Community Acquired Pneumonia (CAP) in Children in Developing countries -A Review

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Abstract

Community-acquired pneumonia (CAP) is a potentially serious infection and is the single commonest and leading cause of death in under 5 children in developing countries. But the crucial first step in tackling childhood pneumonia is being able to diagnose it accurately, particularly after introduction of 2 effective vaccines against two major pathogens responsible for childhood bacterial pneumonia. Radiology and determination of hypoxia by pulse oximetry have been considered the optimal methods for diagnosing pneumonia. This review article has updated the important aspects of childhood pneumonia in developing countries. Early recognition and prompt, appropriate and adequate management can reduce the case fatality as well as morbidity associated with pneumonia.

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Introduction

Pneumonia continues to be the biggest killer worldwide in children under 5 years of age. CAP can be defined clinically as the presence of signs and symptoms of pneumonia in a previously healthy child due to an acute infection (of less than 14 days' duration) of the lower respiratory tract which has been acquired in the community outside the hospital, leading to cough or difficult breathing, tachypnea or lower chest wall indrawing.[1]

With the recent advancement in medical management and economic development as well, there have been enormous reductions in the burden of pneumonia mortality in young children around the world over the past 3 decades. Five countries in Asia and Africa (India, Nigeria, Pakistan, Democratic Republic of Congo and China), where approximately 48% of all pneumonia deaths occur, an understanding of geographic and etiological variability in pneumonia is also important.[2]

Epidemiology : morbidity and mortality burden, and risk factors

Pneumonia remains the leading infectious cause of death, globally among children under 5 years of age, killing approximately 2500 children in a day. Pneumonia accounted for approximately 16% of the 5.6 million underfive deaths, killing around 88,000 children in 2016. Most of these victims were less than 2 years old.[3]

In Bangladesh, Pneumonia is responsible for around 28% of the deaths of children under 5 years of age and around 50,000 children die of pneumonia every year. An estimated 80,000 children under 5 years of age are admitted to hospital with virus associated acute respiratory illness each year. The total number of infections is likely to be higher.[3]

Incidence of total paediatric ARI is 3 to 8 episodes per child per year in urban communities and 1 to 3 episodes in rural communities with most of these being self limiting viral upper respiratory infection.[4]

The incidence of pneumonia in the high income countries (Europe and North America) has been estimated to be approximately 36/1000/year, while here pneumonia related mortality remains relatively low.[4]

The global mortality burden in low-middle-income-countries (LMIC) is disproportionately higher which may be associated with multiple pathogens and inadequate health education (of care givers) regarding early home recognition of signs of severe disease. Globally pneumonia accounted for approximately one-fifth (19%) of the 2 million deaths with 90% of these occurring in a low-middle-income-country population and 50% of these deaths occur in Africa.[4]

Study conducted at Dhaka Hospital of ICDDR,B among 601 under5 children with ALRI (acute lower respiratory infection-it is a practical term in resource poor setting of the developing countries where difficulties in obtaining chest radiograph is present, especially in rural areas[5]), pneumonia (86.5%) was the most common manifestation and respiratory pathogens (both bacterial and viral) were identified.[6]

Prevalence of several risk factors of severe ALRI/pneumonia is higher in poor-resource tropical countries and the predominant host factors are mentioned in Table-1.[7-9]

Table 1: Risk factors for CAP[7,8,9]

Medical
Age <1 year
Prematurity/LBW
Malnutrition
Immunosuppression
Social /Environmental
Overcrowding
Air pollution
Inadequate housing
Passive tobacco smoke exposure
Presence of coughing siblings at home
Indoor fuel combustion
Exposure to environmental pollutants (combustive pollutants of domestic biomass burning)
Winter season
Lack of breast feeding
Poor parental income /literacy
Failure to complete immunization

Aetiological agents

Pneumonia is the inflammation of the lungs, caused by a wide range of bacteria and viruses (and occasionally fungal and parasitic infection). Lung aspirate studies from several countries have shown that bacterial agents like *Streptococcus pneumoniae, Haemophilus influenzae* and *Staphylococcus aureus* are the top three agents accounting for over 60% of pneumonia in the developing world.[10-12]

Table 2: Common causes of CAP in Children

Bacterial
Streptococcus pneumoniae
Moraxella catarrhalis
Hemophilus influenza type B
Staphylococcus aureus
Mycobacterium tuberculosis
Atypical bacteria
Mycoplasma pneumoniae
Chlamydia pneumonia
Chlamydia trachomatis
Pneumocystis jirovecii
Virus
Cytomegalo virus
Respiratory syncytial virus
Rhinoviruses
Adenoviruses
Human metapneumovirus
Parainfluenza virus type 1 and 3
Bocavirus
Influenza A or B
Measles virus

The spectrum of possible pathogens of acute pneumonia varies widely. *Staphylococcus aureus* and *Klebsiella* species are the dominant pathogens of CAP in Nigerian children according to blood culture-generated bacteriological data.[13] Children with measles, malnutrition and other immunocompromised states and also in neonate *Klebsiella, Escherichia coli, Proteus* and *Pseudomonas* species were reportedly common.[14]

Fungal agents like *Candida, Aspergillus, Cryptococcus, Histoplasma, Nocardia* species and *Pneumocystis jiroveci* also accounts for a significant proportion of non-bacterial pneumonia in immunocomprised host.

M tuberculosis usually causes pneumonia which is chronic in nature.

Viral pathogens like *Respiratory Syncytial Virus(RSV)* and *Parainfuenza virus (PIV)* constituting the top two in causing childhood pneumonia in Asia and Sub Saharan Africa.[15] A child with pneumonia who is wheezing is likely to have a viral or atypical pneumonia caused by *Mycoplasma pneumonia* or *Chlamydia pneumonia.*[16]

Induced sputum Gram stain smears and cultures from hospitalized children aged 1-59 months were evaluated and enrolled in a large study of community acquired –pneumonia. The presence of low numbers of squamous epithelial cells (SEC_S) (<10 per LPF) and high numbers of polymorphonuclear (PMN) (>25 per LPF) cells are regarded as indicative of standard lower respiratory tract specimen. Induced sputum culture results were analysed from 3772 of 4232(89.1%) children enrolled in PERCH study of which 2695(71.4%) had severe pneumonia and

1077 (28.6%) very severe pneumonia: 518 from Bangladesh, 596 from Gambia, 592 fron Kenya, 544 from Mali, 824 from South Africa, 191 from Thailand and 507 from Zambia. Detection of 4 major potential pathogens *(Streptococcus pneumoniae, Haemophilus Infuenzae, Moraxella Catarrhalis, Staphylococcus aureus)* was greater in specimens from children without evidence of prior antibiotic use. Gram negative rods like *Acenatobacter* and *Pseudomonas* species were also detected.[17]

Molecular diagnostic methods have the potential to improve our ability to detect small numbers of organisms in tissue and body fluids for diagnosis of childhood pneumonia. Nucleic acid amplification tests (PCR-polymerase chain reaction) can be used to detect nucleic acid from potentially all respiratory pathogens. It is not dependent on viable organism or fastidious culture conditions and are not as affected by prior exposure to antibiotics as conventional culture methods. PCR pathogen detection in paired NP/OP (nasopharyngeal/oropharyngeal) swab and IS (induced sputum) from 1114 hospitalized children (aged 1-59 months) with radiographic pneumonia, the common predominant organisms were *Streptococcus pneumoniae, Moraxella catrrhalis, Haemophilus influenza, Staphylococcus aureus, Pneumocystis jiroveci, Cytomegalovirus, Respiratory syncytial virus, Rhinovirus, Adenovirus, HMPV (human metapneumovirus), Bocavirus, Parainfluenza 1 & 3.*[18]

The *atypical bacteria Pneumocystis jiroveci* whose detection rate was higher in radiologically confirmed pneumonia who were HIV positive but also higher in severe malnutrion with radiographic pneumonia who were HIV negative.[19]

There is approximately 20% reduction of radiologically confirmed pneumonia after introduction of *Haemophilus infuenzae type b (Hib)* vaccine among children in trails in the Gambia and Chile.[19,20] A 9 –valent PCV prevented 37% of cases of radiologically confirmed pneumonia among children in the Gambia who were already receiving Hib vaccine.[21] The global burden of severe pneumonia could be reduced to about half following introduction of conjugate vaccines against these organisms.[22]

Clinical features

The clinical presentation of childhood pneumonia varies with the age of the child and the causative agent; the younger the infant,the less specific is the presentation. In pneumona with severe malnutrition, WHO defined fast breathing and chest indrawing may not be as evident as in other children with pneumonia.[23]

Pneumonia in young infants below 3 months may present with poor feeding, vomiting or irritability, minimum systemic disturbance and cough may be absent despite tachypnea.

Most infants and the majority of school-aged children with *chlamydial* and *mycoplasmal* aetiology are a febrile with minimal systemic toxicity at presentation.

Viral pneumonias usually have a subacute course and may begin with coryzal symptom. Concurrent or antecedent respiratory illness in other dwellers in the household are common. Measles may be complicated by superimposed severe bacterial pneumonia usually by necrotizing agents like *Staphylococcus aureus* or *Klebsiella pneumonia*.

Investigations

The crucial first step of management of childhood pneumonia is being able to diagnose it accurately. Analysis of 1,848 chest radiographs of children in Pakistan hospital outpatients settings who had had non severe pneumonia diagnosed clinically according to WHO guidelines showed that only 14% of the children had radiological evidence of pneumonia.[24] Other community studies in Pakistan also had found to have very low specificity of chestradiograph for pneumonia in young children.[25]

Table 3 : Indications for admission to hospital

All young children <2 months
Children older than 2 months if
Impaired level of consciousness
Inability to drink or eat
Cyanosis
Stridor in calm child
Grunting
Severe chest indrawing
Room air SaO_2 at sea level<90% at higher altitude
Severe malnutrition
Family unable to provide appropriate care
Failure to respond to ambulatory care or clinical determination of treatment failure

Radiological, microbiological and hematological investigations are done where facilities exist, to sort out confusing clinical presentations, identify the extent and severity of the disease, the presence of complications (e.g. pleural effusion, air–leak syndromes), exclude other diagnostic consideration (like foreign body aspiration, pulmonary tuberculosis and congenital heart diseases) and frequently to follow the appropriateness of therapeutic interventions. Relatively invasive investigations (including lung biopsies) may be necessary in the immunocompromised patients, in whom the spectrum of potential pathogens is wider and the presentation frequently atypical.

Non microbiologic laboratory tests have also been widely used in an attempt to differentiate bacterial from non bacterial pneumonia. However they are not much better than chest radiographs. The C-reactive protein (CRP) level and absolute neutrophil count are found to be most helpful.[26] Elevated CRP was positively associated with confirmed bacterial pneumonia

and negatively associated with RSV pneumonia. CRP may be useful for distinguishing bacterial from RSV-associated pneumonia[27]

CBC with differential count usually shows leukocytosis in addition to raised ESR in bacterial pneumonia but in viral pneumonia, a mild leukocytosis or leukopenia with lymphocytosis is expected, while chlamydia trachomatis causes pneumonia associated with eosinophilia in early infancy. Open lung biopsy or bronchoalveolar lavage specimens for histopathology and identification of fungal, bacterial and non-bacterial pathogens.[4]

Treatment

The management of pneumonia may be divided into two concurrently accomplishable components, namely specific and supportive therapy.

Specific Therapy

When treating CAP, the clinical,laboratory and radiographic findings should be considered, specially when the child is hospitalised. As it is difficult to distinguish bacterial from viral pneumonia and because of the frequency of mixed bacterial-viral infections(~30-40%)[1], all children with CAP require an antibiotic. The age of the child, nutritional status of the host, local epidemiology of respiratory pathogens and sensitivity of these pathogens to particular antimicrobial agents and the emergence of antimicrobial resistance usually determine the choice of antibiotic therapy.[28]

The development of revised WHO classification and WHO-approved recommendations for treatment of childhood pneumonia at health facilities, specially for the first-level/primary care level constitutes the current most effective strategy for stemming the mortality burden of pneumonia in LMICs.[28,29]

Staphylococcus aureus and *Klebsiella* species are currently emerging as the top two important pathogens of childhood pneumonia in some urban third world communities such as Nigeria, Colombia and India. Consequently[8], there may be a need to modify the WHO antimicrobial recommendations.

Alternative antimicrobial agents for out-patient cases include oral cephalosporin or clindamycin. The antimicrobial spectrum covered by the new generation macrolides like azithromycin is also good enough to earn a recommendation as an alternative oral medication in the ambulatory treatment of moderately severe cases.

Despite an increasing availability of specific antiviral agents which are of potential value for treating viral pneumonias especially in infants with RSV, the current recommendation is that of 'watchful waiting' while pursuing supportive care. But if facilities are available, infants with RSV disease with concomitant symptom-complex of bronchiolitis and in whom there are risk factors of mortality (i.e. preterm delivary, age<2 months, chronic lung disease/BPD (bronchopulmonary dysplasia)and congenital cardiac lesions), specific antiviral agents like aerosolized ribavirin may be offered.[4]

Supportive Care

This is a crucial aspect of the management for both ambulatory and hospitalised cases of pneumonia. The essential elements of supportive treatment for both categories of patients comprise addressing fever and providing appropriate thermal environment, fluid and nutritional management as well as clearing nostrils. Hypoxaemia is an important risk factor for death as hypoxaemic patients are five times more likely to die than non-hypxaemic patients.[30] Oxygen was never mentioned in the recent publication by the WHO and UNICEF efforts to control pneumonia.[31] Hypoxaemia has been overlooked in world wide strategies for pneumonia control and reducing child mortality.[32]

Therefore provision of oxygen, as well as instituting appropriate medical interventions for complications like congestive heart failure, severe anemia and appropriate surgical intervention for intrapleural complications like pleural effusion including empyema, pneumothorax and air-leak syndromes, constitute important elements of the supportive care of the hospitalised child.

Conclusion

Despite dominating the childhood mortality throughout the developing world, severe pneumonia has received little scientific or public health attention for decades. In developing countries, *pneumococcus* and *H influenzae* type b are the dominant cause of severe pneumonia in children and introduction of conjugate vaccines against these diseases could reduce the global burden of severe pneumonia. The residual cases of pneumonia will have a wide variety of aetiological causes and this broad aetiological diversity will make the diagnosis, classification and management of pneumonia much more complex and expensive in future. The formation of a Global Action Plan for Pneumonia at WHO and the interest of public health foundations in supporting pneumonia research in developing countries are both welcome reversals of this long standing neglect. The focus has extended to reducing the underlying condition recently that put the children at risk of pneumonia mortality including reducing HIV infections through preventing MTCT (maternal to child transmission), preventing and treating malnutrition and undernutrition, reducing household and outdoor air pollution exposure and ensuring that prevention and treatment services are accessible when and where they are needed.

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