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PAEDIATRICS
Perspective

To study prevalence of *Mycoplasma pneumoniae* infection in children less than five years of age and associated risk factors: A prospective observational study

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Received: July 03, 2015; **Published:** August 21, 2015

Abstract

Objective: To identify clinical and demographic profile of lower respiratory tract infections and prevalence of IgM Mycoplasma antibodies in less than 5 year age.

Material and method: Two hundred and ten cases of LRTI in the age group 6 months to 5 years were enrolled. Two hundred and ten healthy children were taken as controls.All patients were subjected for complete blood counts, absolute eosinophil counts, chest x-ray and enzyme immunoassay for IgM Mycoplasma antibodies.

Results: Mycoplasma pneumoniae contributes to 22.70% cases of LRTI in higher age group (3-5 year). Positivity was more seen (14.7%) in cases that having associated wheezing. Incomplete immunization for age, low education level of mother, overcrowding, lack of exclusive breast feeding for 6 months, malnutrition and use of cooking fuel other than LPG were an independent risk factor.

Conclusion: *M. pneumoniae* plays an important role in children with lower respiratory tract infections especially with wheeze, even in children less than 5 years of age so, in LRTI with wheeze in slightly older children (3-5 years) use of macrolides may be considered.

Keywords: *Mycoplasma pneumoniae; Lower respiratory tract infection; Children; IgM Mycoplasma; Antibodies*

Introduction

Acute lower respiratory tract infections (ALRTI) are the leading cause of mortality and a common cause of morbidity in children below five years of age. In developing countries pneumonia alone kills 3 million children every year. It is responsible for 19% of all deaths in children below five years of age and 8.2% of all disability and premature mortality as measured by disability adjusted life years (DALY) [1]. Behrman [2] in a review of epidemiology of ALRTI in developing countries identified low birth weight, malnutrition, vitamin A deficiency, lack of breastfeeding and passive smoking as risk factors for ALRTI. Recent studies have added other risk factors to the list including poor socioeconomic status, large family size, and family history of bronchitis, advanced birth order, crowding, young age, air pollution, and the use of non-allopathic treatment in early stages of illness.

Mycoplasma pneumoniae is a major cause of LRTIs and accounts for 15-20 per cent of all cases of pneumonia [3]. In the majority of cases of suspected *M. pneumoniae*, the presumptive diagnosis is made on history and clinical findings alone. Atypical infections in wheezing children are caused by *Mycoplasma pneumoniae*, pleuro-pneumonia like organisms belonging to the distinctive genus of Mycoplasma. Generally Mycoplasma pneumonia is a benign and self-limiting process, in which the treatment is needed mainly to reduce the morbidity. As most of the patients remain ambulatory, however, it is well documented that with severe infections, admission may be required for oxygen and respiratory support. A specific diagnosis is important because β-lactam antibiotics used empirically in the treatment of

these infections are ineffective. The diagnosis in most cases is confirmed by serology [4]. The commercially available enzyme linked immunosorbent assay (ELISA) is more specific and sensitive. IgM ELISA is the most appropriate among the currently available tests, for the diagnosis of acute *M. pneumoniae* infection.

As majority of the studies conducted in our country has seen prevalence of *M. Pneumoniae* infection in children more than 5 years and rarely it has been conducted till date in under 5 year age children, hence we planned this study to determine the prevalence of *M. Pneumoniae* infection and to study the clinical and demographic profile and also various risk factors of lower respiratory tract infections in under 5 age group children.

Material and Methods

This was a prospective case control, single-centre study. The present study was conducted in the Department of Paediatrics, Umaid Hospital, Dr S. N. Medical College, Jodhpur. A total of 210 admitted children (age group 6 months to 5 years), that fulfilled the study inclusion criteria were enrolled in study. 210 healthy children who were age and sex matched to cases were taken as controls. Inclusion criteria for cases was any patient who presented with complains of cough, fever and breathlessness of less than 30 days duration along with increased respiratory rate as per age (with/without features of respiratory distress) on examination and no past history of previous hospitalization.Those children who had received antibiotics in preceding 48 hours and with any concomitant illness like documented tuberculosis, congenital heart disease, dysentery, severe anaemia (haemoglobin < 7 mg/L) were not included in our study. A written informed consent was taken from patient's attendant before enrolling the patient in our study. The study protocol was approved by the Institutional Research Board (IRB) of the college.

On admission, particulars of the patient (name, age, sex, weight, residence) were noted in an especially-designed, pre-tested performa, for the study. Complete history was elicited regarding onset, duration and progression of symptoms. Patient was also enquired about previous hospital admission, duration of admission, and previous hospital visits for same complaint. History of any atopic or allergic rhinitis or sinusitis was enquired. History of recurrent aspiration was asked. Risk factors which were enquired include malnutrition, lack of breastfeeding, passive smoking, type of fuel used, large family size, family history of respiratory tract infections and overcrowding.

All patients were subjected for complete blood counts, absolute eosinophil counts, chest x-ray and enzyme immunoassays for IgM Mycoplasma antibodies (NOVUM DIAGNOSTICA, Assar Gabrielsson, Germany). The interpretative criteria were consistent with the recommendations of the manufacturer. The mean absorbance value (MN) of the negative controls was determined and the cut-off value (CO) was calculated as:

Cut off = Mean absorbance + 0.300.

The interpretations of the results were done as follows:

Positive: Mean absorbance > 10 per cent above cut off

Negative: Mean absorbance > 10 per cent below cut off

Grey zone: Mean absorbance from 10 per cent above to 10 per cent below cut off.

Statistical Analysis

Data was entered in Microsoft Excel spreadsheet, and analysis was performed using SPSS version 15. Association of each of the categorical variable with pneumonia (outcome variable) was assessed with chi-square test and the strength of their association was computed by unadjusted odds ratio (95% confidence interval).

Observations

In the present study, highest number of cases (54.28%) were in age group of 6 to 23 months followed by 31.42% cases in age group of 36 to 59 months followed by 14.28% cases in age group of 24 to 35 months but there was no statistically significant association between different age group and risk of LRTI ($p > 0.2$).

Most of the cases were males (67.20%) and from urban areas (62.80%) and belonged to Hindu religion (84%). More number of LRTI cases (55%) belonged to joint families as compared to nuclear families (45%) but it was statistically not significant ($p > 0.8$). LRTI was more common (24.3%) in cases who were either incompletely or partially immunized as compared to controls (6.66%) and it was statistically significant ($p < 0.05$). A significantly higher number (64.30%) of LRTI cases were present in children of illiterate mothers as compared to controls (23.30%) ($p < 0.001$) and the risk of LRTI increased by 3.56 times in cases as compared to controls (OR 3.56). Overcrowding was an important predictor of LRTI in 44.30% cases as compared to 23.33% controls. Overall overcrowding was associated with 3-4 times increased risk of LRTI (OR 3.59). A significantly higher (40%) prevalence of LRTI was found in children who were not or partially breastfed for 6 months as compared to (13.33%) controls ($p < 0.01$) and the risk of LRTI increased by 3-4 folds in children who were not breastfed (OR 3.88). Malnutrition was present in 102 (48.60%) cases as compared to 56 (26.6%) in controls and there was a positive correlation between protein energy malnutrition and risk of LRTI ($p < 0.05$). Overall, malnutrition was associated with 2-3 times increased risk of LRTI (OR 2.64). Use of cooking fuel other than LPG was significantly associated with LRTI in 34.30% cases as compared to 13.33% controls ($P < 0.05$). Also, use of biomass fuel causes 3-4 times increased risk of contracting LRTI (OR 3.85) (Table 1). Risk of LRTI was not increased with smoking done by parents and history of respiratory tract infection in other family members in the preceding 2 weeks.

S. No	Variables	Cases n (%)	Controls n (%)	Odds ratio
1	Mother's literacy Illiterate Literate	135 (64.30) 75 (35.70)	49 (23.30) 161 (76.70)	3.56
2	Overcrowding Yes No	93 (44.30) 117 (55.70)	49 (23.33) 161 (76.67)	3.59
3	Exclusive breast feed < 6 months > 6 months	84 (40) 126 (60)	28 (13.33) 182 (86.67)	3.88
4	PEM Absent Present	108 (51.40) 102 (48.60)	154 (73.33) 56 (26.67)	2.64
5	Type of cooking fuel Other than LPG With LPG	72 (34.30) 138 (65.70)	28 (13.33) 182 (86.67)	3.85

Table 1: *Correlation of pneumonia with risk factors by odds ratio.*

Cough was the most common symptom present in 204 (97.14%) cases followed by fever in 195 (92.85%) cases and breathlessness in 189 (90%) cases. Wheezing was present in 45 (21.43%) cases and refusal to feeds was present in 27 (12.85%) cases. The most common sign was rapid breathing 210 (100%) followed by crepitations which were present in 165 (78.57%) cases. Rhonchi was present in 102 (48.57%) cases and chest indrawing was present in 54 (12.85%) of cases.

IgM Mycoplasma antibodies were positive in 22.70% cases in age group 36-59 months followed by 13.04% positive in age group 12-35 months, which is statistically significant ($p < 0.02$) (Table 2). 14.7% cases were positive for IgM Mycoplasma antibodies in cases of LRTI with wheeze as compared to only 8.3% without wheeze (Table 3). 16.23% cases were positive for IgM Mycoplasma antibodies in pneumonia group followed by only 5.5% in severe pneumonia group (Table 4). However, the association was statistically insignificant ($p > 0.3$) while none of our control cases showed positivity for Mycoplasma antibodies.

Age	Cases n = 210 (%)	IgM Antibody Positive percentage n (%)	p
6-11 Months	75 (35.70)	0 (0)	$\chi^2 = 6.38$ $p < 0.02$
12-35 Months	69 (32.80)	9(13.04)	
36-59 Months	66 (31.40)	15(22.70)	
Total	210 (100)	24(11.43)	

Table 2: *Correlation of IgM Mycoplasma antibodies with Age.*

Clinical diagnosis	Cases n = 210 (%)	IgM Mycoplasma Antibody Positive (%)	p
LRTI with wheeze	102 (48.6)	15 (14.7)	$\chi^2 = 0.70$ $p > 0.5$
LRTI without wheeze	108(51.4)	09 (8.3)	
Total	210 (100)	24 (11.4)	

Table 3: *Correlation of IgM Mycoplasma antibodies with clinical diagnosis.*

Classification	Cases (%)	IgM Mycoplasma Antibody Positive (%)	p
Pneumonia	129 (61.43)	21(16.23)	$\chi^2 = 1.28$ $p > 0.3$
Severe Pneumonia	54 (25.71)	03 (5.5)	
Very Severe Pneumonia	27 (12.85)	0 (0)	
Total	210 (100)	24(11.43)	

Table 4: *Correlation of IgM Mycoplasma antibodies with severity of pneumonia.*

Discussion

Pneumonia is a silent global disease which is easily detected and treated effectively in developed countries but in developing countries it mostly results into deaths i.e. it is not easily curable. Various abbreviations e.g. ARI and LRTI used in description of pneumonia, its familiar and benign image in the developed world has brought a wrong perception about this disease as a public health problem thus undermining it as a single, treatable problem. Research on pneumonia can be highly effective, especially if this disease is solely dealt comprehensively.

The majority of the cases of pneumonia in our study were present in age group in between 6-23 months as compared to other age groups and were similar to other studies [5-7]. This might be due to the fact that in young children immunity is not well established, and also because of narrow airways, relatively short bronchial tree and incomplete development of lungs.

Majority of cases (62.80%) in our study were from urban areas but there was no significant association between domicile and pneumonia ($p > 0.5$). This was similar to other researchers [8]. This may be due to the fact that more crowding in urban areas leads to increased risk of infections and also hospital in which our study was undertaken is the main speciality centre in this area and only severe ARI cases from rural areas are referred, while less severe cases are usually managed at primary centres.

The incidence of pneumonia was more in either incomplete or partially immunized ($p < 0.05$). Our observation was similar to other researchers [6,9,10]. This is because Immunization helps to reduce deaths related to childhood pneumonia by preventing children from developing infections that cause pneumonia or can lead to pneumonia as a complication e.g. measles and pertussis.

There was significantly higher number of LRTI cases in children of illiterate mothers as compared to controls ($p < 0.001$).This observation was in concordance with the findings of Savitha MR., *et al*. [10], S Broor., *et al*. [6] and Prasad., *et al*. [9] This may be due to the fact that mother and child has been considered as a single unit. Mother due to her close association with child recognize even the minor changes in child's health and therefore mothers who have more education are more likely to seek appropriate and early care for illnesses in their children. Also, educated mothers can be instructed on how to recognize the signs and symptoms of pneumonia e.g. rapid respiratory rate and the inability to take oral fluids, the importance of childhood immunization and general hygienic measures like use of soap and water.

In the present study, the prevalence of pneumonia was found slightly more in cases as compared to controls that had history of respiratory tract infection in other family members in the preceding 2 weeks. Same type of observations was present in the study by S Broor., *et al*. [21].

In the present study, overcrowding was an important predictor of pneumonia. Overall, overcrowding was associated with 3-4 times increased risk of pneumonia (OR 3.59). Similar results were obtained by others [2,10-12]. Crowding conditions experienced at many homes increases the risk of disease transmission in children and this crowding is mainly caused by living in families of large size, small poor quality houses, and houses with poor sanitation.

The present study showed a significant high risk of contracting pneumonia in cases who were not or partially breastfed for 6 months as compared to controls ($p < 0.01$) and the risk of pneumonia increased by 3-4 folds in children who were not breastfed (OR 3.88). Our findings were comparable with the studies done by S Broor., *et al*. [6] and Savitha MR., *et al*. [10] Breastfeeding has a protective effect which is due to its special or unique anti-infective properties which facilitate passive protection against microorganisms, immune system stimulation and inhibition of gastro-intestinal invasion by Gram negative species. Breast- feeding affords protection against childhood pneumonia which persists beyond the breastfeeding period.

In the study malnutrition was associated with 2-3 times increased risk of pneumonia (OR 2.64). Our findings were comparable with the work done by Tupasi., *et al*. [13], S Broor., *et al*. [6] and Escobar., *et al*. [14]. Similar observations were also noted by Deb SK., *et al*. [15], Mitra NK., *et al*. [16], Biswas A [17], MR Savitha [28] and Pandey A [18]. Malnutrition children have defective cell mediated immunity leading to severe gram negative infection and sepsis. They may also have qualitatively abnormal immunoglobulins and impairment of key enzymes involved in bactericidal action of leucocytes.

In our study, use of cooking fuel other than LPG was strongly associated with pneumonia ($P < 0.05$). Also, use of biomass fuel causes 3-4 times increased risk of contracting pneumonia (OR 3.85). Use of biomass fuels (wood, crop-residues, animal dung), coal and other media (kerosene) are predominant contributors to indoor air pollution. Nearly half the world's households, more so in developing countries and the countryside (90%), use these fuels for cooking. These are burnt in simple stoves with very incomplete combustion generating a lot of toxic products that adversely affect specific and nonspecific local defences of the respiratory tract. The risk is highest for mothers and young children due to longer stay indoors and close proximity during cooking.

In the present study, risk of pneumonia was not significantly associated with smoking done by parents (67.2% in cases as compared to 73.3% in controls) ($p > 0.7$). Our findings were comparable with the study done by Savitha MR., *et al*. [10], S Broor., *et al*. [6] and Rahman MM [12]. This may be because none of the mothers in our study were smokers and the exposure of children due to smoking by fathers may be limited because of relatively greater time spent by fathers outside the home.

The incidences of presenting symptoms in our study were comparable with the studies done by Singhi., *et al*. [19], Kabra., *et al*. [20] and Kumar., *et al*. [21].

Symptoms	Singhi., *et al*. [19]	Kabra., *et al*. [20]	Kumar., *et al*. [21]	Our study
Cough	96.50%	92%	100%	97.14%
Fever	97%	82%	88%	92.85%
Breathlessness	81%	90%	100%	90%
Refusal to feed	31%	42%	22%	12.85%

Tachypnea has been proved to be a sensitive and specific indicator of the presence of pneumonia. Also, the traditional method of making a clinical diagnosis of pneumonia has been by the recognition of chest indrawing and auscultatory signs, in particular crepitations, in a child with cough. In our study, most common signs were rapid breathing (100%) and crepitations (78.57%) for making a clinical diagnosis. Rhonchi (48.57%) and chest indrawing (25.71%) were other important signs.

IgM Mycoplasma antibodies were significantly more common in the 36-59 months as compared to in 12-35 months ($p < 0.02$). Similar results were obtained by Elizabeth., *et al*. [22] who reported 29.2% of IgM Mycoplasma antibodies positive in children of age group less than 5 year old. S Kabra [20] observed 24% and R Chaudhary [23] observed 27.4% in the under 5 age group.

In the present study, among 102 (48.6%) cases of LRTI with wheeze, 15 (14.7%) cases were positive and 87 (85.3%) were negative for IgM Mycoplasma antibodies and among 108 (51.4%) cases of LRTI without wheeze, only 09 (8.3%) were positive and 99(91.3%) were negative for IgM Mycoplasma antibodies. Similar results were obtained by Kashyap., *et al*. [24] showing 21.43% cases of LRTI with wheezing positive for IgM Mycoplasma pneumoniae antibodies.

In the present study, IgM Mycoplasma antibodies were positive in 16.23% in pneumonia group and only 5.5% in severe pneumonia group. This shows that Mycoplasma pneumoniae infection has a propensity to cause pneumonia only. Similar results were obtained by Elizabeth., *et al*. [22] showing 14.8%, Shenoy., *et al*. [25] showing 24%, Pandey., *et al*. [26] showing 24.2% and R Choudhary., *et al*. [23] showing 27.2% in pneumonia patients. A higher incidence of IgM antibodies to M. pneumoniae was reported in earlier studies by Ramamoorthi., *et al*. [27] (31.5%) and Dey., *et al*. [28] (35%).

This may be due to the fact that our study was done in a selected group of patients over a short time. Moreover, the higher number of prevalence of IgM Mycoplasma antibodies in earlier studies may be due to outbreak occurring during that period over which earlier studies were conducted. The strength of the present study includes very large sample size in both group and evaluation of all cases with *M. pneumoniae* antibody.

Conclusion

Incomplete immunization for age, low education level of mother, overcrowding, lack of exclusive breastfeeding for 6 months, malnutrition and use of cooking fuel other than LPG was found as an independent risk factor for pneumonia. *M. pneumoniae* plays an important role in children with lower respiratory tract infections.

Financial Disclosure: The authors have no financial relationships relevant to this article to disclose.

Conflicts of Interest: The authors have no conflicts of interest relevant to this article to disclose.

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Volume 2 Issue 1 August 2015