

Original Research Article

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A study to assess the prevalence of atypical organisms in pneumonia in children aged 1 month to 3 years by serum polymerase chain reaction in KIMS Hospital, Bangalore, India

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ABSTRACT

Background: Atypical organisms are a common causative agent of pneumonia in children more than 3 years of age. Though atypical pathogens are said to cause relatively milder form of pneumonia severe manifestations can also occur. Very few studies are available on the prevalence of atypical pneumonia in children less than 3 years. Hence in this study the prevalence of atypical organisms in pneumonia was identified by using serum Polymerase chain reaction (PCR).

Methods: This is a prospective observational study conducted in children between 1 month to 3 years of age with clinical diagnosis of pneumonia admitted in wards and PICU in KIMS hospital. Authors excluded Immuno compromised children. Detailed history and clinical examination was done. Investigations - complete hemogram, Chest X-ray, blood Culture and sensitivity and serum PCR was done for a sample size of 50 children.

Results: Among the three atypical organisms, *Legionella pneumoniae* was identified in 4% (2/50) cases by serum PCR.

Conclusions: In this study it was found that the prevalence of 4%. *Legionella pneumonia* can be fatal in 10% of cases. Hence atypical pathogens like *Legionella* should be kept in mind even in children less than 3 years when pneumonia is not responding to beta lactam antibiotics, in such cases macrolides to be considered.

Keywords: Atypical pneumonia, *Legionella*, Less than 3 years, Polymerase chain reaction

INTRODUCTION

Atypical organisms are identified as the causative agent of pneumonia in 15-30% of pediatric cases.¹ Atypical organisms include *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* and *Legionella*. They are characterised by atypical features such as a less virulent course, but sometimes they can also cause severe manifestations.² They have presence of signs more than symptoms (walking pneumonia), patchy infiltrates on chest radiographs, and lack of response to beta lactam antibiotics. Most of the times they have a clinical picture

similar to typical organisms and they are difficult to detect by routine investigations.

The effectiveness of serum PCR in the diagnosis of atypical pathogens have been found to be 52%, 70%, 50% for *Mycoplasma*, *Chlamydia* and *Legionella* respectively.³⁻⁵ By doing PCR in serum samples the advantages are that serum is easily stored and handled, and the pathogen is detected from a sterile site, where colonization can be ruled out. Other tests used to diagnose atypical pathogens include Serology ELISA (requires fourfold increase in titre), cold agglutinins for

mycoplasma, Polymerase chain reaction (PCR) respiratory secretions, pleural fluid, blood Culture and sensitivity.⁶ Although atypical pathogens are a common cause of community acquired pneumonia in children aged more than 3 years, very few studies are done to find there prevalence in younger children. In this study the prevalence of atypical organisms in children between 1 month to 3 years will be studied by serum PCR along with the clinical spectrum of pneumonia in this age group.

METHODS

This is a prospective observational study conducted in children between 1 month to 3 years of age with clinical diagnosis of pneumonia admitted in wards and Pediatric intensive care unit in KIMS hospital. Authors excluded Immuno compromised children.

The study was approved by the Institutional Ethics Committee of the institute. Informed consent was obtained from the parents or the legal guardians of the study participants. Detailed history and clinical examination was done. The diagnosis of pneumonia in children clinically was made according to the WHO guidelines.

- Cough
- Tachypnea /chest retraction.

Criteria for tachypnea according to age

- 1month-2months->60/min
- 6month to 1 year- > 50/min
- 1 year to 3 years- >40 /min
 - Fever >100 degree Fahrenheit.
 - Respiratory signs
 - Radiological evidence of pneumonia.

Investigations includes complete hemogram, Chest Xray, blood Culture and sensitivity and serum PCR was done for a sample size of 50 children over a study period of 14 months from January 2018 to March 2019. On the day of admission to the hospital, samples were collected by sterile technique and PCR samples were stored in appropriate conditions. Serum RT-PCR (reverse transcriptase polymerase chain reaction) was done using a kit to detect 33 respiratory pathogens (Fast track diagnostics kit) by trained professional.

Statistical analysis was done using software stata version 14, p value of less than 0.05 was considered significant.

RESULTS

Patient characteristics

Of the 50 children enrolled in the study 62% were boys and 38% girls. The mean age of the children was 17

months ; 6% were between 1 month to 6 months, 48% were between 6 months to 1 year, 14 patients 28% were between 1 year to 2 year , and 18% between 2 year to 3 years old (Table 1).

Table 1: Distribution of pneumonia according to age.

Age categories	Frequency(n=50)	Percentage(%)
1-6 months	3	6
6-12 months	24	48
1- 2 years	14	28
2- 3 years	9	18
Total	50	100

The seasonal distribution of cases showed that the maximum number of cases were between the month of august to October which was during the rainy season.

Etiology

The cause of pneumonia by Polymerase chain reaction of serum samples was identified in 66% of the cases, they have been shown in Table 2.

Bacterial pathogen as the sole causative agent was identified in 29 cases (58%), viral pathogen in 1 case (2%), atypical pathogen in 1 case (1%), bacterial and atypical pathogen in 1 case (2%) and bacterial and viral co-infection in 1 case (2%). Blood culture and sensitivity did not identify the causative organism in any of the cases. Among the atypical pathogens only Legionella pneumoniae was detected in 4% cases.

Table 2: Etiological agents identified by serum PCR.

Organisms	Frequency	Percentage
Streptococcus pneumoniae	26	52%
Staphylococcus aureus	9	18%
Bordetella pertussis	2	4%
Legionella	2	4%
Human metapneumo virus(HMPV)	2	4%
Coinfection (Streptococcus pneumoniae+ Legionella-1 Staphylococcus aureus + HMPV -1)	2	4%
Unknown	17	34%

Cases of pneumonia due to atypical organisms and other typical organisms could have been missed by serum PCR probably because bacteremia wouldn't have occurred during admission and hence genetic material could not be detected or the organisms were not a part of the panel for 33 respiratory organisms used.

Also these results did not aid in the treatment as the samples for PCR were not processed immediately, as this study was for research purpose.

Comparative clinical and radiological data

From the table 3 it can be seen that there is no statistically significant differences in the clinical and radiological features of the different groups. Chest retractions with

tachypnea was found in 36 cases (72%), belonging to the category of severe pneumonia according to WHO and very severe pneumonia in 6 cases (12%). The mean duration of hospital stay was 3-5 days. There was no mortality in any of the cases.

Table 3: Demographic and clinical characteristics associated with bacterial, atypical, viral, combined or unknown pathogens.

Variable	Bacterial (n=29)	Atypical (n=1)	Viral (n=1)	Combined (n=2)	Unknown (n=17)	p value
Age in months, md(range)	18 (12-24)	12 (12-12)	7 (7-7)	21 (12-30)	12 (8-24)	0.41
Sex, male n (%)	17 (54.8)	1 (3.2)	0	2 (6.5)	11 (3.5)	0.45
Fever duration before admissions, m(sd)	3.7 (1.2)	6	2	5	4.2 (1.7)	0.2
Cough duration before admissions, m(sd)	2.1 (1.9)	6	2	5	4.6 (1.8)	0.48
Total fever Duration, m(sd)	5.7 (1.6)	7	5	5.5 (0.7)	6.9 (2.3)	0.24
Creptitations with wheeze, n (%)	16 (64)	0	1 (4)	2 (8)	6 (24)	0.216
Previous antibiotics, n (%)	19 (63.3)	1 (3.3)	0	2 (6.7)	8 (26.7)	0.28
Chest retractions, n (%)	23 (59.0)	1(100)	1 (2.6)	0	15 (38.5)	0.055
Need for ventilator, n (%)	3 (100)	0	0	0	0	0.68
Elevated Total Count	21 (65.6)	1 (3.1)	1 (3.1)	1 (3.1)	8 (25.0)	0.37
Positive CRP	19 (70.4)	0	1 (3.7)	0	7 (25.9)	0.133
Need for ventilator, n (%)	3 (100)	0	0	0	0	0.68
Duration of hospital stay, m(sd)	5 (2.4)	3	5	5	5.4 (2)	0.88

Table 4: Chest radiograph findings.

Distribution	Number (n=50)	Percentage
Unilateral	12	24%
Bilateral	38	76%
Involvement of only 1 lobe	6	12%
Lower lobe	3	6%
Middle lobe	0	0%
Upper lobe	6	12%
Patterns		
Bronchopneumonia	32	64%
Lobar/airspace pneumonia without effusion	8	16%
Interstitial pneumonia	8	16%
Lobar pneumonia with effusion	2	4%

Table 4 shows that Bronchopneumonia was the commonest radiological finding (64%). Among 2 cases were associated with pleural effusion one was a case of Streptococcus Pneumoniae pneumonia and other coinfection of Staphylococcus aureus with Human metapneumovirus. Xray features of legionella cases were bilateral interstitial infiltrates and bronchopneumonia.

Table 5 shows the clinical features of the two cases with Legionella pneumoniae. Both were 9 month old infants, with clinical features of cough, fever, loose stools,

vomiting, anemia and positive CRP. One case required PICU admission and another cases was co-infection with Streptococcus pneumoniae.

Table 5: Clinical spectrum of the two cases which were positive for legionella.

Case 1	Common Features	Case 2
Male	9 Months	Female
Fever-3 days	Loose stools, vomiting	Fever-5 days
Cough-6 days	Chest retractions	Cough-5 days
CXR-bilateral interstitial infiltrates	Anemia	bronchopneumonia
PICU admission	Positive C-reactive protein (CRP)	Coinfection with s.pneumoniae

DISCUSSION

Legionella pneumonia has not been considered as a prominent pathogen causing pneumonia in children below 3 years.

In this study Legionella Pneumonia was identified in 2 cases(4%), both of them were infants. In this study, both of them were infants. Both of them were healthy subjects.

Fever, cough, loose stools and vomiting were found in both the cases. Both the cases were admitted during August which was during the rainy season which favours the growth of the organism.⁷ One case was sick with respiratory distress, this shows that *Legionella pneumonia* can also cause severe respiratory infections. Among the atypical organisms *Legionella pneumoniae* has a clinical picture similar to *S.pneumoniae* and can cause severe respiratory infection.⁸

Similar to this study, conducted by US Centre of disease control 2008 in Geneva over, 5 year Legionnaires disease in children was reported in 1.7% of reported cases. The incidence in infants is reported to be 0.11 per 100,000.⁹

Appropriate macrolide therapy is critical in maximizing the survival in atypical organism. In the 2006 study conducted by Alexander et al, mortality was 23% for those who received correct therapy and was 70% for those who did not.¹⁰

CONCLUSION

In this study it was found that the prevalence of 4%. *Legionella* is not considered as a common causative agent in children with pneumonia, hence appropriate antibiotic therapy is not initiated. Clinically legionellosis is not easily distinguishable from other bacterial and viral pathogens, hence a high degree of suspicion is required while treating children with pneumonia. If facilities for PCR are available it can be considered. If not adding macrolides along with other antibiotics will benefit the patient outcome and reduce the hospital stay.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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