

Original Research Article

Clinical spectrum of pneumonia in children aged 1 month to 18 years by serum polymerase chain reaction, in a tertiary care centre in Bengaluru, Karnataka, India

Ramya H. S.¹, Anjana Gopi², Vivetha Elango^{1*}, Dona Joseph¹

¹Department of Pediatrics, ²Department of Microbiology, Kempegoda Institute of Medical Sciences, Bengaluru, Karnataka, India

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*Correspondence:

Dr. Vivetha Elango,

E-mail: vivethu@yahoo.co.in

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ABSTRACT

Background: Pneumonia accounts for 15% all deaths in children under 5 years of age, being the single largest infectious cause of deaths in children worldwide according to WHO. Establishing the exact etiological factor is a difficult task, as there are no definite clinical, radiological markers to differentiate between causative organisms. Hence by detecting the genetic material of causative organism by serum PCR (polymerase chain reaction) and correlating it with the clinical and radiological features can help in appropriate use with antibiotics.

Methods: It is an observational study conducted in department of paediatrics KIMS hospital Bangalore, India which included inpatients admitted with clinical and radiological features of pneumonia over a study period from February 2018-April 2019. In this study we excluded immunocompromised children. After obtaining informed written consent, detailed history and clinical examination was done. Investigations including complete hemogram, CXR were done. Under sterile precautions, blood samples for serum PCR and blood culture and sensitivity were obtained. Serum PCR was done for a panel of 33 respiratory pathogens.

Results: Etiological agents were identified in 63% of cases. *Streptococcus pneumoniae* was the most common causative agent being detected in 50.6% of the cases. *Staphylococcus aureus* has been detected to be the second common organism 16%.

Conclusions: In our study Pneumococci was identified in 50.6% of cases. Multiplex serum PCR could be a useful rapid diagnostic tool to identify the etiological agents. Introduction of pneumococcal vaccine worldwide in government immunization schedule, nationwide will help to reduce the disease burden caused by *Streptococcus pneumoniae*.

Keywords: Clinical spectrum, Children, Pneumonia, *Streptococcus pneumoniae*

INTRODUCTION

Pneumonia is the first largest infectious cause of death in children worldwide. According to UNICEF in 2018, Pneumonia killed around 8,00,000 children accounting for 14-15% of deaths in children of under age group of 5 years with India accounting for 1,27,000 of the deaths.¹ The most common causative agent causing pneumonia

depends on the age of the child with viruses are the most common cause of pneumonia in the first two years of life, followed by bacteria in the later ages.²

In children up to 15 years of age, *S. pneumoniae* accounts for 17% -28% of pneumonia cases, with a mortality rate of 26.7 /1000 under 5 cases.³⁻⁵ Establishing the exact etiological agent is difficult as there are no definite

clinical/laboratory/ radiological features that effectively distinguish between the various bacterial and viral agents.

Blood culture and sensitivity is considered as the gold standard in diagnosis. But it is difficult to isolate as >80-90% of children with pneumonia would not have developed bacteremia at the time of hospital admission which is needed for the diagnosis.⁶ Newer molecular diagnostic tests like Polymerase Chain Reaction (PCR) which gives reports in 6-24 hours can help in rapid diagnosis. It has been showed that PCR of serum samples was significantly better than culture in the detection of organisms causing pneumonia with sensitivity of 75-88% and specificity to be 96-100%.^{7,8}

Diagnosis of the etiological agents by multiplex serum PCR will help in rapid detection causative organism which inturn will help in appropriate treatment.

Therefore we conducted a study to identify the etiological and clinical spectrum of pneumonia in children aged 1month to 18 years by serum polymerase chain reaction (PCR).

METHODS

This was a prospective observational study conducted over a period of 15 months from February 2018 to April 2019 on children aged 1 month to 18 years admitted with diagnosis of pneumonia in wards and intensive care unit in the department of Pediatrics in Kempegowda institute of medical sciences. The sample size was 150 children.

Inclusion criteria

Children aged 1 month to 18 years with clinical diagnosis of pneumonia admitted as inpatients in wards and paediatrics intensive care unit (PICU).

Exclusion criteria

Immunocompromised 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. Investigations included complete hemogram, Chest X ray, blood Culture and sensitivity and serum PCR.

The diagnosis of pneumonia in children clinically was made according to the WHO guidelines. That is presence of Cough, Tachypnea /chest retraction, [Criteria for tachypnea according to age: 1month-2months->60/min, 6month to 1 year- > 50/min, 1 year to 5 years- >40 /min , more than 5 years- >30/min, fever >100 degree Fahrenheit, respiratory signs on auscultation and radiological evidence of pneumonia.

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 (real time polymerase chain reaction) was done using a kit to detect 33 respiratory pathogens (Fast track diagnostics kit) by trained professional.

Statistical analysis

Data was analysed on Microsoft excel and analysed using STATA version 13. The p value <0.05 was considered significant.

RESULTS

Patient characteristics

A total of 150 children were enrolled in the study of which 54.7% were boys and 45.3% were girls. 4% of the children were between 1month - 6 months, 14% between 7 months to 1 year, 35.3% between 1 year to 3 years, 26% between 3 years to 5 years, 12% between 6 years to 10 years and 8.7% more than 10 years. The mean age was 4.16 years, and 79% of the children were under 5 years. Maximum number of cases were during the rainy season from July-September 2018 (Figure 1).

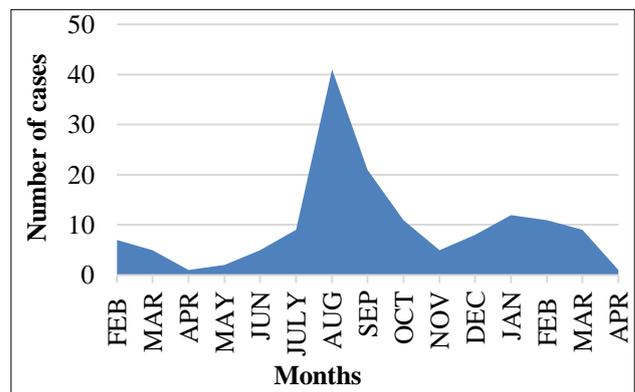


Figure 1: Seasonal distribution of cases with pneumonia.

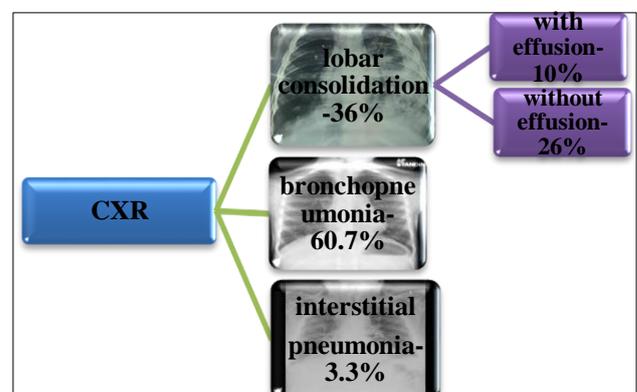


Figure 2: Distribution of chest radiograph findings.

Clinical features

The average total duration of fever was 6.8 days and average duration of cough prior to admission was 5.17 days. 67% of the cases had chest retractions indicating severe pneumonia. Anemia was seen in 56% of cases and protein energy malnutrition was seen in 62% of the cases. Bronchopneumonia was the most common radiological finding (60.7%), followed by lobar consolidation (36%), of which 10% had pleural effusion (Figure 2). The etiological agent was identified in 63% of the cases by serum polymerase chain reaction. Blood culture failed to identify the etiological agent in any of the cases. The

exact distribution of the etiological agents are shown in the above table (Table 1). Single etiological agent was seen in 47.3% of the cases, 12.6% was due to coinfection with 2 organisms and 2.6% due to coinfection of 3 organisms.

About 58% of the cases were due to bacterial etiology, 4% due to coinfection of bacteria and viruses, 1% due to virus. The organism couldn't be identified in 37% of the cases. *Streptococcus pneumoniae* was the most common causative agent accounting for 50.6% of the cases of which 38.6% was due to *S. pneumoniae* alone and 11.4% was due to coinfection with other bacteria or virus.

Table 1: Distribution of etiological agents by serum PCR.

	S.P	S.A	B.P	K.P	L.P	HMPV	HADV	HRV
<i>Streptococcus pneumoniae</i> (S.P)	58	7	2	2	1	0	2	1
<i>Staphylococcus aureus</i> (S.A)	7	10	1 (S.P)	2+1 (HADV)	2 (S.P)	2	1 (K.P)	0
<i>Bordetella pertusis</i> (B.P)	2+1 (S.A)	1 (S.P)	1	0	0	0	0	0
<i>Legionella pneumoniae</i> (L.P)	1+2 (S.A)	2 (S.P)	0	0	1	0	0	0
<i>Klebsiella pneumoniae</i> (K.P)	2	2	0	0	0	0	0	0
Human metapneumo virus (HMPV)	0	2	0	0	0	1	0	0
Human Adeno virus (HADV)	2	1 (K.P)	0	0	0	0	0	0
Human Reo virus (HRV)	1	0	0	0	0	0	0	0
Total	76 (50.6%)	25 (16%)	4 (2.6%)	5 (3.3%)	4 (2.6%)	3 (2%)	3 (2%)	1 (0.6%)

Table 2: Comparison of clinical and laboratory parameters.

Variables	Bacteria alone	Bacteria+ Viral	Virus alone	Unknown	Total	p value
Age in years	4.61±3.91	3.83±1.47	1.00±0.00	3.56±2.43	4.16±3.38	0.237
Hemoglobin (g/dl)	10.7±1.7	10.23±0.54	6.70±0.00	10.49±1.64	10.63±1.72	0.080+
Total count (mm ³)	14350.57±9076.17	13130±7422.63	7780.00±0	12023.04±6262.39	13389.00±8082.48	0.348
CRP (>0.5)	68 (78.2%)	5 (83.3%)	0	43 (76.8%)	116 (77.3%)	0.444
ESR (mm/hr)	27.9±23.24	66.83±51.93	12.00±0.0	24.66±21.33	28.19±25.23	0.001*
Fever before admission (days)	5.1±3.14	4.67±1.86	2.00±0.00	4.32±1.85	4.78±2.70	0.259
Duration of fever (days)	7.4±4.27	6.67±2.73	3.00±0.00	5.96±2.04	6.85±3.60	0.063+
Cough (days)	5.8±3.46	4.67±1.86	2.00±0.00	4.27±2.00	5.17±3.02	0.014*
PICU	35 (40.2%)	2 (33.3%)	0	6 (10.7%)	43 (40.2%)	<0.001*
Duration of hospital stay (days)	5.5±2.31	5.00±2.61	3.00±0.00	4.36±1.31	5.05±2.07	0.007*

The above table shows the laboratory and clinical profile of the various groups (Table 2). Though p value is

significant in terms of ESR, CRP, duration of fever and PICU stay but this cannot be considered as the group with

virus has only one case and hence is not comparable to other groups.

DISCUSSION

In this study etiological agent was identified in 63% of the cases. The British thoracic guidelines for management of community acquired pneumonia in children in 2011 states that, with the development of newer molecular diagnostic techniques like PCR the yield of detecting the causative organism of pneumonia can be as high as 65-86% in high resource settings.⁹ The variation in the detection rates depend upon parameters like inclusion criteria, age group, criteria for admission, geographic location, diagnostic modalities and vaccination status.

The identification of organisms from plasma is better than nasopharyngeal samples as most of the common respiratory pathogens like *Streptococcus pneumoniae*, *Hemophilus influenza*, *Staphylococcus aureus* are commensals of the upper respiratory tract.¹⁰

The main causative agent in our study was *S. pneumoniae* being responsible for 50.6% of the cases, either alone or as a coinfection. The next common pathogen was *S. aureus* responsible for 16% of the cases. This is higher in comparison to study done by Bjarson et al, in Texas which showed prevalence of *S. pneumoniae* to be 20%.¹¹ This high prevalence of *Streptococcus pneumoniae* is probably because pneumococcal vaccination is not a part of the national immunisation programme in the state and none of the children had received the vaccination.

Pleural effusion in chest radiograph was present in 10% (15/150) of the cases. About 60% of the cases with pleural effusion were due to *Streptococcus pneumoniae*, 33% were due to *Staphylococcus aureus*. Only 4% (6/150) of the cases were complicated with empyema and needed surgery. 3 of the cases were due to *S.pneumoniae* and 2 cases were due to *S. aureus*

In a study done by V. C vikovic spik in Slovenia showed that RT-PCR was significantly better than culture in the detection of organisms causing pneumonia. This study showed that in the detection of *Streptococcus pneumoniae* blood culture detected only 5% of cases as compared to PCR of plasma samples which detected 27% of the cases.⁷

Statistically 53% of the cases had received antibiotics prior to admission. Among the 53% of the cases, in 58/70 (82%) of the cases the etiological agent was identified. This shows that prior antibiotic administration does not affect the result of PCR.

Hence PCR from serum samples would be better in diagnosing the etiological agent with pneumonia rather than nasopharyngeal samples as it rules out colonization. Rapid diagnosis of the various etiological agents by multiplex PCR can help in judicious use of antibiotics,

which can help in reducing the rate of antimicrobial resistance.

CONCLUSION

This was a prospective observational study to know the clinical spectrum of pneumonia in children with etiological diagnosis by serum PCR. The etiological agent was identified in 63% of the cases. *Streptococcus pneumoniae* was the most common causative agent followed by *Staphylococcus aureus*. Multiplex serum PCR could be a useful rapid diagnostic tool to identify the etiological agents.

All our patients belonged to lower and middle socioeconomic status, according to modified kuppuswamy classification and most of the children were anemic, malnourished and none of the patients had received vaccination against pneumococci .Hence awareness has to be created regarding the importance of nutrition, balanced diet and hygienic measures. Introduction of pneumococcal vaccine worldwide in government immunization schedule, nationwide will help to reduce the disease burden caused by *Streptococcus pneumoniae*.

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Conflict of interest: None declared

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

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