022).** Etiology and the challenge of diagnostic testing of community-acquired pneumonia in children and adolescents. BMC pediatrics, 22(1), 1-14.
11. **Johnston, C., Campo, N., Bergé, M. J., Polard, P., & Claverys, J. P. (2014). Streptococcus** pneumoniae, le transformiste. Trends in microbiology, 22(3), 113-119.
12. **Esposito, S., & Principi, N. (2019).** Defining the aetiology of paediatric community-acquired pneumonia: an unsolved problem. Expert Review of Respiratory Medicine, 13(2), 153-161.
13. **Ticona, J. H., Zaccone, V. M., & McFarlane, I. M. (2021).** Community-acquired pneumonia: A focused review. Am J Med Case Rep, 9(1), 45-52.
14. **Cilloniz, C., Martin-Loeches, I., Garcia-Vidal, C., San Jose, A., & Torres, A. (2016).** Microbial etiology of pneumonia: epidemiology, diagnosis and resistance patterns. International journal of molecular sciences, 17(12), 2120.
15. **Zambare, K. K., & Thalkari, A. B. (2019).** Overview on Pathophysiology of Pneumonia. Asian Journal of Pharmaceutical Research, 9(3), 177-180.
16. **Ghia, C.J.; Dhar, R.; Koul, P.A.; Rambhad, G.; Fletcher, M.A.** Streptococcus pneumoniae as a cause of community-acquired pneumonia in Indian adolescents and adults: A systematic review and meta-analysis. Clin. Med. Insights Circ. Respir.
17. **Driver, C. (2012).** Pneumonia part 1: pathology, presentation and prevention. British Journal of Nursing, 21(2), 103-106.
18. **Seramo, R.K., Awol, S.M., Wabe, Y.A., & Ali, M.M. (2021).** Determinant of Pneumonia Among Children Aged 2-59 Months in Public Health Facilities in Worabe Town, Southern Ethiopia: Facility-Based Case Control Study.
19. **Bradley JS, Byington CL, Shah SS, et al. (2011):** The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the pediatric infectious diseases society and the infectious diseases society of America. Clin Infect Dis . ;53(7):617–630.
20. **O'Grady, K. A. F., Torzillo, P. J., Frawley, K., & Chang, A. B. (2014).** The radiological diagnosis of pneumonia in children. Pneumonia, 5, 38-51.
21. **Ruuskanen, O., Lahti, E., Jennings, L. C., & Murdoch, D. R. (2011).** Viral pneumonia. The Lancet, 377(9773), 1264-1275.
22. **Lynch, T., Bialy, L., Kellner, J. D., Osmond, M. H., Klassen, T. P., Durec, T., ... & Johnson, D. W. (2010).** A systematic review on the diagnosis of pediatric bacterial pneumonia: when gold is bronze. PloS one, 5(8), e11989..
23. **Kelly M S, Sandora T J (2020):Community-Acquired Pneumonia, Nelson Textbook of Pediatrics, ROBERT M.** KLIEGMAN, JOSEPH W. ST GEME NATHAN J. BLUM, SAMIR S. SHAH ROBERT C. TASKER , RICHARD E. BEHRMAN, 21 EDITION, Elsevier Inc. ISBN:978-0-323-52950-1IE ISBN: 978-0-323-56890-6, 8956-8977.
24. **Matteo Bassetti, Elda Righi, Antonio Vena, Elena Graziano, Alessandro Russo, and M. P. (2018).** Risk stratification and treatment of ICU-acquired pneumonia caused by multidrug-resistant/ extensively drug-resistant/pandrug-resistant bacteria Matteo. CURRENT OPINION, 24(5), 385–393.