

Acute *Chlamydia Trachomatis* Respiratory Infection in Infants

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ABSTRACT

Objectives: This designed was designed to estimate the prevalence of *Chlamydia trachomatis* infection in infants of up to 6 months of age and to assess clinical and laboratory indicators as predictors of Chlamydia etiology. **Materials and Methods:** A hospital-based study was conducted in Department of Pediatrics, Maharani Laxmi Bai Medical College, Jhansi, Uttar Pradesh, India, where infants up to 6 months of age ($n=50$) with features of lower respiratory tract infection of at least 1 week duration and fulfilling the inclusion criteria were assessed clinically and underwent laboratory investigations using hemogram, Chest X-ray, and IgM ELISA. **Results:** Out of 50 infants, 12 (24%) were tested positive by IgM ELISA test for *C. trachomatis* infection. In age group of up to 2 months 25% positivity was seen whereas it was found to be 31.81% in age group of 2–4 months and 15% in age group 4–6 months. With the 'P' value less than 0.05, it was found that there may be an association of seropositivity of *C. trachomatis* with duration of cough and absolute eosinophil count. **Conclusion:** *Chlamydia trachomatis* is an important cause of lower respiratory tract infection in infants below six months of age. The prolonged duration of cough and increased absolute eosinophil count may be good indicator of its etiology.

Key words: *Chlamydia trachomatis*, Infants, Seroprevalence

INTRODUCTION

Acute lower respiratory tract infection (ALRI) is the leading cause of death in children.^[1,2] In developing countries, it causes 19% of all deaths among children younger than 5 years and 8.2% of all disability. In these countries, it is estimated that ALRI kills 4 million children every year: 3 million of these die from pneumonia.^[3]

There is a current widely held belief that the causative organisms vary according to the age of the child, viruses being most common in children under 5 years old. Respiratory syncytial virus, adenovirus, parainfluenza virus, influenza virus, and more recently metapneumovirus virus^[4] have all been identified in this age group. *Pneumocystis carinii* had been implicated as a causative agent of pneumonia in malnourished and immunodeficient children.

Etiology of pneumonia in younger infants less than 6 months of age is not very well documented. Nearly half of all pneumonia occurring in children less than 5 years age group of children occurs in those less than 6 months of age. Pneumonia in this age group is the leading cause of death, accounting for about 16% of all deaths in the neonatal period. Moreover, pneumonia in this age group may lead to septicemia and meningitis due to physiological and immunological immaturity in these infants. Documentation of the causative agents of the lower respiratory tract infection in this age group is therefore important for therapy of pneumonia. *Chlamydia trachomatis* has been documented to be pathogen causing lower respiratory tract infection in this age group. Different studies showed that *Chlamydia pneumoniae* is a common respiratory pathogen, responsible for about 10% of community acquired pneumonia (CAP).^[5]

In *C. trachomatis* pneumonia, the illness tends to be of subacute onset. The organism may be causally associated with wheezing, asthmatic bronchitis, and adult onset asthma.^[6] Fever is usually absent.

The infant usually acquires the organism during passage

Access this article online	
Quick Response Code: 	Website: www.jgid.org
	DOI: 10.4103/0974-777X.83525

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through the birth canal from chronically infected mothers. Usual age of presentation is at 3 weeks to 3 months of life, but sometimes patient presents at even younger age. The prevalence of *C. trachomatis* was reported as 15.8% in infants younger than 3 months of age, who had pneumonia, sepsis, and meningitis.^[7] Similarly, a different study showed that *C. trachomatis* is not an infrequent cause of respiratory distress even in early childhood, where 8/103 (7.8%) preterm neonates were positive for *C. trachomatis* as early as within 24 h of life.^[8] Most cases of LRTI respond to conventional antibiotics such as amoxicillin, co-trimoxazole, or oral cephalosporin within 1 week, but in *C. pneumoniae* the course of illness is protracted and a specific diagnosis is important because β -lactam antibiotic treatment is ineffective in infections due to Chlamydia.^[9] Macrolides are treatment of choice for this type of pneumonia.

Culture of the organism from nasopharyngeal secretions remains the gold standard for the diagnosis of *C. trachomatis* infection. Ligase chain reaction, direct immunofluorescence test, microimmunofluorescence test, and ELISA are the other tests used for diagnosis of *C. trachomatis*.^[10,11] ELISA test is relatively easier to carry out, less costly, have good sensitivity (75%) and specificity (88%). Other above investigations were not available in our hospital. In developing country like India, cost factor is very important, so we used ELISA method in our study.

This study was conducted to find out the seroprevalence of *C. trachomatis* infection in young infants up to 6 months of age with lower respiratory tract infection of more than 1 week in Bundelkhand region. These patients were also assessed for clinical indicators (association with conjunctivitis, fever, and cough) and laboratory indicators (absolute eosinophil count and chest X-ray) as predictors of Chlamydial etiology.

MATERIALS AND METHODS

Inclusion criteria

1. Infants up to 6 months of age, attending Pediatric OPD or admitted in Pediatrics ward of Maharani Laxmi Bai Medical College, Jhansi.
2. Cough and tachypnea with or without chest wall retraction for more than 1 week duration despite conventional treatment for pneumonia. Tachypnea was defined as respiratory rate more than 60 per minute in a child less than 2 months or more than 50 per minute in an infant two or more than two months.

Exclusion criteria

Infants with defects known to be associated with prolonged lower respiratory tract infection such as congenital heart disease, congestive heart failure, bronchopulmonary dysplasia, or a history consistent with tracheoesophageal fistula were excluded from study.

Design and sample size

This was a cross-sectional study, where 50 cases were taken to find out the prevalence of *C. trachomatis* associated pneumonitis in patients with lower respiratory tract infection in the first 6 months of life.

Methodology

This study was conducted in the Department of Pediatrics, Maharani Laxmi Bai Medical College, Jhansi. Data were collected over a period of 1 year in active collaboration with Department of Microbiology after taking due clearance from the ethical committee. Infants up to 6 months of age, attending Pediatric OPD or admitted in Pediatrics ward of Maharani Laxmi Bai Medical College, Jhansi, who presented with features of lower respiratory tract infection of at least 1 week duration and fulfilling the inclusion criteria were taken as subjects. The subjects were divided into three groups on the basis of age, into less than 2 months, 2–4 months, and 4–6 months. A complete clinical examination was done. In the investigations hemoglobin percent, total leukocyte count, absolute eosinophil count, and chest X-ray were done. Blood samples were withdrawn from a peripheral vein with all precautions and asepsis. Serum was separated by centrifugation and stored in deep freezer at -20°C . Repeated freeze-thawing was avoided. Grossly hemolysed, icteric, or grossly lipemic samples were discarded. Measurement of serum IgM antibody against *C. trachomatis* was detected using ELISA method, following all the steps given by the manufacturer of ELISA kit (CHLM0070, Novatec, Immundiagnostica, Germany). The gold standard for diagnosis of *C. trachomatis* pneumonia is isolation by culture of a specimen from the nasopharynx. However, this facility was not available in our hospital and ELISA test is a simple and reliable test which gives rapid results, so we used ELISA method in our study. The association among *C. trachomatis* and fever, duration of cough, mode of delivery, conjunctivitis, total leukocyte count, and absolute eosinophil count was measured using χ^2 test and Fisher's exact test.

Undertaking of consent

During the conduct of study, detailed information about the study was given to the parents to obtain their willingness to participate in the study and for providing sera samples of the infants with informed and written consent of the parents.

RESULTS

Fifty cases were recruited into the study. There were 8 (16%) infants below 2 months, 22 (44%) between 2 and 4 months, and 20 (40%) between 4 and 6 months of age group [Table 1]. In 50 infants of up to 6 months of age with atypical features of lower respiratory tract infection, the seroprevalence of *C. trachomatis* was found to be 12 (24%) by ELISA method. Test positivity in three defined age group of less than 2 months, 2–4 months and 4–6 months was 2 (25%), 7 (31.81%), and 3 (15%), respectively [Table 1].

There were 40 (80%) males and 10 (20%) females. Around 38 (76%) infants were born by vaginal delivery and 12 (24%) by cesarean section. Positivity for *C. trachomatis* was not significantly associated with mode of delivery [Table 2].

Among 50 infants, duration of cough was prolonged in 38 (76%) infants. Out of these 38 infants, 6 (15.8%) infants were found to be positive for *C. trachomatis*. In remaining 12/50 (24%) infants where duration of cough was less than 2 weeks, 6/12 (50%) infants were found to be positive for *C. trachomatis*. Duration of cough and seropositivity of *C. trachomatis* was found to be statistically significant [Table 3]. Seven (58.3%) patients with *C. trachomatis* etiology had some elements of conjunctivitis. Thus, while the presence of conjunctivitis was quite reliable as a marker of Chlamydia infection, but the absence of conjunctivitis did not rule out infection with *C. trachomatis*. Seven (58.3%) infants positive for *C. trachomatis* were afebrile.

Association of eosinophilia (i.e., absolute eosinophil count more than 300 per cu mm) with positivity of *C. trachomatis* was found to be statistically significant. A total of 83.3% of infants positive for *C. trachomatis* had eosinophilia [Table 4].

Among 12 infants, who were positive for *C. trachomatis*, 75% did not have leucocytosis (i.e., leucocytes count more than 11,000 per cu mm). These results may be due to low antigenicity of *C. trachomatis*. X-rays of the infants positive for *C. trachomatis* had variable findings. Most common finding in these X-rays was the patchy infiltrates. Besides that minimal infiltrates and hyperinflation were also found. The classical features of *C. pneumoniae* as hilar and perihilar infiltrates and reticular parenchymal infiltrates were not

found in our study. Thus, X-rays were not found to be much specific for Chlamydial etiology.

Overall among the various clinical and laboratory parameters studied, significant association with disease etiology was seen with prolonged and distressing cough, and increased absolute eosinophil count in blood.

DISCUSSION

Etiology of pneumonia in early infancy is not well described in developing countries, although a number of investigations have focused on later infancy and preschool years. *C. trachomatis* is responsible for about one-third cases of atypical pneumonia in infants up to 6 months of age.

Table 1: Age wise distribution of cases with positivity for IgM antibodies to *C. trachomatis*

Age groups (months)	No. of infants (n=50)	IgM ELISA-positive for <i>C. trachomatis</i>
Up to 2 months	8	2 (25)
2–4 months	22	7 (31.81)
4–6 months	20	3 (15)

Figures in parenthesis are in percentage

Table 2: Association of *C. trachomatis* positivity with mode of delivery

Mode of delivery	No. of infants (n=50)	IgM ELISA positive for <i>C. trachomatis</i>	P-values from Fisher's exact test
Vaginal	38	10 (26.3)	>0.05
Cesarean	12	2 (16.6)	

Figures in parenthesis are in percentage

Table 3: Association of *C. trachomatis* positivity with clinical features

Clinical findings	No. of infants (n=50)	IgM ELISA positive for <i>C. trachomatis</i>	P-value from Fisher's exact test	
Duration of cough (weeks)	≤2 weeks	38	6 (15.8)	0.024
	>2 weeks	12	6 (50)	
Conjunctivitis	Absent	32	5 (15.6)	0.06
	Present	18	7 (38.9)	
Fever	Absent	32	5 (15.6)	0.06
	Present	18	7 (38.9)	

Figures in parenthesis are in percentage

Table 4: Association of *C. trachomatis* positivity with laboratory findings

Laboratory findings	No. of infants (n=50)	Positive for IgM against <i>C. trachomatis</i>	Chi-square value ^a	P-value	
Absolute eosinophil count (per cu mm)	≤300	22	2 (9.09)	4.79	<0.05
	>300	28	10 (35.7)		
Total leucocytes count (per cu mm)	<11,000	21	3 (14.28)	1.07	>0.05
	≥11,000	29	9 (31.03)		

^aχ² values are calculated at df=1; Figures in parenthesis are in percentage

ELISA test was used to detect the serum IgM antibodies against *C. trachomatis*. This test is a simple and reliable test, which gives rapid results.

This study showed that seroprevalence of *C. trachomatis* in infants of up to 6 months of age having lower respiratory tract infection with features of atypical pneumonia was 24%.

Close to the results of this study was a study conducted by Muhe *et al.* in Ethiopia (1999), in which they reported *C. trachomatis* in 15.8% infants younger than 3 months of age, who had pneumonia, sepsis, and meningitis.^[7] In another study conducted at All India Institute of Medical Sciences, Delhi, India, by Kabra *et al.*, to identify pathogens responsible for ALRI in under 5 children (mean age 11.2 months), they found the seroprevalence of *C. trachomatis* to be 11%.^[12] Wubbel *et al.* (USA) in 1999 found the seroprevalence of Chlamydia to be 6% in 6 months to 6 years ambulatory children.^[13] The low prevalence rate in these studies compared to our study can be attributed to older age group of the study sample and acute symptoms taken in these studies.

This study was conducted at Maharani Laxmi Bai Medical College, which comes under Bundelkhand region. Bundelkhand is an area where most of the people are in low socioeconomic group and maternal infection with *C. trachomatis* is more in this socioeconomic group of patients. Thus, in infants of this area, when taken up to 6 months of age with features of atypical pneumonia, the prevalence rate of *C. trachomatis* was found to be more. Nonetheless, all these studies show that Chlamydia is an important cause of lower respiratory tract infection with symptoms of atypical pneumonia in children, and it is not a rare cause as previously thought.

On analysis of the prevalence of *C. trachomatis* in different age groups, we found that 8 (75%) of cases with lower respiratory tract infections positive for *C. trachomatis* were of below 4 months of age.

Colarizi *et al.* found in their study that *C. trachomatis* was also detected within 24 h of life, from preterm infants born by cesarean section without premature rupture of membranes.^[8] In a study conducted by Pao *et al.*, they detected *C. trachomatis* DNA sequences in the amniotic fluid of a substantial proportion of women with urogenital Chlamydia infection, thus suggesting an in-utero mechanism by which Chlamydia can be transmitted before birth.^[14] Thus, while infants born by vaginal route have more chances of Chlamydial infection, infants born by cesarean section are also at risk of getting this infection.

In our study infants having cough of more than 1 week duration were more likely to be ELISA positive for *C. trachomatis* and it was found to be statistically significant (Fisher's exact test value 0.024). Margaret *et al.*, in their study, found that 59% of Chlamydia positive infants had paroxysm of staccato coughing.^[15] Schacter found that distinctive cough was present in many of infants with this type of pneumonia.^[16] Beem and Saxon found that a distinctive cough was an important finding in infants having pneumonia due to *C. trachomatis*.^[17] Cough usually occurs as staccato paroxysms that may be followed by periods of vomiting or apnea. Thus, prolonged and distressing cough can give an important clue for the clinical diagnosis of *C. trachomatis* in these infants.

In our study, out of 12 infants positive for *C. trachomatis*, 7 (58%) had fever while 5 (42%) did not have fever. This association was not found to be statistically significant (Fisher's exact test value 0.06). The present finding in the study may be because of the fact that infection with *C. trachomatis* is of low virulence and usually fever is absent in this infection. Schacter *et al.* in 1978 also found that this pneumonia is characterized by an afebrile course.^[16] Salaria and Singh found that in spite of extensive pneumonia, the infant almost always remains afebrile.^[18]

An important observation which we found in our study was that positivity of infants for *C. trachomatis* was more in those having absolute eosinophil count more than 300 per cu mm. A total of 35.7% of cases with absolute eosinophil count more than 300 per cu mm were positive for *C. trachomatis* whereas only 9.09% cases with absolute eosinophil count less than or equal to 300 per cu mm were positive for *C. trachomatis*. In our study, 83% of total cases positive for *C. trachomatis* had absolute eosinophil count more than 300 per cu mm. By application of χ^2 test, this association was found to be significant. Margaret *et al.* found in their study that absolute eosinophil count values were commonly elevated in these infants.^[15] A total of 71% of total positive infants had count more than or equal to 300 per cu mm. According to Salaria and Singh blood examination in these children often shows absolute eosinophilia.^[18] The eosinophilia found in these infants positive for *C. trachomatis* could be due to allergic response from *C. infection*, thus eosinophilia is an important associated finding in infants of lower respiratory tract infection positive for *C. trachomatis*.

We found in our study that infants positive for *C. trachomatis* had variable findings on chest X-ray. Most common finding was of patchy infiltrates. Besides that minimal infiltrates and hyperinflation were also found in the chest X-rays. The classical picture of *C pneumoniae* of hilar and perihilar

infiltrates and reticular parenchymal infiltrates was not found in our study. Hence, X-rays were not found to be of much significance for Chlamydial etiology.

Limitations of study

The study used ELISA for establishing the diagnosis of *C. trachomatis* instead of the gold standard. As the sample size of the study was 50, similar study on larger sample size should be planned for generalizing the results.

ACKNOWLEDGEMENT

The authors would like to thank Department of Microbiology, MLB Medical College, Jhansi, for conducting ELISA test.

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How to cite this article: Mishra KN, Bhardwaj P, Mishra A, Kaushik A. Acute *Chlamydia trachomatis* respiratory infection in Infants. *J Global Infect Dis* 2011;3:216-20.

Source of Support: Nil. **Conflict of Interest:** None declared.

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