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Original article

# The incidence of *Mycoplasma pneumoniae* in community acquired pneumonia among children: One centre study

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**ABSTRACT**

**Background:** *Mycoplasma pneumonia*e (*M. pneumonia*e) is an important cause of pediatric community acquired pneumonia (CAP). **Aim**: The aim of this study was to determine the incidence of *M. pneumonia*e in pediatric community acquired pneumonia and to determine the most frequent clinical findings of *M. pneumonia*e CAP. **Methods:** A total of 83 pediatric CAP patients were subjected to history taking, clinical examination, chest X-ray, CBC, CRP and serum antimycoplasma pneumonia IgM and IgA by ELISA. **Results:** Twenty-nine (34.9%) out of 83 patients were positive for *M. pneumonia*e Ig M while 2 (3.4%) patients were positive for *M. pneumonia*e IgA. There was more infection (54%) in age group (5-9 years; *p value <0.001*). *Mycoplasma pneumoniae* pneumonia infected patients were presented with cough (29/29; 100%), fever (29/29; 100%), malaise (18/29; 43.8%), headache (16/29; 33.8%), wheeze (21/29; 52.5%), chest discomfort (13/29; 44.8%), sore throat (13/29; 46.4%), rhinitis (8/29; 27.5%) and pharyngitis (6/29; 24%). The most frequent X ray findings in *M. pneumoniae* pneumonia was air space pneumonia (71%); segmental more than lobar form (*p-value < 0.0001*). **Conclusions:** The findings of this study highlight the clinical significance of *M pneumoniae* in pediatric community acquired pneumonia.

## Introduction

*Mycoplasma pneumonia*e (*M. pneumonia*e) is a slowly growing, pleomorphic, non-motile bacteria that lacks cell wall. It was first identified by **Eaton et al.** then cultured by **Chanock et al.** and eventually classified as *M. pneumonia* in 1963 [1]**.** It can cause many clinical manifestations of variable severity [2]. It can cause upper respiratory congestion, pharyngitis or trachea-bronchitis [3]. It also can cause pneumonia and extra-pulmonary manifestations as encephalitis, or Stevens-Johnson syndrome [4-6]. The infection occurs in all age groups, but older children and young adults are affected at a higher frequency than other age groups [7].

Community acquired pneumonia (CAP) is one of the most common serious infections in children and an important cause of death in children under 5 years old in developing countries and in adults over 65 in developed countries [8]. In children, *M. pneumoniae* pneumonia causes up to 40% of (CAP) and as many as 18% of cases require hospitalization [9]. Epidemics of *M. pneumonia* infections can occur in the community, or in closed settings such as military persons,

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schools and facilities for the mentally disabled personnel [10]. The aim of this study was to determine the incidence of *M. pneumoniae* in pediatric community acquired pneumonia and to determine the most frequent clinical findings of *M. pneumonia*e CAP.

**Patients and Methods**

The present study is cross sectional study done according to the international guidelines of Strengthening the Reporting for Observational Studies in Epidemiology (STROBE) [11]. It was done in Pediatric and Medical microbiology and Immunology Departments, Faculty of Medicine, Zagazig University. It included 83 children with ages ranging 2 to 12 years old attending the Zagazig University Pediatric Hospital with acute pneumonia in the period from January to July 2013. The study was approved by the research and ethical committees of the Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. An informed consent was taken from parents or guardians of study subjects.

**Inclusion criteria**

Age between 2-12 years, both sexes, any child with community acquired pneumonia, defined as acute infection of the pulmonary parenchyma in a previously health child who acquired the infection in the community [12].

**Exclusion criteria**

Age < 2 years or > 12 years, children with evidence of *Streptococcus pneumonia*e or *Streptococcus pyogenes* infection, chronic respiratory illness as cystic fibrosis, children with other underlying chronic disease that predispose to pneumonia, patients with nosocomial infection and children recently received antibiotics active against *M. pneumoniae*

All patients were subjected to history taking stressing on family history, onset, course, duration, cough, rhinitis, sore throat, malaise, headache, chest discomfort, nocturnal symptoms, history of asthma, previous medications. All children were also subjected to clinical examination for fever, heart rate, pharyngitis, respiratory distress signs (respiratory rate, chest retractions, and cyanosis), degree of air entry, chest wheezes. Investigations done were chest X-ray, complete blood count (CBC), C-reactive protein (CRP). Serum anti-*Mycoplasma pneumoniae* IgM and IgA were determined by ELISA using commercial kit REIDASCREEN (Biopharm, Darmstadt, Germany) *M. pneumoniae* IgM and IgA imported by Clinilab, Cairo, Egypt.

**Specimen collection**

Five ml of blood were withdrawn by venipuncture from each patient. Two ml of them were mixed with ethylenediamine tetraacetic acid (EDITA) for CBC determination and 3 ml of collected blood are left to coagulate at 37◦C then, centrifuged for 10 minutes and serum separated for CRP and ELISA.

**Serum anti-*Mycoplasma pneumoniae* ELISA** [13]: Serum anti-*Mycoplasma pneumoniae* IgM and Ig A were determined by ELISA using commercial kit REIDASCREEN *M. pneumoniae* IgM and IgA imported by Clinilab, Cairo, Egypt. After preparation of the reagents following the manufacturer instructions, 100µl of diluted sera and ready to use controls were pipette into corresponding wells, then incubated at 37◦C for 30 minutes. Washing was done using diluted wash buffer 4 times. 100µl of conjugate was added to each well. Second incubation was done at 37C for 30 minutes, and then washing was done 4 times. 100 µl of substrate was added to each well and incubated for at 37◦C for 30 minutes. The enzyme converts the colorless substrate (H2O2/TMB) to a blue end product. The reaction was stopped by adding100 µl stopping solution and the colour of the mixture switches from blue to yellow at the same time. The final measurement was carried out at 450 nm on a photometer using a reference wavelength ≥ 620 nm. The results of the samples were calculated according to the manufacturer instructions.

**Case definition**

Patients with *M pneumoniae* pneumonia infection were defined as children admitted to the pediatric intensive care unit (PICU) or pediatric chest unit with both positive laboratory results and a clinical presentation consistent with pneumonia and positive for *M. pneumonia*e IgM or Ig A [14].

**Statistical methods**

Data was coded, entered and analyzed using Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. Qualitative data was represented as number and percentage. Quantitative data was represented by mean ± SD. Chi Square test was used to assess statistical significance of difference between two qualitative variables. If an expected number is less than 5, Fisher's exact test of independence was applied. Student's t–test was used to compare the mean value of the measurement variables. P value was set at

*<0.05* for significant results and *<0.001* for highly significant results.

**Results**

Among 83 patients of this study, 47 were males and 36 females; 37 were of age 5-9 years, 20 aged 9-12 years and 26 aged 2-5 years. As shown in **table (1)** and **figure (1)**, 29 (34.9%) out of 83 patients were positive for *M. pneumonia*e IgM while 2 (3.4%) patients were positive for *M. pneumonia*e IgA. As shown in **table (2)**, *M pneumoniae* was significantly higher in the age group (5-9 years) (54%) (*p value= 0.0001*). As regard to sex distribution, there was no statistical significance between male and female patients (*p value =0.8*).

As shown in **table (3)**, all *M. pneumoniae* pneumonia patients presented with cough 29/29 (100%), fever 29/29 (100%). Other manifestations were malaise 18/29 (43.8%), headache 16/29 (33.8%), wheeze 21/29 (52.5%), chest discomfort 13/29 (44.8%), sore throat 13/29 (46.4%), rhinitis 8/29 (27.5%) and pharyngitis 6/29 (24%). There were, statistical significance for chest discomfort with *p value=0.000*, Wheezes with *p value=0.001*, malaise with *p value=0.007*, and headache with *p value=0.001*.

As shown in **table (4)**, the most frequent X ray findings in *M. pneumoniae* pneumonia was air space pneumonia (71%); segmental more than lobar form. It was statistically more significant than other x-ray findings (The chi-square = 24.931 & the *p-value is <0.00001*). As shown in **table (4)**, leucocytes count and granulocyte count were significantly higher in pneumonia types other than *M. pneumoniae* pneumonia (the *p-value 0.0245*, and *< 0.00001*) respectively. Lymphocyte count was also significantly lower in types of pneumonia other than *M. pneumoniae* pneumonia (the *p-value is < 0.0001*). There was no significant difference in CRP between *M.pneumoniae* pneumonia and other types of pneumonia (the *p-value = 1*).

**Figure 1.** Serological results for *Mycoplasma pneumoniae* among the patients

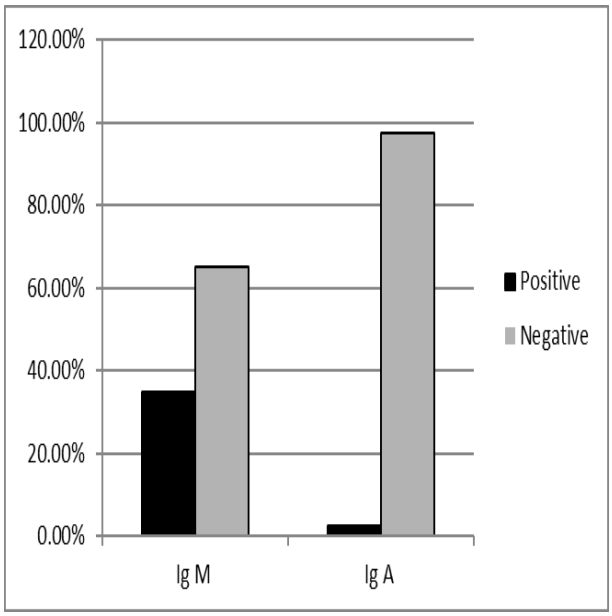


**Table 1.** Serological results for *Mycoplasma pneumoniae* among the patients.

| | IgM No (%) | IgA No (%) |
|---|---|---|
| **Positive** | 29 (34.9%) | 2 (2.4%) |
| **Negative** | 54 (65.1%) | 81 (97.6%) |
| **Total** | 83 (100%) | 83 (100%) |

**Table 2.** Age and sex distribution among children with M *pneumoniae* pneumonia according to serology.

| Age | Male | % | Female | % | Total | |
|---|---|---|---|---|---|---|
| 2:5y | 1/26 | 3.8 | 2/26 | 7.6 | 3/26 | 11.5 |
| 5:9y [1] | 12/37 | 32.4 | 8/37 | 21.6 | 20/37 | 54 |
| 9:12y | 2/20 | 10 | 4/20 | 20 | 6/20 | 30 |
| Total | 15/83 | 18 | 14/83 | 16.8 | 29/83 | 34.9 |

1p = 0.001

Male v female: The chi-square statistic is 0.0418. The *p*-value is .838036

**Table 3.** Comparison between *M pneumoniae* Ig M positive children and children with other types of pneumonia as regards clinical signs and symptoms.

| **Characteristic** | **Clinical signs and symptoms of children with pneumonia** | | | |
|---|---|---|---|---|
| | ***M.pneumoniae* IgM Seropositive (29)** | ***P value*** | ***M.pneumoniae* Ig M seronegative (54)** | **Total** |
| Cough | 29(100%) | *0.1* | 54(100%) | 83 (100%) |
| Fever | 29(100%) | *0.1* | 54(100%) | 83 (100%) |
| Chest discomfort[1] | 13(44.8%) | *0.000* | 1 (7%) | 14 (16.8%) |
| Wheeze[2] | 21(52.5%) | *0.001* | 19 (57.5%) | 40 (48.2%) |
| Sore throat | 13(46.4%) | *0.15* | 15(67.5%) | 28(31.3%) |
| Malaise[3] | 18(43.8%) | *0.007* | 17(53.6%) | 35(42.2%) |
| Asthma exacerbation | 3(37.5%) | *0.6* | 5(62.5%) | 8(8%) |
| Rhinitis | 8(27.5%) | *0.9* | 15(62.3%) | 23(27.7%) |
| Headache[4] | 16(33.8%) | *0.001* | 11(66.2%) | 27 (100%) |
| pharyngitis | 6(24%) | *0.1* | 19(76%) | 25(30%) |

[1]*p = 0000* [2]*p = 001* [3]*P = 0.007* [4]*p = 0.001*

**Table 4.** Comparison between MP IgM positive children and children with other types of pneumonia as regards X- ray findings and laboratory data.

| **Chest X- ray finding** | *Mpneumoniae* pneumonia No (%) | Other pneumonia No (%) | chi-square | *p*-value |
|---|---|---|---|---|
| Air space pneumonia<br>Segmental<br>Lobar | 20 (71.2)<br>12(42.1)<br>8(29.1) | 6 (11.1)<br>2<br>4 | 29.3558 | *< 0.00001* |
| Interstitial pneumonia | 4 (13.1) | 28 (51.8) | 11.5361 | *0.000683.* |
| Bronchopneumonia | 5 (13.7) | 20 (38) | 3.5127 | *0.0609* |
| **Laboratory data** | | | t* | P |
| Hb (mg/dL) mean±SD | 11.2 ± 0.9 | 11.3 ± 0.9 | 0.4826 | *0.6307* |
| Leucocytes (x$10^3$/µL) | 7.9 ± 3.5 | 11.2 ± 7.3 | 2.2923 | *0.0245* |
| Granulocytes (%) | 47± 14 | 61± 14 | 4.3437 | *< 0.0001* |
| Lymphocytes (%) | 42± 13 | 29± 13 | 4.3437 | *< 0.0001* |
| Monocytes (%) | 9 ± 3 | 8 ± 3 | 1.4479 | *0.1515* |
| Platelet (x $10^3$ /µL) | 266 ± 91 | 251± 75 | 0.8055 | *0.4229* |
| CRP (mg/dL) | 48 ± 12 | 48± 16 | 0.0000 | *1.0000* |

*t= *Student t test*

N.B. Chi-square = 24.931. *p-value is < 0.00001* between different X ray findings in *M pneumoniae* pneumonia

**Discussion:**

*Mycoplasma pneumoniae* causes a significant burden of disease in children especially upper and lower respiratory tract infections. *M. pneumoniae* is a major cause of pneumonia in children. Clinical practice requires rapid and accurate detection for effective treatment [15].

In the current study, *M. pneumonia*e IgM was positive in 34.9% of 83 pediatric CAP cases while only 2 (3.4%) patients were positive for *M. pneumonia*e IgA. A study done in India reported positive *M. pneumoniae* IgM in 29.4% [16]. **Harris et al**. also reported a positive pharyngeal polymerase chain reaction or serology for *M. pneumoniae* can be found in 4–39% of children hospitalized with community-acquired [17]. The presence of *M. pneumoniae* IgM is associated with current infection with *M. pneumoniae*, especially in children, but *M. pneumoniae* IgM is difficult to be detected in adult's pneumonia [18]. In Madagascar, a prevalence of 18.2% for *M. pneumoniae* infection in children was reported [19]. Specific serum immunoglobulin IgM can be detected within 1 week after initial infection and about 1–2 weeks before IgG [20]. Specific serum IgA rises, peaks and decreases earlier than IgM, but is less frequently detected [21]. Detection of *M. pneumoniae* IgM was more sensitive than *M. pneumoniae* IgA in school-age children with *M. pneumoniae* pneumonia [22]. Although culture is the gold standard for *M. pneumoniae* pneumonia diagnosis, this approach is time-consuming and requires specialized media and trained laboratory personnel. PCR-based methods are increasingly used in daily clinical practice, as well as in clinical studies, for the detection of *M. pneumoniae* because they provide fast and sensitive results in the acute phase of an infection [23]. Both culture and PCR cannot differentiate between carriage and infection by *M. pneumonia* [21, 23] so antibody testing is one of the main diagnostic tools for *M. pneumoniae* infection detection [14, 24].

Age is an important factor that can affect pathogen distribution. The incidence of *M. pneumoniae* infection is highest among children aged 3–7 years, while respiratory viral infections are more common in children younger than 2 years [25]. In the current study, *M. pneumoniae* was significantly higher in the age group (5-9 years) (54%, *p value= 0.0001*). This result agrees with a study done in India [16] reporting that *M. pneumoniae* was positive in 23.2% in children <5 years and 54.0% in children ≥5 years of age, and this difference was statistically significant (*P <0.001*). In china [26], Among 110 patients with *M pneumoniae* positive, the median age was 5 years. As regard to sex distribution, there was no statistical significance between male and female patients (*p value =0.8*). The gender distribution did not differ significantly between children with *M. pneumoniae* positive and CAP (*P=0.094*).

In the current study, all *M. pneumoniae* pneumonia patients presented with cough 29/29 (100%), and fever 29/29 (100%). Other reported manifestations were malaise (43.8%), headache (33.8%), wheeze (52.5%), chest discomfort (44.8%), sore throat (46.4%), rhinitis (27.5%) and pharyngitis (24%). A study by **Defilippi et al.** [27] found cough and fever were the two most frequent symptoms in *M. pneumoniae* infection. However, dyspnea, upper respiratory tract involvement, diarrhea and vomiting were reported as more common manifestations in patients <2 years old children. **Gordon et al**. [28] reported that the clinical presentation of pediatric *M. pneumoniae* infections accompanied by fever in 33.4% of patients, and duration of symptoms was between 3 and 9 days. Fever, cough, and sore throat were the three most common symptoms of children with *M. pneumoniae* positive [26]. Runny nose was more common in patients with *M. pneumoniae* -virus co-detection [26]. Signs and symptoms of *M. pneumoniae* infections are not unique, and physical examination findings can be minimal initially. Pulmonary symptoms may occur later on the course of disease and even be absent. Clinicians should be aware about mycoplasma in pediatric patients having prolonged fever without a focus [29]. **Xia et al.** [30] reported expectoration and wheezing, accompanied by low-grade fever as common presentations among infants with *M. pneumoniae* infection. They observed gastrointestinal symptoms as the most common extra-pulmonary manifestation among infants who had evident pulmonary signs. In contrast, the majority of the school-age children presented with high fever and severe dry cough. Studies have reported rash as the most common extra-pulmonary manifestation in these patients [30].

In the current study, the most frequent X ray findings in *M. pneumoniae* pneumonia was air space pneumonia (71%); segmental more than lobar form. It was statistically more significant than other x-ray findings (The chi-square = 24.931 & the p-value is < *0.00001*). In a study done by **Lu et al.** [31], Children <5 years age more commonly displayed evidence of bronchopneumonia on chest radiographs compared with that of children in the ≥5 years age group

(*P<0.05*). Approximately 58.1% of the children in ≥5-year age group had segmental/lobar pneumonia, and frequently presented with pleural effusion and atelectasis. The incidence of interstitial pneumonia in children aged 6 months and 1-year age group was higher (6.3%) than that in other age groups (*P<0.05*) [31].

In the current study, there was significant difference between *M. pneumoniae* pneumonia and other types of pneumonia as regards to total leucocytes count, granulocytes and lymphocyte count (the *p-value* is *0.0245*, *<0.00001* and *<0.0001* respectively).The leukocyte count in *M. pneumoniae* pneumonia may or may not increase [32,33]**.** Significant differences were present in white blood cells counts, proportion of neutrophils, platelet count and CRP levels among different age groups. Absolute lymphocyte count was significantly different between the bronchopneumonia group and the severe segmental/lobar pneumonia group [34].

**Conclusion:**

The findings of this study highlight the clinical significance of *M. pneumoniae* in pediatric community acquired pneumonia.

**Recommendations:**

The study recommends pediatricians to highly consider *M pneumonia*e in the differential diagnosis of pediatric CAP in especially in the age group (5-9 years).

**Limitations of the study:**

The study depends on only serology besides clinical manifestations to diagnose *M. pneumoniae* pneumonia. The number of patients included in the study was only 83 patients.

**Conflict of interests:**

The authors declare no conflicts of interest.

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