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Community Acquired Pneumonia In Children- Contemporary Issues And Current Concerns

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Abstract

Community acquired pneumonia (CAP) remains the leading cause of mortality in children less than five years of age. This article reviews the main issues related to CAP in children namely recognition of seriousness, need for standardized case management, use of appropriate antibiotic therapy, predictors of treatment failure, role of chest radiography and prevention of CAP. Early recognition and use of appropriate effective antibiotic therapy can significantly reduce mortality of childhood pneumonia. Education of primary care-givers in the community especially parents and community health workers is an important and much needed measure to help achieve the above. Effectiveness of standardized case management can be further improved by addressing the various risk factors associated with poor response to antibiotic therapy namely malnutrition, incomplete immunizations and hypoxemia at presentation since these are amenable to interventions. Primary prevention of pneumonia through appropriate vaccination policies is likely to reduce the burden significantly.

Key Words: Community acquired pneumonia, children, prevention, recognition, standardized case management, immunization

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Introduction

Pneumonia is the single most important cause of death in children (1). It is estimated that each year, over 2 million children die of pneumonia; which translates to 20% of the mortality among under five children. Pneumonia accounts for more childhood deaths than diarrhoea and is responsible for greater mortality than malaria, measles and AIDS put together (2). This relatively high mortality is not restricted to developing countries; even in industrialised nations, pneumonia is responsible for a disproportionately large share of childhood mortality. UNICEF data show that a handful of 15 countries account for over three-quarters of childhood pneumonia across the world; India has the dubious distinction of topping this list, contributing 44 million (39%) of the estimated 113 million global episodes. What is more alarming is that these 44 million episodes of pneumonia also translate to the highest number of episodes per child per year. Therefore, the importance of appropriate health care interventions at the individual, community national and regional levels cannot be over-emphasized. It has recently been calculated that standard case management of pneumonia is likely to have an impact even greater than that of oral rehydration therapy for diarrhoea; this is an important observation considering that the latter is often universally hailed as the most effective heath intervention over the past century (3). Therefore, it is pertinent to examine contemporary issues and current concerns related to community acquired pneumonia in children.

Issue 1: Recognition Of Seriousness

The first step to accessing effective health care is the recognition of seriousness of the problem. Unfortunately, for pneumonia there is considerable deficiency on the part of primary care-givers in this aspect, which results in poor health-seeking behaviour. There could be many reasons for this, including confusing symptoms and signs of pneumonia with trivial childhood illnesses, failure to recognise danger signals and putting off a visit to health care centre until advanced stages. It is indeed unfortunate that appropriate health care is sought in only about 50% cases of childhood pneumonia. Table 1 reflects the burden of childhood pneumonia and the health seeking behaviour of populations in developing countries within UNICEF regions. These data imply that about half the children with pneumonia do not present to a health provider. These dismal trends prevail for both genders, and also in rural as well as urban areas of

Table 1: Burden of childhood pneumonia and health-seeking behaviour

UNICEF region	Episodes per child per year	Percentage taken to appropriate health care provider
Developing countries in general	0.29	54%
South Asia	0.36	59%
Sub-Saharan Africa	0.30	41%
CEE/ CIS	0.29	50%
Middle East and Sub-saharan Africa	0.26	66%
Latin America	0.22	52%
East Asia and Pacific	0.24	62%
Middle East	0.26	66%

Data from reference 2

residence, although it is worse in the rural areas.

Recognition of seriousness is hampered by the fact that less than 20% primary care-givers are aware that common physical signs such as fast breathing and difficult breathing, independently herald serious disease. There is some evidence that children of less educated mothers are less likely to be taken to a health care provider (Table 2A). There is also emerging evidence that the likelihood of visiting a health centre is directly proportional to the level of economic capacity, although it must be emphasized that even 'rich' parents display 'poor' health seeking behaviour (Table 2B). These findings argue for educating primary care-givers in the community about the importance of childhood pneumonia as well as imparting knowledge and skill to identify simple symptoms and signs of severe disease. This is particularly important because recent management protocols are emphasizing the importance of home-based treatment, which again necessitates that caregivers should understand and be convinced of treatment efficacy.

Issue 2: Standard Case Management

Standard case management depends on correct diagnosis and classification of severity of children with pneumonia. The Integrated

Table 2: Factors affecting health-seeking behaviour

2A. Relationship of health-seeking behaviour and maternal education	
Level of maternal education	Percentage of under-five children taken to appropriate health-care provider
Secondary education	59%
Primary education	47%
No formal education	43%
2B. Relationship of health-seeking behaviour to economic status	
Relative economic status	Percentage of under-five children taken to appropriate health-care provider
Richest	53%
Middle	45%
Poorest	40%

Data from reference 2

Management of Childhood Illness (IMCI) guidelines (4, 5) define pneumonia among children upto 5 years of age, as the presence of cough with fast or difficult breathing. Fast breathing is defined as respiratory rate greater than 50 per minute for children aged 2 to 12 months old and more than 40 per minute for those 12 months to 5 years old. Pneumonia is categorised as severe when there is lower chest wall indrawing (retractions) and as very severe pneumonia in presence of cyanosis and/or inability to drink. It is immediately evident that this diagnosis and classification system is practical, simple to apply and does not require sophisticated instruments or advanced training. Further, there is evidence which suggests that tachypnea may be a characteristic sign of pneumonia across all ages (6). However, it should be noted that the case definition does not give importance to fever and estimates of oxygenation. This may be because the former is very non-specific and the latter difficult to measure in community settings. Similarly, auscultatory signs have not been included in the standard case definition because it requires considerable training and skill, and yet has low specificity and poor inter-observer concordance (7).

As per the standard case management guidelines, only children

aged 2 months to 5 years with 'non-severe' pneumonia may be treated at home. These children should receive a complete course of antibiotic therapy. Children with severe pneumonia and infants less than 2 months old with any pneumonia should be referred to the nearest health facility immediately. It may be prudent to administer the first dose of antibiotic before referral to a facility where oxygen and injectable antibiotics can be administered. The effect of community based management of pneumonia has been recently established through a meta-analysis of trials on this intervention. This showed that there was significant decline in all-cause mortality as well as pneumonia-specific mortality across all age groups in those who received community based management (Table 3).

Table 3: Impact of community-based management of pneumonia

Age group	Reduction in all cause mortality	Reduction in pneumonia related mortality
Neonates	27%	42%
Infants	20%	36%
Children	24%	36%

Data from reference 2

Issue 3: Appropriate Antibiotic Therapy

Although it may appear strange to discuss something as obvious as antibiotic therapy for pneumonia, this is a very important issue because data from various developing countries shows that only a small fraction of children with pneumonia receive antibiotic therapy. Figure 1 shows the dismal scenario in these countries across all continents. India fares slightly better than some of these countries, but the level of coverage is far below that expected. Although some countries have shown progress, what is alarming is that some other countries actually report a further decline in the number of children receiving antibiotics for pneumonia (Table 4).

Clinical experience in many developing countries suggests that cotrimoxazole and amoxicillin are effective antibiotics to treat childhood community acquired pneumonia in developing countries. The key factor is the completion of a full-course of therapy.

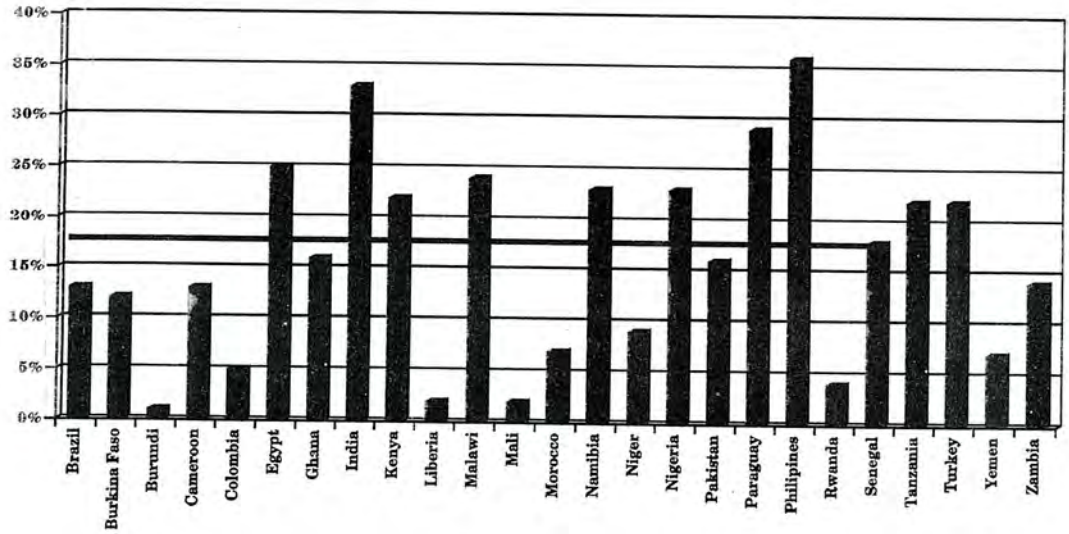

Figure 1: Proportion of children receiving antibiotic therapy for pneumonia.

The solid line indicates the average data of 27 developing countries
Data from reference 2

Table 4: Change in trends of antibiotic therapy for children with pneumonia

Country	Year	Percentage of under five children treated with antibiotics
Brazil	1991	13%
	1996	15%
Colombia	1986	5%
	1990	30%
Dominican Republic	1991	29%
	1996	10%
Egypt	1992	25%
	2000	75%
Ghana	1993	24%
	1998	16%
Philippines	1993	44%
	1998	36%

Recent years have witnessed a spate of studies that confirm the clinical success of therapy with amoxicillin or cotrimoxazole in children with pneumonia. A summary of these is presented in Table 5 (8-13). A more recent randomized trial has confirmed that oral therapy may be as efficacious as intravenous therapy; this trial with almost 250 participants demonstrated the equivalence of efficacy with oral amoxicillin as compared to intravenous benzyl-penicillin, with respect to treatment success, duration of fever and time to complete resolution of symptoms (14). Further, it is now evident that treatment duration as short as three days may be adequate, in terms of comparable efficacy of the longer five-day course (12).

The trend towards progressively shorter antibiotic courses for non-severe pneumonia had led to a pertinent question whether such children require antibiotics at all. This is a natural extension of the question on the likely etiology of pneumonia in

Table 5: Efficacy studies on antibiotic therapy in developing countries

Study	Country	Sites	Year	Population	Intervention and outcome			
					Antibiotic	Treatment failure	Antibiotic	Treatment failure
Strauss et al	Pakistan	2	1991-1992	595 children, age 2-59 month	Amoxicillin 45mg/kg/day for 5 days.	13%	Cotrimoxazole 20/4 mg/kg/day for 5 days	23%
COMET study	Pakistan	9	1995-1996	1143 children, age 2-59 month	Cotrimoxazole 20/4 mg/kg/day for 5 days	19%	Cotrimoxazole 40/8mg/kg/day for 5 days	21%
CATCHUP study	Pakistan	8	1998-1999	1471 children, age 2-59 months.	Amoxicillin 45mg/kg/day for 5 days.	16%	Cotrimoxazole 20/4 mg/kg/day for 5 days	19%
MASCOT Pneumonia Study group	Pakistan	7	1999-2001	2000 children, age 2-59 months.	Amoxicillin 45 mg/kg/day for 3 days.	21%	Amoxicillin 45 mg/kg/day for 5 days.	20%
ISCAP Study	India	7	2000-2002	2188 children, age 2-59 months.	Amoxicillin 31-54mg/kg/day for 3 days.	11%	Amoxicillin 31-54mg/kg/day for 5 days.	10%
Hazir T et al	Pakistan	4	2003-04	896 children, age 2-59 months.	Amoxicillin 45 mg/kg/day for 3 days.	5.9%	Amoxicillin 90 mg/kg/day for 3 days.	7.9%

children. It has been known for long that majority of childhood pneumonia in developed countries is related to viral infection, whereas it is predominantly bacterial in developing countries. Further, the frequent isolation of atypical organisms in children with pneumonia could argue against prescribing antibiotic treatment. If children in developing countries also have predominantly 'viral' pneumonia, it could account for the 'success' of a short course of oral antibiotic therapy. Short of determining the etiology of pneumonia through sophisticated investigations, the only way to determine this indirectly would be to with-hold antibiotic treatment in a cohort of childhood pneumonia and assess the outcome. This important issue has recently been addressed in an elaborately designed double-blind multi-centric trial in India. This trial was designed to evaluate whether 'placebo administration in children with non-severe pneumonia and wheezing, had equivalent effects compared to therapy with amoxicillin (15). Wheezing is a common presentation in childhood pneumonia, especially viral and atypical pneumonia. Table 6 shows the primary outcome (treatment failure) for each of the centres that participated in the trial. It is interesting that although the effect was comparable between the two

Table 6 : Is antibiotic therapy required in children with non-severe pneumonia: results of a double-blind multicentric trial in India.

Place	Treatment failure in Placebo arm	Treatment failure in Amoxicillin arm	OR (95% CI)	RR (95% CI)
New Delhi	23/92	14/93	1.88 (0.90-3.94)	1.66 (0.91-3.02)
Chandigarh	4/81	3/79	1.32 (0.28-6.08)	1.30 (0.30-5.62)
Nagpur	5/108	10/110	0.49 (0.16-1.47)	0.51 (0.18-1.44)
Trivandrum	32/128	20/127	1.78 (0.96-3.32)	1.59 (0.96-2.62)
Mumbai	19/108	17/109	1.16 (0.56-2.36)	1.13 (0.62-2.05)
Chennai	54/120	49/118	1.15 (0.69-1.92)	1.08 (0.81-1.45)
Vellore	34/111	30/111	1.19 (0.67-2.13)	1.13 (0.75-1.72)
Lucknow	31/91	23/88	1.46 (0.77-2.78)	1.30 (0.83-2.05)
Overall	202/839	166/835	1.28 (1.01-1.52)	1.21 (1.01-1.45)

arms within each centre, the pooled effect was in favour of therapy with amoxicillin as compared with placebo. The importance of this landmark trial is that it not only demonstrates that the beneficial effect of short course antibiotic therapy in childhood pneumonia has a scientific basis, but also indirectly points towards bacterial etiology of this condition, which is also amenable to other interventions such as vaccination.

Issue 4: Predictors Of Treatment Failure In Childhood Pneumonia

From the foregoing sections, it is clear that although short course of oral antibiotic therapy is successful in childhood pneumonia, there are a significant number of children encountering treatment failure. A number of reasons could be responsible for this; such as greater severity of disease within a category, presence of co-morbid conditions, organisms that respond poorly to the antibiotics used, and of course inadequate antimicrobial therapy. An emerging factor is the trend of antimicrobial resistance among many bacterial species. Therefore, it would be of immense clinical value, if one could predict the likelihood of treatment failure in a given patient. The multi-centric WHO-SPEAR study (16) assessed treatment failure between treatment arms based on chloramphenicol versus ampicillin with gentamicin, in children with very severe pneumonia, at serial intervals (5 days, 10 days and 21 days). Although the latter combination therapy proved to be superior, the trial provided a number of risk factors that were associated with treatment failure. These included female gender (OR 1.95, 95% CI 1.11-3.43), incomplete immunization (OR 1.77, 95% CI 1.00-3.15), severe malnutrition defined as weight for age Z-score less than -3.0 (OR 1.48, 95% CI 0.69-3.19) and the presence of hypoxemia (OR 4.7, 95% CI 2.29-9.67). The latter is clinically important as this is easily correctable at short notice. Univariate analysis of data from Chandigarh showed that children with treatment failure had significantly higher temperature at admission, hypoglycemia and a positive blood culture at admission. An important difference among those in whom treatment was successful compared to treatment failure, was the degree and duration of hypoxemia. The latter group had hypoxemia that was more severe and lasted longer than the former (Fig. 2). The recent multi-centric Indian trial in children with non-severe pneumonia demonstrated that the presence of vomiting was a significant independent risk factor associated with

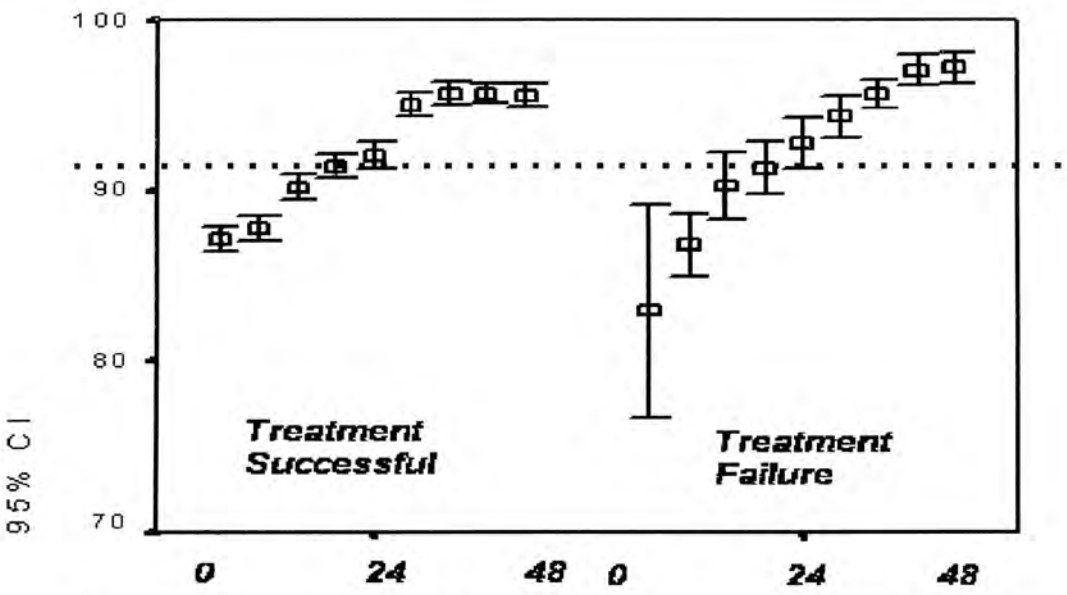

Figure 2: Oxygenation and relationship to outcome in children with pneumonia

worse outcome. Another very significant clinical finding predictive of treatment failure was a respiratory rate more than 10 breaths per minute beyond the cut-off.

Issue 5: Role Of Chest Radiography

It is interesting that there is scant mention of the role of chest radiography in most of the recent guidelines for the management of community acquired pneumonia in children. This is because of three major reasons, first it has little impact on treatment policy in the setting of community acquired pneumonia, especially where home-based care is concerned, second it has poor specificity to identify bacterial infection (where antibiotics are necessary) as against viral infection (wherein antibiotics may not be necessary) and third, the radiological definitions of pneumonia are very variable and have poor specificity (17, 18). Therefore current treatment protocols of non-severe community acquired pneumonia do not lay much stress on chest radiography.

Issue 6: Co-Infection With HIV

Pneumocystis jiroveci (formerly *P. carinii*) pneumonia is the most common opportunistic infection in HIV positive children. It is responsible for about 25% deaths in HIV positive infants. These

data argue strongly in favour of antibiotic prophylaxis in all HIV positive children and babies born to IIIV infected mothers. There is empiric data that attests to improved outcome with such intervention. The WHO therefore recommends cotrimoxazole prophylaxis in all such children

Issue 7: Prevention Of Community Acquired Pneumonia

The high morbidity and mortality associated with childhood pneumonia makes it necessary that every possible effort be made to prevent its occurrence. Potentially beneficial measures are community education, improvement of nutrition and vaccination against preventable causes of pneumonia (19-22).

Vaccination for the prevention of pneumonia has been in practice for several decades in developed countries and for about 30 years in most developing countries. Measles immunization and universal immunization with DPT have resulted in significant decline in morbidity and mortality across the world. This is true in developing countries as well. It is expected that vaccination against *Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae*, for

Table 7 : Efficacy of Hib and Pneumococcal vaccines in developing countries

Country	Vaccine used	Study design	Vaccine efficacy (95% CI)
Colombia	Hib conjugate vaccine	Case-control	55% (7-78)
Chile	Hib conjugate vaccine	RCT	22% (7-43)
Brazil	Hib conjugate vaccine	Case-control	31% (9-57)
Gambia	Hib conjugate vaccine	Double blind RCT	22% (2-39)
Indonesia	Hib conjugate vaccine	Double blind RCT	12%
Bangladesh	Hib conjugate vaccine	Case-control	44% (20-61)
South Africa	9 valent Pneumococcal conjugate vaccine	Double blind RCT	25% (4-40)
Philippines	11 valent Pneumococcal conjugate vaccine	Double blind RCT	22.9% (1-41)
Gambia	9 valent Pneumococcal conjugate vaccine	Double blind RCT	35% (26-43)

which safe vaccines are currently available, can further improve child survival. This is based on the calculation that *Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae* are the leading causes of childhood pneumonia; together accounting for more than half the mortality related to childhood pneumonia (23,24).

The early randomized controlled trials in developing countries proved that Hib vaccination resulted in significant protection against pneumonia and meningitis; although it is estimated that the burden of pneumonia prevented is nearly ten-fold higher. Similar observations have emerged from case–control studies also. Similarly, a limited number of trials of Pneumococcal conjugate vaccine in the developing world have reported encouraging results. The World Health Organization has been pressing all countries; especially developing countries to include both Hib and Pneumococcal conjugate vaccine into individual routine immunization programmes (25, 26). It is expected that the financial assistance extended through international organizations such as GAVI Alliance will help make this a reality in resource poor settings.

Conclusion

Globally, childhood pneumonia is a problem of enormous public health importance; it remains the leading cause of mortality in under five-children, with an undesirably high disease burden in resource poor countries. Early recognition and use of appropriate effective antibiotic therapy that can be delivered at patients' door-step can have significant impact on pneumonia mortality. Educating and empowering primary care-givers in the community, particularly parents and community health workers, to enhance the proportion of children who receive antibiotic therapy, has the potential to reduce mortality. The current IMCI guidelines for recognition and categorisation of childhood pneumonia facilitate this process. The yield of standard case management can be further improved by addressing various risk factors associated with poor response to antibiotic therapy; malnutrition, incomplete immunizations, hypoxemia at presentation; that are eminently amenable to interventions. Primary prevention of pneumonia through appropriate vaccination policies is likely to reduce the burden significantly.

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