Occurrence and clinicolaboratory profile of mycoplasma infection in children hospitalized with lower respiratory tract infection – A prospective study

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ABSTRACT

Background: *Mycoplasma pneumoniae* (MP) is a common cause of lower respiratory tract infection (LRTI) in children between 5 and 15 years of age. The clinical and laboratory findings are usually non-specific and extrapulmonary manifestations can be devastating. **Objectives:** The objectives of the study were to study the occurrence, clinical features, and laboratory profile of MP infection in children presenting with LRTI to a tertiary care hospital. **Materials and Methods:** This was a hospital-based prospective study done in the inpatient department of pediatrics of a tertiary care teaching hospital in South India from November 2014 to April 2016. Children aged 1 month–18 years, admitted with LRTI were included in the study. A pre-tested semi-structured questionnaire was used to collect history. MP infection was confirmed using mycoplasma immunoglobulin M enzyme-linked immunosorbent assay. Clinical and laboratory findings were compared between mycoplasma positive and negative groups. **Results:** Among a total of 268 children with LRTI, MP infection was diagnosed in 41 children (15.3%). The peak occurrence was in 9–12 years (30%) followed by 6–9 years (25.4%) and 3–6 years (21.7%) age group. MP infection was more common among malnourished (29.4%) than well-nourished children (13.1%). None of the clinical and laboratory parameters were specific for the infection. Extrapulmonary manifestations were not seen in our study. **Conclusion:** MP infection can occur even in children in 3–6 years age group. The clinical and laboratory findings in MP infection are non-specific necessitating empirical treatment with macrolide antibiotics in children more than 3 years of age. It is more common among malnourished children and extrapulmonary manifestations are rare in our population.

Key words: *Lower respiratory tract infection, Mycoplasma immunoglobulin M enzyme-linked immunosorbent assay, Mycoplasma infection*

Pneumonia, defined as the inflammation of lung parenchyma, is the leading infectious cause of death globally among children younger than 5 years. Pneumonia accounted for 15% of all deaths of children under 5 years of age in 2017 [1]. Viruses, atypical microorganisms, and bacteria cause the vast majority of childhood pneumonia [2-4]. It can be difficult to identify whether the cause of pneumonia in a given patient is bacterial or non-bacterial [5]. *Mycoplasma Pneumoniae* (MP) accounts for 20–40% of all community acquired pneumonia (CAP) among children and adults. Spread is largely through school contacts. Secondary attack rate among household members is 40% [6].

MP typically presents with sore throat, hoarseness of voice, and fever with dyspnea occurring in severe cases. Symptoms can persist for weeks to months. Children under 5 years of age are most likely to manifest coryza and wheezing, and progression to pneumonia is relatively uncommon, whereas older children aged 5–15 years are more likely to develop bronchopneumonia in one or more lobes. Chest auscultation may show scattered or localized rhonchi [7,8]. Extrapulmonary manifestations occur in 25% of children with MP infection. They may occur from 3 days of onset of illness to 3 weeks after resolution.

The most common and life threatening are the neurological manifestations such as meningoencephalitis and Guillain–Barré syndrome [9], followed by Stevens–Johnson syndrome, erythema multiforme, and toxic epidermal necrolysis [10]. Hematological manifestations include autoimmune hemolytic anemia, autoimmune thrombocytopenia, and disseminated intravascular coagulation. Clinical diagnosis of MP infection is difficult due to non-specific signs and symptoms. The most common finding on chest X-ray is an interstitial infiltrate followed by alveolar infiltrates and sometimes pleural effusion [11]. Computed tomography chest may show bronchial wall thickening [12].

Cultures require specialized techniques and are positive in only 30–60% [13]. Therefore, serological testing is the most common means of diagnosing MP infection. The "gold standard" is a demonstration of a 4-fold rise in antibody titers [14]. Cold agglutinins and complement fixation tests have poor sensitivity

and specificity [15,16]. Enzyme immunoassays on paired samples have high sensitivity (92%) and specificity (95%) and are comparable to polymerase chain reaction (PCR). However, it may be positive in asymptomatic carriers [17]. Hence, a combination of PCR and immunoglobulin M (IgM) enzyme-linked immunosorbent assay (ELISA) is considered to be a useful approach in children [18].

Although fluoroquinolones and tetracyclines are effective against MP, macrolides, especially azithromycin, are the preferred antibiotic in children [19]. Macrolide resistance has been noted recently, but treatment failure is unlikely even in macrolide-resistant infections [20]. This study was done to determine the occurrence, clinical features, and laboratory profile of MP infection in children presenting with lower respiratory tract infection (LRTI).

MATERIALS AND METHODS

This hospital-based descriptive study was done in the department of pediatrics of a tertiary care hospital in South India. Institutional Ethical Committee clearance was taken before the commencement of the study. The study was conducted from November 2014 to April 2016. The participants consisted of children aged 1 month–18 years, admitted with LRTI. Seriously ill patients requiring mechanical ventilation, children whose parents did not give consent or were unwilling for mycoplasma IgM antibody testing or children who were known cases of bronchial asthma were excluded from the study. Informed consent was obtained from the parents and assent of children was taken before the study.

Sampling technique used was non-probability purposive sampling technique. History was collected using a pre-tested semi-structured questionnaire. After a thorough physical examination, participants were subjected to routine laboratory investigations. Blood sample for mycoplasma IgM ELISA was collected in the 2nd week of illness. LRTI was considered in the presence of fever along with cough and either of the following; fast breathing, respiratory distress (chest retractions, grunting, and flaring of ala nasi), and crepitations or wheeze. MP infection was considered in children tested positive for mycoplasma IgM. Based on the WHO classification, stunting was defined as height for age <−2 standard deviation (SD) and wasting as a weight for height <−2SD.

The data collected were compiled in MS Excel and analyzed using SPSS.V.16.0. Continuous variables were expressed in the mean and SD, categorical data are expressed in number and percentage. Chi-square test was applied to test the significance of association and $p<0.05$ was considered as statistically significant.

RESULTS

A total of 268 children participated in the study. There was a preponderance of males with 151 males (56.3%) and 117 females (43.7%); although, the difference was not statistically significant, as shown in Table 1.

The clinical features, nutritional status, and chest X-ray findings are discussed in Table 2. MP infection was present in 41 (15.3%) children out of 268 children with LRTI. The occurrence of MP infection was minimal (2.15%) in children <3 years. Among children with MP infection, 17 (41.5%) were female and 24 (58.5%) were male. This difference was not statistically significant (Table 2).

All children had a fever and cough. The average duration of fever was 3.5 days (range: 1–10 days). MP infection was strongly associated with fever >3 days duration (p=0.025). Average duration of cough was 3.16 days (range: 1–12 days). No significant association was noticed between cough and MP infection. Although wheezing was found to be more common in MP-positive group, difference was not statistically significant (p=0.07). In the study population, malnutrition as per the WHO classification was seen in 17.5%. Wasting was observed in 15.2% and stunting in 2.2% of children. A greater percentage of malnourished children (29.4%) suffered from MP infection compared to those with normal nutrition (13.1%). This association was found to be statistically significant (p=0.03) (Table 2).

Chest X-ray abnormalities were seen in 69.4% of the study population (Table 2). There was no statistically significant difference in X-ray patterns between MP-positive and negative groups. The findings on complete blood count also showed no significant association with MP infection.

DISCUSSION

The occurrence of MP infection among children with LRTI was 15.3% in our study. There was no statistically significant difference in occurrence between males (56.3%) and females (43.7%). Kashyap *et al*. [21] reported an incidence rate of 24% among 75 children with CAP, using a combination of culture/serology and PCR. Shenoy *et al*. [22] used mycoplasma IgM ELISA and reported an incidence of 24% among children hospitalized for pneumonia. Chaudhry *et al*. [23] reported 27.4% MP seropositivity among children with CAP. None of the earlier studies have documented a gender preference.

Detection of IgM in a single serum sample for diagnosis of MP infection is considered significant in children who had fewer opportunities for repeated exposure [24]. Nadal *et al*. compared mycoplasma IgM serology with paired serology and found its sensitivity and specificity to be 78.1% and 87.1%, respectively [25]. Chang *et al*. used reverse transcription PCR as a standard and found sensitivity and specificity of IgM serology to be 62.2% and 85.5%, respectively [26]. In our study, mycoplasma IgM ELISA was positive in 41 children (15.3%). As sensitivity of the test is determined by timing of specimen collection, we had ensured that sera were taken in the 2nd week of illness. However, as shown in the study by Kashyap *et al*., a combination of paired serum samples for IgM and IgG in combination with PCR is ideal [21]. However, this was not possible in our study due to financial constraints.

In our study, the frequency of MP infection was the highest in 9–12 years (30%) followed by 6–9 years (25.4%) and 3–6 years (21.7%) age group and the difference was significant (p=0.001). The significant finding here is the high frequency of MP infection

Table 1: Age and sex distribution of the study population

Character	Number (%)	MP negative (%)	MP positive (%)	p value
Age group (years)				
Up to 3	93 (34.7)	91 (97.8)	2 (2.15)	0.001
3.1–6	69 (25.7)	54 (78.3)	15 (21.7)	
6.1–9	63 (23.5)	47 (74.6)	16 (25.4)	
9.1–12	20 (7.46)	14 (70)	6 (30)	
>12	23 (8.58)	21 (91.3)	2 (8.7)	
Total	268 (100)	227 (84.7)	41 (15.3)	
Age (months)*		59.9±48.3	86.9±38.1	0.001
Sex				
Female	117 (43.6)	100 (85.5)	17 (14.5)	0.75
Male	151 (56.34)	127 (84.1)	24 (15.9)	
Total	268 (100)	227 (84.7)	41 (15.3)	

*Independent t-test. MP: *Mycoplasma pneumoniae*

Table 2: Clinical features, nutritional status, and chest X-ray findings in the study population

Parameters	MP negative, n (%)	MP positive, n (%)	Total, n (%)	p value
Fever (days)				
1–3	142 (88.7)	18 (11.25)	160 (60)	χ^2=5.022
>3	85 (78.7)	23 (21.3)	108 (40)	p=0.025
Cough (days)				
1–3	166 (84.7)	30 (15.3)	196 (73.1)	χ^2=0
>3	61 (84.7)	11 (15.3)	72 (26.9)	p=0.99
Respiratory distress				
Present	132 (87.4)	19 (12.6)	151 (56.34)	χ^2=1.96
Absent	95 (81.2)	22 (18.8)	117 (43.65)	p=0.16
Wheezing				
Present	184 (82.9)	38 (17.1)	222 (82.8)	χ^2=3.30
Absent	43 (93.5)	3 (6.5)	46 (17.2)	p=0.07
Nutritional status				
No malnutrition	192 (86.9)	29 (13.1)	221 (82.5)	χ^2=4.61
Malnutrition	35 (74.47)	12 (25.5)	47 (17.5)	p=0.03
Chest X-ray findings*				
Normal	73 (89)	9 (11)	82 (30.6)	χ^2=1.7039
Lobar consolidation	109 (77.3)	32 (22.7)	141 (52.6)	p=0.1917
Hyperinflation	37 (100)	0 (0)	37 (13.8)	
Patchy infiltration	8 (100)	0 (0)	8 (3)	
Total	227 (84.7)	41 (15.3)	268 (100)	

*Pooled Chi-square test is applied. MP: *Mycoplasma pneumoniae*

in the 3–6 years age group because MP infection is considered to rarely affect children <5 years of age [6]. In a study by Shenoy *et al*., the highest incidence was in the 2–5 years and 5–10 years age group [22]. This finding is also supported by other studies from the Western world [27]. However, Kashyap *et al*. did not find a significant difference in incidence of <5 years and >5 years age group [21].

In our study, none of the clinical signs and symptoms showed any significant association with MP infection, though wheezing was found to be more common in the MP-positive group. One significant finding in our study was the association of malnutrition with MP infection. A greater percentage of malnourished children suffered from MP infection compared to those with normal nutrition (p=0.03). Extrapulmonary complications were not seen in our study. Other studies have reported 25% incidence of extrapulmonary manifestations [7,9,10].

In our study, the only X-ray finding observed in MP infection was lobar consolidation (78%). Hyperinflation and patchy infiltration were seen only in the MP-negative group. There was no significant association between X-ray findings and MP infection. In the study by Puljiz *et al*., chest X-ray abnormalities included interstitial infiltrate (90.48%), alveolar infiltrates (8.84%), and pleural effusion (8.84%) [11]. In the study by Kashyap *et al*., the X-ray findings were infiltrates (34.67%), hyperinflation

(26.67%), consolidation (25.33%), and bronchopneumonia (17.33%) [21]. Blood counts showed no significant difference between the MP-positive and negative groups.

Our study has several limitations. Accurate diagnosis of MP infection requires a combination of serology and PCR. However, PCR was not used due to financial constraints. Attempt could have been made to isolate other etiological agents as MP can coinfect with other organisms.

CONCLUSION

MP infection is traditionally considered to be rare in children <5 years of age. However, our study showed a significant occurrence of MP infection in the 3–6 years age group. The clinical, radiological, and hematological findings in MP infection are non-specific necessitating empirical treatment with macrolide antibiotics in children more than 3 years of age.

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