

# Acute Upper Respiratory Tract Infections in Children and Mode of Delivery

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## ABSTRACT

**Background:** Studies on prevalence of acute respiratory tract infections (ARTIs) exclusively on the infant population in India, and their association with mode of delivery are lacking.

**Aims and objectives:** To assess the incidence of ARTIs in infants aged <12 months and to delineate its association with the mode of delivery (cesarean and vaginal). We also evaluated the antibiotic use for management of ARTIs in the study population.

**Study design:** This single-center retrospective analysis was carried out in a private hospital (Cloudnine Hospitals) in Karnataka, India, over a period of 12 years from 2007 to July 2019.

**Participants:** The study included 51,850 infants up to 1 year of age who were outpatients or admitted to the hospital with infections.

**Intervention:** In this retrospective study, infection type, mode of delivery, and antibiotic use were recorded.

**Outcomes:** Both upper and lower respiratory tract infections (URTI and LRTI) were observed. Mode of delivery recorded included both cesarean and vaginal, and some infants received antibiotics for ARTI treatment.

**Results:** Higher prevalence of cesarean mode of delivery (71%) was recorded, which was associated with a higher incidence of ARTIs, compared to vaginal delivery (5,648 vs 2,420). Among the ARTI patients, antibiotics were prescribed to 2,635 (21.7%) infants. The commonly prescribed antibiotics were penicillin-type and aminoglycoside antibiotics.

**Conclusion:** The incidence of ARTIs in infants was 23.4%, with URITs being more prevalent than LRTIs. The prevalence of cesarean delivery was found to be highest and was associated with a higher incidence of ARTIs. Use of antibiotics was observed in 21.7% of infants with ARTIs.

**Keywords:** Antibiotics, Infants, Lower respiratory tract infection, Mode of delivery, Respiratory tract infection, Retrospective analysis, Single center, Upper respiratory tract infection.

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## INTRODUCTION

Globally, acute respiratory tract infections (ARTIs) largely account for morbidity and mortality in pediatric patients.<sup>1</sup> A higher frequency of respiratory infections is observed in early life compared to adulthood, with the annual infection rate being 5–6 infections.<sup>2</sup> Respiratory tract infections (RTI) cause approximately 1.9 million deaths among children worldwide, with 70% of such deaths occurring in southeast Asia.<sup>3</sup> In India, acute respiratory infections account for 15–30% of all under-5 deaths.<sup>4</sup>

The various manifestations of RTIs include a combination of wheeze, sore throat, rhinitis, cough, and fever. Although majority of these infections in children are managed in a primary care setting, a few require hospital admissions. Acute respiratory infections contribute to 25% of all pediatric admissions from developing countries.<sup>5,6</sup> Environmental factors and housing standards, such as the type of house (kutcha/pucca), overcrowding, adequate ventilation, type of cooking fuel, and presence of window or chimney in the kitchen, are key determinants accounting for acute respiratory infections among children.<sup>7</sup> The type of feeding in infants, acquiring RTIs from older siblings in nursery or school, passive smoking (especially maternal), presence of diseases or congenital disorders [chronic lung diseases (CLD) like cystic fibrosis or premature baby, congenital heart disease, congenital or acquired immune deficiencies, neuromuscular disorders, and severe gastroesophageal reflux diseases], and the need of supplemental oxygen therapy at home owing to premature-birth related CLDs are some of the risk factors of RTIs among children.<sup>6</sup> Besides, exposure

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to air pollution, low birthweight, lack of measles immunization, crowding, and malnutrition also contribute to RTIs, with low birthweight and malnutrition accounting for a higher number of childhood RTIs in developing countries.<sup>7</sup>

The mode of delivery affects child health even 3–6 years after birth, particularly respiratory health.<sup>8</sup> It has been demonstrated that when compared to vaginal delivery, cesarean section (C-section)-delivered children have higher rates of infectious diseases, including ARTIs, thereby resulting in a higher rate of neonatal respiratory morbidity. Moreover, delayed gut colonization in these infants results in an altered immune system.<sup>9</sup> An Indian study revealed that the fecal microbiota of vaginally delivered babies are distinctly different from infants born through C-section mode of delivery.<sup>10</sup>

Although globally several population-wide registry research studies have reported the effects of C-section delivery on infant health, there is paucity of such studies in the Indian setting. This is a crucial issue in the Indian scenario, as the rate of C-section delivery is high in India and is increasing nationwide.<sup>11</sup>

Mortality caused by bacterial infections can be reduced by the appropriate use of antibiotics. Multiple studies from India have demonstrated that antibiotics are among the most commonly prescribed drugs in pediatric patients. However, inappropriate prescription of antibiotics, in the absence of such indications, contributes to the development of antibiotic resistance. It has been observed that pediatric patients are often prescribed antibiotics for nonbacterial infections. Therefore, it is essential to monitor local antibiotic use in pediatric patients to improve the prescribing practices. In a study by Sharma et al. conducted in two hospitals in India, broad-spectrum antibiotics were found to be frequently prescribed to treat infections in pediatric patients, although the World Health Organization (WHO) recommends administering broad-spectrum antibiotics only when treatment with specific antibiotics has been proven ineffective.<sup>12</sup>

In India, private hospitals are the major health service providers, while most Indian studies on antibiotic use in pediatric patients have been conducted in outpatients and public health care facilities.<sup>12</sup> With this background, the present study aims to determine the effects of mode of delivery on the incidence of ARTIs in infants, along with the corresponding antibiotic prescription patterns in a private hospital in India. Comparing these findings with other studies across different regions in India will help document ARTI incidence in infants, along with the appropriate antibiotic prescription practices.

**MATERIALS AND METHODS**

This single-center retrospective analysis was carried out in a private hospital (Cloudnine Hospitals) in India, over a period of 12 years from 2007 to July 2019. The study included 51,850 infants up to 1 year of age who were seen as outpatients or admitted to the hospital with ARTIs. The patients were from all over India as the parents attending Cloudnine came from all over India with 40% being from outside Karnataka.

All ARTIs were reviewed after 72 hours of symptom presentation or earlier if there were other concerns or worsening of symptoms. Diagnosis of URTI was made based on absence of chest symptoms or signs, while LRTI was diagnosed if chest symptoms or signs were present. In order to rule out and differentiate between viral and bacterial infections, blood cultures were done, C-reactive protein (CRP) levels were measured, and in some cases throat swabs were collected after 72 hours, if the symptoms persisted. To avoid antibiotic overuse and use of antibiotics for viral infections, emphasis on NO antibiotics as a standard operating policy (SOP) was circulated and monitored in the hospital, both in inpatient and outpatient settings. Antibiotics were not prescribed unless there was a good indication of bacterial ARTIs.

The infants included were either born in the same hospital (Cloudnine babies; C9) or other hospitals (non-Cloudnine babies; non-C9). Along with the type of infection, the mode of delivery and the type of antibiotic prescribed to the infants who attended the outpatient department and were admitted to the hospital with infections were recorded.

This study was performed in accordance with the ethical principles consistent with the Declaration of Helsinki, International

Conference on Harmonisation-Good Clinical Practice (ICH-GCP), and the applicable legislation on noninterventional studies.

**Statistical Analysis**

Statistical analysis was done using appropriate statistical tests. Chi-square test was used for *p* value calculation to determine statistical significance. *p* value <0.05 was considered significant.

**RESULTS**

A total of 51,850 infants were included in the study who visited Cloudnine Hospital from 2007 to July 2019. Since the study was conducted in a private hospital, all the participants belonged to a medium-to-high socioeconomic strata. The mean age of presentation ( $\pm$ standard deviation, SD) was 197.31  $\pm$  97.13 days for C9 babies and 226.98  $\pm$  85.26 days for non-C9 babies. Only infants presenting with upper respiratory tract infections (URTI) or lower respiratory tract infections (LRTI) within 1 year of age were included in this study (Table 1).

The modes of delivery recorded for the infants included lower segment C-section (LSCS), forceps delivery, vacuum-assisted delivery, and normal vaginal delivery (NVD). In the study population, the proportion of LSCS babies was highest (71.0%), followed by NVD (23.7%) (Table 2).

Among the total 51,850 infants included in the study, 12,148 (23.4%) patients presented with either LRTIs or URTIs. A higher number of ARTIs were recorded in the C-section babies (8,068) compared to the NVD (4,080). In both the C9 and non-C9 infants, the incidence of URTIs was significantly higher as compared to LRTIs (Table 3). It was observed that as compared to URTIs, the incidence of LRTIs was significantly associated with the mode of delivery (*p* value = 0.0031) (Table 4).

Among 12,148 RTI patients in the total study population, 2,635 (21.7%) received antibiotics. Among the antibiotics prescribed, the

**Table 1:** Baseline patient characteristics

<i>Patient characteristics</i>	<i>Details</i>
Total study population (N)	51,850
Age	Infants within one-year age
Mean age ( $\pm$ SD)	197.31 $\pm$ 97.13 days for Cloudnine babies, 226.98 $\pm$ 85.26 days for non-Cloudnine babies
Socioeconomic background	Medium-to-high economic strata
Infection type	
URTI, <i>n</i> (%)	10,728 (21%)
LRTI, <i>n</i> (%)	1,420 (3%)
Other RTIs, <i>n</i> (%)	12,148 (23.4%)

RTI, respiratory tract infection; URTI, upper respiratory tract infection; LRTI, lower respiratory tract infection

**Table 2:** Mode of delivery for the study population

<i>Type of delivery</i>	<i>Number of patients (n)</i>	<i>Percentage of total</i>
LSCS	36,820	71
Forceps delivery	527	1
Vacuum assisted	2,191	4.2
NVD	12,312	23.7

LSCS, lower segment cesarean section; NVD, normal vaginal delivery

use of aminoglycoside antibiotics ( $N = 1,858$ ) and penicillin-type antibiotics ( $N = 1,063$ ) was the highest. Other antibiotics that were commonly prescribed included cephalosporins and macrolides (Fig. 1).

**DISCUSSION**

In the present single-center observational retrospective study, the overall incidence of ARTIs was 23.4% among infants up to 1 year age who visited a private hospital in Karnataka, India. The incidence of URTIs was found to be much higher than LRTIs. A higher prevalence of LSCS mode of delivery was observed when compared to NVD, vacuum-assisted, and forceps delivery methods in the infants. This could be because the study center is a tertiary referral high-risk perinatal unit. A higher incidence of URTIs was observed as compared to LRTIs. Among patients with ARTIs, a significant association was observed between the mode of delivery and the incidence of LRTIs. The incidence of ARTIs was highest in babies born by LSCS mode of delivery. Approximately 21.7% of total ARTI patients were prescribed antibiotics, including aminoglycosides and glycopeptides. These findings highlight the increasing prevalence of LSCS mode of delivery, increased incidence of ARTIs in infants

with LSCS mode of delivery, and rational use of antibiotics as first-line therapy for treating infants with ARTI.

Despite being the single most prominent cause of under-5 morbidity, ARTIs have not been studied adequately across India.<sup>13</sup> Therefore, several global healthcare agencies such as the United Nations Children’s Fund (UNICEF), World Health Organization (WHO), national and state governments, and local and international agencies involved in research, academics, and aid have all focused on this area.<sup>14</sup> However, adequate nationwide studies on the incidence of ARTI in large population size are sparse. Several studies have been conducted across various regions of the country to study the prevalence of ARTI in children below 5. The regions studied include Puducherry, peri-urban area of Delhi, Delhi slum area, Kozhikode district of Kerala, central Andhra Pradesh, Assam, Tamil Nadu, Tripura, Ahmedabad, and a rural region of North India, reporting RTI prevalence within the range of 14.6–59.1%.<sup>4,6,14–23</sup> In fact, a study by Walke et al. reported a decreased incidence of ARTIs with increasing age.<sup>13</sup> However, although there are quite a few reports on the incidence and prevalence of ARTIs in under-5 children, such studies exclusively for the infant population in India, along with their association with mode of delivery, are lacking. In this scenario, our study reveals the incidence of RTIs in exclusively infant population, up to 12 months age. The prevalence of RTIs in infants was found to be 23.4% in and around Karnataka, South India. There were no mortalities during this period in the study population. More studies are essential in this age group for estimating the overall prevalence of acute respiratory infections in this age group of infants across the country.

Several studies indicate that infants born by C-section delivery have a higher incidence of respiratory distress.<sup>24</sup> This is particularly well explored in the incidence of asthma, followed by RTIs.<sup>24–28</sup> This phenomenon has been explained by the “hygiene hypothesis,”

**Table 3:** Type of RTIs in the patients

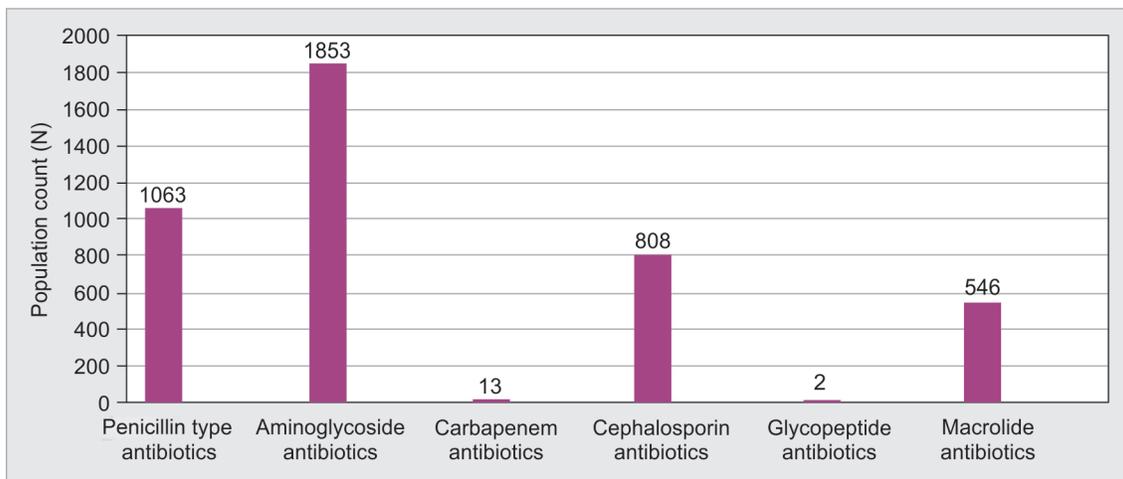
	Total (n)	Infection type	Number of patients (n)	Percentage of total
C9 babies	8,068	URTI	7,358	60.6
		LRTI	710	5.8
Non-C9 babies	4,080	URTI	3,370	27.7
		LRTI	710	5.8

RTI, respiratory tract infection; URTI, upper respiratory tract infection; LRTI, lower respiratory tract infection

**Table 4:** Association between incidence of RTI and mode of delivery in the Cloudnine babies

Infection type	Mode of delivery				p value
	LSCS	Forceps	NVD	Vacuum-assisted	
Infection (overall)	5,648 (15.3%)	89 (16.9%)	1,985 (16.1%)	346 (15.8%)	0.1629
URTI	5,170 (14%)	82 (15.6%)	1,779 (14.4%)	327 (14.9%)	0.3757
LRTI	478 (1.3%)	7 (1.3%)	206 (1.7%)	19 (0.9%)	0.0031*

\*Significant p value; RTI, respiratory tract infection, URTI, upper respiratory tract infection; LRTI, lower respiratory tract infection; LSCS, lower segment cesarean section, NVD, normal vaginal delivery



**Fig. 1:** Type of antibiotics prescribed for RTI



according to which C-section delivery impedes the development of healthy immune system of the infant, as they are not exposed to mother's intestinal and vaginal microbes at birth and have altered flora than vaginally delivered infants.<sup>11</sup> However, there are some conflicting reports in this regard. For example, Moore et al. demonstrated in a population-based longitudinal data that respiratory morbidity and hospitalization after 3 years of age due to asthma are strongly dependent on recurrent hospitalization during infancy due to RTIs and not on the mode of delivery.<sup>29</sup> In 2017, Lavin et al. reported that in India, C-section birth might be associated with an increased risk of childhood asthma.<sup>30</sup> A prospective pregnancy cohort study from a peri-urban region of Telangana State in India reported that unlike reports from Western countries, C-section delivery associates with higher reports of respiratory infant outcomes.<sup>11</sup> Given the increasing trend in delivery by C-section in India,<sup>11</sup> it is a matter of utmost importance to conduct studies on the association between the mode of delivery and the incidence of RTI in infants in India. At present, there is dearth of information in this area in the Indian context. Therefore, the present study elucidated the association between the mode of delivery and RTIs in infants. Our findings demonstrated a significant association between RTI incidence and mode of delivery; both LRTIs and URTIs were found to be higher in infants born by LSCS.

Pediatric RTIs are a leading cause of antibiotic prescriptions. Frequent prescription of antibiotics, even for URTIs of viral origin, is a common practice. Evidence indicates that the number of prescriptions of broad-spectrum antibiotics has increased, even in those cases where no therapy is essential, or when narrow-spectrum antibiotics are appropriate. Such misuse or overuse of antibiotics contributes to drug-related adverse events, incurs evitable medical costs, antibiotic resistance, increased clinical failure, and limited efficacy of antibiotics for long-term treatment in case of recurring RTIs.<sup>31</sup> In this context, the present study was conducted under strict vigilance to prevent antibiotic misuse, which is not commonly observed in Indian hospitals. This indicates growing awareness and practice regarding prevention of antibiotic overuse and misuse for treating viral infections in the Indian healthcare scenario.

In case of pneumonia, the use of antibiotics such as penicillin/ampicillin and macrolides is common, while azithromycin is used for bronchitis.<sup>7</sup> In order to curb antibiotic misuse in children with RTIs, the Ministry of Health and Family Welfare, Government of India has detailed guidelines, which mentions the use of antibiotics such as amoxicillin, cotrimoxazole, cloxacillin, gentamicin, ceftriaxone, penicillin, and ampicillin for different RTIs such as pneumonia and influenza. The guidelines also specify the conditions that do not require antibiotics, like asthma.<sup>32</sup> Along with some broad-spectrum antibiotics, the present study revealed penicillin and aminoglycosides to be the most commonly prescribed antibiotics for the treatment of RTIs in the population studied. These findings are in keeping with an earlier report published in the WHO bulletin, which suggests penicillin and cephalosporins to be the commonly used antibiotics in Vellore, India, followed by macrolides.<sup>33</sup> However, similar studies in the Indian setting on the antibiotic use related to RTIs in infants are sparse.

This study has several strengths, including the duration (12 years) and a large study population. To our knowledge, this is the first detailed study in the Indian setting on the incidence of RTIs solely in the infant population. Moreover, this study also highlights the association between the incidence of RTI in infants and the

mode of delivery; the use of antibiotics for management of RTIs in such infants has also been studied.

Our study has a few limitations. Being a retrospective design of a longer duration might have led to unintentional bias during data extraction and reporting. Further, the subtypes of LRTIs or URTIs in the study population, the risk factors associated with RTIs, variations in the incidence of RTIs in urban and rural populations, or with gender, dependence on the incidence of RTI on the type of feeding of the infant, and seasonal variations in the prevalence of the disease have not been studied. Moreover, although the list of antibiotics has been provided, data on their condition-specific use has not been considered. Again, the presence of any comorbidities along with RTIs and genetic predispositions have not been explored.

## CONCLUSION

To our knowledge, this is the first Indian study reporting all the aspects of RTI including its incidence, treatment, and association with the mode of delivery in infants up to 1 year of age. Further similar studies are required from different regions across the country, in order to improve treatment and develop guidelines for appropriate management of RTIs in infants.

## KEY MESSAGES

### What is Already Known?

Globally, the incidence of RTI is high in the under-five population, and cesarean mode of delivery associates with higher incidence of RTI as compared to vaginal birth.

### What this Study Adds?

The retrospective study conducted exclusively in infants up to one-year age, reflects the current scenario of RTI incidence, treatment, antibiotics use, and association with mode of delivery, in Indian infants of this age-group.

## AUTHOR CONTRIBUTIONS

Kishore Kumar has contributed toward concept, data collection, data analysis, review and approval of manuscript. Nandini Nagar has contributed toward data analysis. Sowmya MV has contributed toward data collection.

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