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CLINICAL PATTERNS, RISK FACTORS, AND EARLY DIAGNOSIS OF PNEUMONIA CAUSED BY ATYPICAL BACTERIA IN CHILDREN

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ABSTRACT **Background:** Community-acquired pneumonia is a leading cause of mortality in developing countries, particularly in children under 5. Atypical pneumonia, caused by viruses and bacteria like Mycoplasma pneumoniae, Legionella pneumophila, Chlamydia pneumoniae, and Coxiella burnetti, is a significant cause of this disease. The study aims to identify the clinical characteristics and risk factors of Atypical Community-Acquired Pneumonia and develop a cost-effective, rapid multiplex PCR for rapid diagnostic testing. **Objectives:** 1. To determine the clinical pattern and risk factors among children acquiring Atypical Pneumonia. 2. To develop a cost-effective, rapid multiplex PCR-based assay for detecting respiratory bacterial pathogens causing Atypical Pneumonia in children. **Methods:** The study involved 96 children aged 1 month to 18 years admitted to Tertiary care hospitals with severe pneumonia. Basic demographic details, clinical features, and risk factors were obtained from parents using a standard questionnaire. RT-PCR was used to detect bacterial pathogens, both atypical and Typical bacteria. **Results:** Mycoplasma pneumoniae was the most common infection at 43.8%, followed by Chlamydia at 39.6% and Legionella at 38.5%. Passive smoke exposure and overcrowding were risk factors for pneumonia caused by atypical bacteria. Clinical symptoms related to atypical bacteria in children were dry cough, wheezing, diarrhea, vomiting, and rashes. The most prevalent comorbidity among children hospitalized with pneumonia was anemia (32.2%), followed by malnutrition (17%). 72% of children with atypical bacteria had chest X-ray findings indicating Bronchopneumonia, while 57% with typical bacteria had homogenous consolidation indicating lobar pneumonia pattern.

KEYWORDS : Atypical bacteria; Pneumonia; Children; Etiology; Risk factor

INTRODUCTION

Pneumonia, also known as the silent killer, is the leading cause of infant deaths globally, with India accounting for 26% of the global pneumonia cases between 2019 and 2021, with one child being afflicted every second [(1)]. According to the Health Management Information System (HMIS), there were a total of 473,780 documented cases of childhood pneumonia in the year 2022-23. Among these instances, there were 11,497 deaths in babies and 4,571 deaths in children under the age of 5 due to pneumonia [(2)]. The disease is characterized by lung inflammation, with bacterial infections, such as Streptococcus pneumoniae, Staphylococcus aureus, and Haemophilus influenzae, being the primary pathogens. Viruses account for 90% of pneumonia cases in children during the first two years of life [(3)].

As individuals age, the likelihood of developing pneumonia decreases, but bacterial infections caused by Mycoplasma pneumoniae, Legionella pneumophila, and Chlamydia pneumoniae contribute to an increase in atypical pneumonia. Viruses are responsible for only half of the cases of pneumonia in school-aged children. Mycoplasma pneumoniae is the second most prevalent causative agent, behind Streptococcus pneumoniae, and is the primary pathogen seen in early adolescents, accounting for up to 50% of cases. Chlamydia pneumoniae is the second most prevalent pathogen in young adolescents, following Mycoplasma. It is responsible for approximately one-third of all occurrences of pneumonia [(2)].

The inflammation of lung parenchyma characterizes pneumonia. Community-acquired pneumonia is categorized into two types: Typical and Atypical Pneumonia. Atypical pneumonia is named due to its distinguishing characteristics, such as clinical features, chest X-ray findings, total leucocyte count, and lack of susceptibility to beta-lactam antibiotics. Mycoplasma pneumoniae affects school-aged individuals and young adults, with outbreaks typically occurring during winter. Chlamydia pneumoniae has a similar clinical presentation but higher CRP levels. Legionella pneumophila impacts those mainly with risk factors like prolonged hospital stay, diabetes, immunosuppression, and malignancy.

METHODOLOGY

Sample Size: 96 children admitted to MS Ramaiah hospitals, Bengaluru for Severe Pneumonia between the age group 1 month to 18 years from August 2022 to January 2024 who fulfilled the inclusion criteria were enrolled in the study.

Study Design: Cross-Sectional Study

Inclusion Criteria:

All children aged 1 month to 18 years who were diagnosed with Severe Pneumonia as per IMNCI Guidelines.

Exclusion Criteria:

1) The child who had taken three or more days of antibiotics for the present episode
2) Chemical Pneumonitis
3) Aspiration Pneumonia (secondary to GERD and in patients with Cerebral Palsy)
4) Hypostatic Pneumonia

Procedure

The study enrolled 96 children admitted to MS Ramaiah Hospital with Severe Pneumonia, assessing their clinical manifestations and risk factors. Data was collected through a standardized questionnaire and analyzed using Complete blood count, C reactive protein, Blood culture, and Chest X-ray. Sputum/gastric aspirate samples were collected and processed for RT-PCR to detect atypical and typical bacteria causing pneumonia. DNA extraction was performed using a Qiagen DNA mini kit, and atypical pneumonia was confirmed among children diagnosed with these etiological agents. The data was analyzed using SPSS 22 version software. Categorical data was represented as frequencies and proportions, while qualitative data was represented using chi-square or Fischer's exact. Continuous data was represented as mean and standard deviation and an independent t-test was used to identify the mean difference between two quantitative variables. A p value of <0.05 was considered statistically significant after assuming all the rules of statistical tests.

RESULTS

Mycoplasma pneumoniae was the most common infection at 43.8%, followed by Chlamydia at 39.6% and Legionella at 38.5%. Haemophilus influenzae was found in 19.8% and Streptococcus pneumonia 14.6% (Figure 1). Mycoplasma pneumoniae was most common in toddlers, Legionella in newborns, and Streptococcus in adolescents.

Table 1 Demographic Characteristics Of Hospitalized Children With Severe Pneumonia

Variables	Measure
Number of children	96
Age (in years) Infants Toddler Preschool School going Adolescent	36(7 - 96) 34 (45.4) 13 (13.5) 17 (17.7) 17 (17.7) 15 (15.6)
Gender Male Female	 57 (59.4) 39 (40.6)
Incident Season Monsoon (June, July, August, September) Autumn (October, November) Winter (December, January, February) Summer (March, April, May)	 7 (7.3) 14 (14.6) 58 (60.4) 17 (17.7)

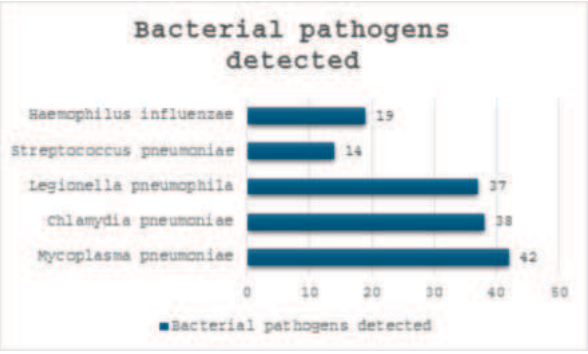

Figure 1 - Bar Chart Representing The Distribution Of Bacterial Pathogens In The Study Population(N=96)

Atypical bacteria were more prevalent in children with a running nose, vomiting, diarrhea, chest pain, and wheezing. The cold in the form of a running nose was more prevalent in children with atypical bacteria. Mycoplasma was found in 60.5% of cases where individuals were exposed to passive smoke, 59% of cases with overcrowding, and 100% of cases where the child stayed at a hostel. Passive smoking and overcrowding had strong statistical significance, with p-values of 0.004 and 0.021, respectively. Mycoplasma was present in all individuals with a history of hostel stay, although this finding did not reach statistical significance. The odds ratio for mycoplasma infection was 2.88 for overcrowding and 3.54 for passive smoking exposure, with overcrowding significantly amplifying the likelihood of infections by a factor of 2.88. Winter had the most children hospitalized for pneumonia in the current study of all bacterial infections, followed by summer, autumn, and monsoon.

72% of children with atypical bacteria had chest X-ray findings suggestive of Bronchopneumonia while 57% with typical bacteria had homogenous consolidation suggestive of lobar pneumonia pattern (Figure 2). Out of the children diagnosed with typical bacteria, 57.1% (n=16) had Lobar pneumonia on the chest X-ray, with a p-value of 0.009 indicating statistical significance. On the other hand, 72% (n=49) of the children diagnosed with atypical bacteria had Bronchopneumonia on the chest X-ray, although the p-value of 0.098 was not statistically significant(Table 2)

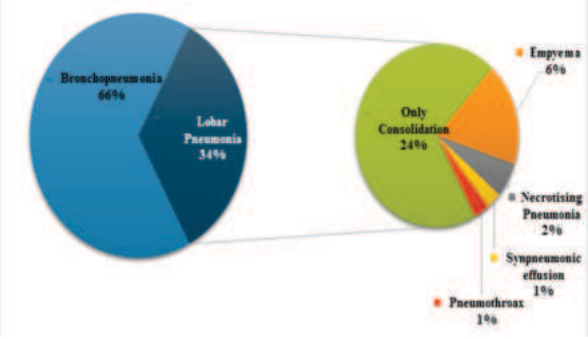

Figure 2 - Pie Of Pie Chart Showing The Chest X-ray Findings In The Study Population(n=96)

Table 2 – Correlation Of Chest X-ray With Bacterial Pathogen Detected

Bacterial pathogen detected	Bronchopneumonia on Chest X-ray	Lobar Pneumonia on Chest X-ray	P value
Typical bacteria	12	16	0.009
Atypical bacteria	49	15	0.098
Co-infection	11	9	0.302

In children hospitalized with pneumonia, children with comorbidities were higher than the ones without any underlying comorbidity. Anemia was the most prevalent medical condition observed in 19.8% (n=19) of children who were hospitalized with Pneumonia. Undernutrition was the second most prevalent underlying condition, accounting for 10.4% (n=10) of cases. This was followed by 15.3% (n=9) each in children with a history of preterm birth and neurological disease. Among the children hospitalized with pneumonia, 6.3% (n=6) had congenital heart disease, specifically ventricular septal defect (n=5) and atrial septal defect (n=1).

The median duration of hospital stay was 8 days. Respiratory support was applied for 84.4 %(n=81), including invasive mechanical ventilation for 30.2%(n=29), and 81.2%(n=78) of patients were managed in the intensive care unit. The median duration of PICU stay was 5 days. Mortality was noted in 6.3%(n=6) cases.

Anemia also correlated with the severity of Pneumonia in the form of higher duration of oxygen support and PICU stay.

DISCUSSION

Pneumonia can be caused by various pathogens, including typical and atypical bacteria and viruses. Accurate and fast detection of the etiological agent is critical for timely patient management, reduction of hospital stay, guiding the usage of antibiotics, and preventing antibiotic resistance. This study was conducted to determine clinical patterns, risk factors associated with pneumonia caused by atypical bacteria, and its early diagnosis using RT-PCR.

Bacterial pathogens were identified in 81.3% of cases of community-acquired pneumonia in the study population. Mycoplasma pneumoniae was the most detected bacteria, accounting for 42 cases (43.8%). The prevalence of bacterial infections was highest in the infantile age group (n=51), followed by the school-going age group (n=31). Legionella was the most common pathogen found in the group of infants, being detected in 68% of them, with 23 cases of co-detections. Mycoplasma pneumoniae was the predominant pathogen in both toddlers and the preschool age group. Chlamydia pneumoniae was found to be 70.6%, with 22 cases of co-infection with other pathogens. The prevalence of Mycoplasma pneumoniae and Chlamydia pneumoniae was evenly distributed across adolescents, with a 40% prevalence for each bacterium. In hospitalized children aged 1 to 3 years, the prevalence of Mycoplasma pneumoniae was higher at 61% (8 out of 13), which aligns with the findings of Oumei et al. Their analysis indicated that 25.2% (378 out of 1500) of children under 5 years old tested positive for Mycoplasma [4].

The winter season had the highest frequency of admission with community-acquired pneumonia, accounting for 60.4% of cases. Mycoplasma pneumoniae and Chlamydia pneumoniae were frequently found in children who were exposed to passive smoking and lived in overcrowded families. A case-control study conducted by Yun et al from 2015 to 2018 also observed that second-hand smoking exposure was linked to community-acquired pneumonia [5].

The most common presenting clinical features included fever, cold in the form of running nose, fast breathing and vomiting. Fever, cough, headache, Myalgia, sore throat, hoarseness of voice and presence of skin rashes in the form of maculopapular rashes were distributed almost equally among both typical and atypical bacteria. Children diagnosed with atypical bacteria had a cold(82.7% vs 70%), vomiting(62% vs 43.3%), diarrhea(22.4% vs 13.3%), and wheezing(22.4% vs 10%) as predominantly associated complaints when compared with typical bacteria. Pleuritic type of chest pain was more seen in association with typical bacteria(10% vs 1.7%). Cold and dry cough were found to be higher in those children detected with Mycoplasma pneumoniae which was statistically significant. This was in concordance with the study conducted by Elkolaly et al, which showed that 79.5% of individuals diagnosed with Mycoplasma pneumoniae had a dry cough, whereas only 20.5% had a productive cough [6].

The presence of concurrent bacterial infection was observed to exacerbate the intensity of pneumonia. 54%(n=37 out of 68) of the children with atypical pathogens detected required oxygen support in the form of HFNC and ventilator, which was lower than the demand in children with co-infection, which was observed to be 70%(n=14 out of 20). The mortality rate in children who tested positive for solely atypical bacterial pathogens was 5.4%(n=4 out of 68), while children with co-infections had a mortality rate of 10%(n=2 out of 20). This finding is in line with the study conducted by Huong et al, which similarly observed that co-infections can lead to severe pneumonia [7].

Children with underlying medical issues required ventilator support at a much higher rate (40.7% vs 13.5%) compared to healthy children. This study was comparable to the research conducted by Suh et al., which similarly demonstrated that children with a pre-existing medical problem required respiratory assistance (82.6%) and intensive care unit (ICU) treatment (18.1%) more frequently than healthy children.[53] This was also reported in a systematic review done by Wilkes et al., which demonstrated malnutrition, the presence of anemia, and the existence of an underlying chronic condition exacerbated the severity of the disease and mortality [8].

CONCLUSION

Atypical bacteria play an important role as etiological agents in pneumonia in children. Demographics, risk factors, and clinical patterns can be used to suspect Pneumonia caused by atypical bacteria. Confirmation can be done by RT-PCR, which is useful for rapid detection of atypical bacteria. Early detection and appropriate treatment are crucial in preventing complications and reducing mortality rates in paediatric pneumonia cases. It can also guide us in antibiotic usage in children and thus prevent antibiotic resistance.

Limitation

The Small sample size and urban population of the study population, potentially limiting generalizability and the study also excluded cases of Severe Pneumonia, potentially missing atypical pneumonia cases.

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