Etiology of Acute Respiratory Infections in Infants
A Prospective Birth Cohort Study

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Background: There is paucity of studies on etiology of acute respiratory infections (ARI) in infants. The objective of this study is to document incidence and etiology of ARI in infants, their seasonal variability and association of clinical profile with etiology.

Methods: A birth cohort was followed for the first year of life; for each episode of ARI, nasopharyngeal aspirates were collected to identify the causative respiratory virus(es) using multiplex real-time polymerase chain reaction assay. For lower respiratory tract infections, blood culture, serum procalcitonin, serum antibodies to Mycoplasma and Chlamydia and urinary Streptococcus pneumoniae antigen were also assayed.

Results: A total of 503 ARI episodes were documented in 310 infants for an incidence rate of 1.8 episodes per infant per year. Of these, samples were processed in 395 episodes (upper respiratory tract infection: 377; lower respiratory tract infection: 18). One or more viruses were detected in 250 (63.3%) episodes and viral coinfections in 72 (18.2%) episodes. Rhinovirus was the most common virus [105 (42%)] followed by respiratory syncytial virus [50 (20%)], parainfluenza virus [42 (16.8%)] and coronavirus [44 (17.6%)]. In lower respiratory tract infections, viral infections were detected in 12 (66.7%) episodes, bacterial infections in 17 (94.4%) episodes and mixed bacterial–viral infections in 8 (44.4%) episodes. Peak incidence of viruses was observed during February–March and September–November. There was no significant difference in symptom duration with virus types.

Conclusion: In this cohort of infants, ARI incidence was 1.8 episodes per year per infant; 95% were upper respiratory tract infections. Viruses were identified in 63.3% episodes, and the most common viruses detected were rhinovirus, respiratory syncytial virus and parainfluenza virus.

Key Words: acute respiratory infections, etiology, infants, pneumonia

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Acute respiratory infections (ARI) continue to be the leading cause of mortality and morbidity from infectious diseases in young children worldwide. According to the World Health Organization estimates, in 2012, globally 15% of the 6.5 million deaths in children <5 years of age were because of ARI. In India, 14% of 1.4 million deaths in this age group in 2012 were attributed to ARI. Children with ARI contribute to the majority of consultations and admissions to health care facilities. A study from India reported that ARI constitute 20%–40% of all outpatient and 12%–35% of inpatient hospital visits. ARI has a huge economic burden on both families and societies, especially in developing countries.

Several studies have shown that viruses are the most common cause of ARI in young children. Over 200 viruses have been recognized as associated with ARI and this number is increasing every year. Clinically, it is usually difficult to accurately differentiate between different etiologies, which lead to inappropriate use of antibiotics even at the best health centers.

The etiologic diagnosis of ARI is challenging because of the limited availability of noninvasive investigations until recently. For the last 2 decades, serology and virus isolation were the mainstay of investigations for the detection of viruses. With the advent of molecular method such as multiplex real-time polymerase chain reaction (RT-PCR), now it is possible to identify a number of pathogens on single sample. This technology may be helpful in estimating the epidemiologic pattern of ARI accurately; it may also bolster judicious use of antibiotics and prevent antibiotic resistance on long term.

Most of the available studies on the etiology of ARI are from developed countries, mainly focusing on detection of viruses and including children up to 5 years of age. There is paucity of studies on epidemiologic pattern and etiology of ARI in infants from developing countries like India. The aim of this study was to determine the incidence and etiology of ARI in infants, their seasonal variability and association of clinical profile with the etiology.

MATERIALS AND METHODS

Study Design and Ethical Clearance
This prospective cohort study was carried out at the Department of Pediatrics, All India Institute of Medical Sciences (AIIMS), New Delhi, India from August 2012 to December 2014. Part of the investigations was carried out at Translational Health Science and Technology Institute (THSTI), Faridabad, India. The study was approved by the institute ethics committee of both the institute. Written informed consents were obtained from the parents or the guardians.

Study Population
All neonates born in the hospital during the study period were screened for eligibility in this study. The inclusion criteria were term, appropriate for gestational age babies with uneventful perinatal period. Presence of congenital anomalies and refusal to consent were exclusion criteria. The enrolled babies were examined clinically and anthropometric measurements were recorded at the time of enrollment. They were followed regularly for 1 year and parents were asked to consult immediately for any respiratory symptoms. One research staff enquired periodically (2–4 weekly) over the phone about presence of respiratory symptoms. If babies had respiratory symptoms or other complaints, the parents were advised to come to the hospital. Home visits were made if family could not be contacted.

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Definitions
ARI: Presence of cold or cough with or without fever, fast breathing or breathing difficulty.\textsuperscript{11}
Upper respiratory tract infections (URTI): ARI in the absence of fast breathing for age as defined by the World Health Organization.\textsuperscript{11}
Lower respiratory tract infection (LRTI): ARI in the presence of fast breathing for age as defined by World Health Organization (respiratory rate, <2 months: >60/min; 2–12 months: >50/min).\textsuperscript{11}

Microbiologic Sampling
Babies with respiratory symptoms were subjected to a clinical evaluation. Based on the above-mentioned criteria, diagnosis of URTI or LRTI was made, and the predefined microbiologic samples were taken and analyzed (Table 1).

Nasopharyngeal Aspirates
Nasopharyngeal aspirate (NPA) was collected by gently inserting a feeding tube (5 or 6 Fr) into the posterior nasopharyngeal space through one of the nostrils with babies in supine position and applying low suction pressure with 10-mL disposable syringe.

Aspirated fluids were mixed with normal saline to make it to a volume of 3 mL and stored at −80°C till further use.

Multiplex RT-PCR
Viral RNA/DNA from centrifuged NPA samples were extracted with QIAampMiniElute virus spin kit according to the manufacturer’s instructions (QIAGEN, Limburg, Netherlands). The extracted material was analyzed by multiplex real-time PCR assay for qualitative detection of 21 respiratory pathogens according to the manufacturer’s instructions (Fast-Track Diagnostic, Junglinster, Luxembourg). The respiratory pathogens (20 viruses and 1 atypical bacteria) detected were as follows: influenza A, influenza A (H1N1) swl, influenza B, coronaviruses (CoV) NL63, 229E, OC43 and H1K1; paramyxovirus (PIV) 1, 2, 3 and 4; human metapneumovirus (HMPV) A and B; rhinovirus (RV); respiratory syncytial viruses (RSV) A and B; adenovirus (AV); enterovirus (EV); parechovirus (PV); bocavirus (BoV) and Mycoplasma pneumoniae.\textsuperscript{12}

Other Investigations
In children with clinical diagnosis of LRTI, blood culture was done, and for this purpose, 1 mL of blood was collected under aseptic condition in blood culture bottle containing 10 mL of BH1 broth (Difco, Durham, NC) and immediately transported to the microbiologic lab, where it was kept in the incubator at 37°C. At 24 hours of incubation, subculture was done on sheep blood agar (BioMerieux, Durham, NC) and MacConkey agar (HiMedia, Mumbai, India) media and was repeated at 48 and 72 hours. The culture was reported as negative if no growth was observed after 72 hours.

Procalcitonin (PCT) assay was performed on serum sample using VIDAS B.R.A.H.M.S PCT (BioMerieux SA, Marcy-l’Etoile, France) kit; PCT value >0.5 ng/mL was taken as positive (suggestive of bacterial infection) according to the manufacturer’s instruction. Culture of NPA was done in pleuropneumonia-like organisms (mycoplasma) broth and pleuropneumonia-like organisms (mycoplasma) agar and observed for 21 days for growth of Mycoplasma. EUROIMMUN (Lubeck, Germany) enzyme-linked immunosorbent assay kits were used for serology for Mycoplasma and Chlamydia (immunoglobulin G and immunoglobulin M). PCR was also done for detection of PI gene of M. pneumoniae. Urine was tested for Streptococcus pneumoniae antigen with rapid assay—BinaxNOW S. pneumoniae Antigen Card (Alere, Ireland).

Statistical Analysis
The data were managed in Microsoft Access and analyzed using STATA v.12 (StataCorp, College Station, TX). The data on etiology were analyzed using descriptive statistics, and results were expressed as rates and proportions.

RESULTS
A total of 310 newborns [169 (54.5%) boys] were enrolled after screening of 3421 neonates. The mean (standard deviation) gestational age and birth weight of the enrolled neonates were 268 (22) days and 2648 (690) g, respectively. The summary of the demographic characteristics is given in Table 2.

Incidence of ARI
The babies enrolled in this study had a mean (standard deviation) follow up of 11.5 (1.2) months. A total 503 episodes of ARI were

| TABLE 2. Demographic Characteristics of Enrolled Neonates (n = 310) |
|---------------------------------------------------------------|
| **Characteristics** | **Values*** |
| Gender | \begin{tabular}{l}  
Males & 169 (54.5) \\
Females & 141(45.5) \\
\end{tabular} |
| Anthropometry, mean (SD), years | \begin{tabular}{l}  
Birth weight (g) & 2648.2 (689.2) \\
Length (cm) & 47.7 (6.4) \\
Gestation, mean, (SD), d & 267.9 (22.6) \\
Mode of delivery | \begin{tabular}{l}  
Vaginal & 179 (58.9) \\
Caesarean & 101 (32.3) \\
Instrumental & 24 (7.9) \\
\end{tabular} |

*Values are expressed in n (%), unless otherwise specified. SD indicates standard deviation.

**Mother**

| Age of parents, mean (SD), years | 26.5 (3.9) |
| Education level of parents | \begin{tabular}{l}  
Undergraduate & 157 (50.6) \\
Graduate & 102 (32.9) \\
Postgraduate & 51 (16.5) \\
\end{tabular} |
| Number of family members in house, mean (SD) | 5.3 (2.8) |

**Father**

| Living accommodation | \begin{tabular}{l}  
Urban & 296 (96.1) \\
Rural & 12 (3.9) \\
\end{tabular} |
| Family history of any allergy | \begin{tabular}{l}  
Asthma & 82 (26.5) \\
Allergic rhinitis & 99 (31.9) \\
Atopic dermatitis & 32 (10.3) \\
\end{tabular} |

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documented in the first year in 310 enrolled babies at the incidence rate of 1.8 episodes per infant per year. URTI were documented in 476 (94.6%) and LRTI in 27 (5.4%) with incidence rate of URTI and LRTI being 1.7 and 0.1 episodes per infant per year, respectively. Out of 503 ARI episodes, microbiologic samples were analyzed in 395 episodes, which included 377 (95.4%) URTI and 18 (4.6%) LRTI episodes.

### Viruses and ARI

A total of 329 viruses were detected in 250 (63.3%) ARI episodes: 312 (94.8%) viruses from 238 URTI and 17 (5.2%) viruses from 12 LRTI episodes. Single virus was detected in 178 (54.1%) ARI episodes, while 2 and 3 viruses were identified in 65 (16.4%) and 7 (1.8%) episodes, respectively.

**RV** was the commonest virus detected in 105 (42%) ARI episodes (out of 250) followed by RSV in 50 (20%), PIV in 42 (16.8%), human CoV (HCoV) in 44 (17.6%). HKU subtype was the commonest HCoV detected in 16 (6.4%) episodes, while serotype 3 was the commonest PIV detected in 27 (10.8%) episodes. The summary of proportion of different viruses detected is given in Table 3.

Coinfection with 2 or more viruses was observed in 72 (18.2%) of ARI episodes; 2 viruses were detected in 65 (16.4%) and 3 viruses in 7 (1.8%) episodes. RV was the commonest virus among coinfected viruses detected in 26 (36.1%) coinfected ARI episodes. The respiratory viruses like AV, human monocytivirus among coinfected viruses detected in 26 (10.8%) episodes; 2 viruses were detected in 65 (16.4%) episodes, while 2 and 3 viruses were identified in 65 (16.4%) and 7 (1.8%) episodes, respectively.

### Seasonal Variability of ARI

ARI episodes were observed throughout the year with 2 peaks: first peak in February–March and second peak in October–November (Fig. 1). ARI episodes were commonest in March [60 (15.2%)] and least common in June [15 (3.8%)].

### Seasonal Variability of Detected Viruses

The RV episodes were detected throughout the year with 2 peaks: first peak in March and second peak in July–October. RSV showed clear-cut seasonal variation: first in February–March and second in September–November. PIV also showed 2 peaks: first peak in March and second peak in July–September, while influenza virus (IV) was more commonly observed in July. HCoV also showed 2 peaks in March–April and September–October. HMPV were commonly recovered in January–March. Seasonal variability of common viruses is summarized in Figure 2.

### Clinical Characteristics of ARI

The mean (standard deviation) age at the time of first ARI episode was 6 (3) months, and the maximum number of episodes was observed in 6-month-old infants [60 (15.2%)]. In the first 6 months of life, 240 (60.8%) ARI episodes were documented; 109 (27.6%) episodes were in first 3 months and 46 (11.7%) were in first month of life.

### Types of Virus at Different Ages

Viruses were detected in more than half of ARI episodes [144 (57.6%)] that occurred <6 months of age. RV was the commonest virus throughout infancy except in the 9–12 months age group in which RSV was the most common virus detected. The other common viruses detected were RSV, PIV, HCoV and HMPV in 3–6 months of age groups, while IV, HBoV and EV were more commonly detected in 6–9 months age groups (Table 4).

### Clinical Features

Rhinorrea was the most common symptom, observed in 372 (94.8%) ARI episodes followed by cough in 320 (81%), fever in 140 (35.4%), breathing difficulty in 19 (4.8%) and feeding difficulty in 28 (7.1%) of the episodes. A total of 105 (26.6%) episodes had 1 or more other associated symptoms like diarrhea, vomiting, ear itching or skin rash.

### Lower Respiratory Tract Infection

Of 503 ARI episodes, 27 (5.4%) were diagnosed as LRTI on clinical criteria; collected samples were processed and analyzed in 18 (4.6%) episodes. LRTI was most commonly diagnosed in >6 months of age [14 (77.8%)] and only 1 case (5.6%) was documented in the first 3 months. Compared with URTI, the mean (standard deviation) duration of fever was significantly prolonged in LRTI [LRTI: 5 (1.6) days; URTI: 2.6 (1.4) days; P < 0.001]. Viruses were detected in 12 (66.7%) LRTI episodes in which RSV was the commonest [5 (27.8%)] followed by RV in 4 (22.2%) episodes. Epidemiologic agents for LRTI are shown in Table 5.

Virus coinfection was detected in 3 (16.7%) episodes in which RV was the commonest followed by HBoV. LRTI was attributed to mycoplasma pneumonia, chlamydia pneumonia and streptococcus pneumonia in 1 (5.6%), 3 (16.7%) and 7 (38.9%) episodes, respectively (Table 4). Six LRTI episodes had indirect evidence of bacterial infection (raised PCT), although no organism was isolated.

### Viral–Bacterial Coinfection

In 8 (44.4%) LRTI episodes, mixed virus and bacterial infections were observed in which RSV was the most commonly detected virus [4 (22.2%)].

### Outcome of ARI

Infants required hospitalization in 13 (3.3%) episodes with an incidence rate of 0.04 per infant per year; the rest of the episodes were managed on an outpatient basis. Viruses were detected in all the hospitalized cases in which RV was the commonest, detected in 7 (53.8%) episodes followed by RSV in 6 (46.2%) episodes. Virus coinfection was observed in 7 (53.8%) episodes in which RSV was isolated from 3 (23.1%) episodes.

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**TABLE 3. Proportion of Different Viruses Detected in 250 ARI Episodes in 310 Infants**

| Virus Type | Proportion of Viruses* n (%) |
|------------|-----------------------------|
| RV         | 105 (42)                    |
| RSV A and B| 50 (20)                     |
| PIV        | 42 (16.8)                   |
| PIV 4      | 10 (4)                      |
| PIV 3      | 27 (10.8)                   |
| PIV 2      | 2 (0.8)                     |
| PIV 1      | 3 (1.2)                     |
| HCoV 4     | 44 (17.6)                   |
| HCoV 43    | 11 (4.4)                    |
| HCoV 68    | 12 (4.8)                    |
| HCoV HKU   | 16 (6.4)                    |
| HCoV 229   | 5 (2)                       |
| HMPV       | 23 (9.2)                    |
| IV A       | 11 (4.4)                    |
| IV A H1N1  | 2 (0.8)                     |
| IV B       | 3 (1.2)                     |
| EY         | 14 (5.6)                    |
| HBoV       | 19 (7.6)                    |
| EV         | 11 (4.4)                    |
| PV         | 5 (2)                       |
| Total      | 329                         |

*In 72 episodes, more than 1 virus was identified.
In this cohort, 3 deaths were reported: 2 in home (1 had metabolic disease and 1 had congenital heart disease—both were diagnosed after enrollment during follow up) and 1 in hospital (admitted for fever and hepatosplenomegaly at 5 months of age). None of the deaths were assessed to be related to ARI.

### DISCUSSION

We observed 503 ARI episodes in 310 babies followed for 1 year, with the incidence rate of 1.8 episodes per infant per year. The incidence rate of URTI and LRTI were 1.7 and 0.1 episode per infant per year. Nearly 95% of the ARI episodes were URTI. The available evidence on etiology of ARI in children is very heterogeneous in literatures as most study had also included child beyond infancy, but in this study, we had included infants up to 1 year of age only. Similarly, some studies were from rural area, while others were from urban population only.\(^\text{13–15}\)

A study carried out in children <5 years of age from rural Bangladesh had estimated the incidence of 5.5 episodes of ARI per child per year.\(^\text{13}\) Chhabra et al\(^\text{14}\) from India had observed incidence rate of 2.5 episodes of ARI per child per year in which 87.5% of the episodes were URTI and 12.5% were LRTI in children <5 years of age.

Although ARI episodes in this study were documented throughout the infancy, the mean age at first ARI episode was 6 (3) months. A community-based birth cohort study from Switzerland also observed that the median age of ARI was 6 (range, 0.5–12) months.\(^\text{15}\)

### TABLE 4. Types of Virus With Age

| Age Groups (mo) | 0–3 mo | 3–6 mo | 6–9 mo | 9–12 mo |
|-----------------|--------|--------|--------|--------|
| RV              | 26 (10.4) | 22 (8.8) | 20 (8.0) | 11 (4.4) |
| RSV             | 10 (4.0)  | 12 (4.8) | 9 (3.6)  | 12 (4.8) |
| PIV             | 6 (2.4)   | 12 (4.8) | 11 (4.4) | 8 (3.2)  |
| CoV             | 6 (2.4)   | 16 (6.4) | 9 (3.6)  | 2 (0.8)  |
| IV              | 3 (1.2)   | 4 (1.6)  | 5 (2.0)  | 3 (1.2)  |
| HMPV            | 5 (2.0)   | 12 (4.8) | 3 (1.2)  | 0       |
| EV              | 2 (0.8)   | 3 (1.2)  | 4 (1.6)  | 3 (1.2)  |
| HBoV            | 2 (0.8)   | 1 (0.4)  | 3 (1.2)  | 2 (0.8)  |
TABLE 5. Etiology of LRTI Episodes (n = 18)

| Etiology of LRTI | Proportion | Total |
|------------------|------------|-------|
|                 | n (%)      | n (%) |
| Viruses (RT-PCR) |            |       |
| RSV             | 5 (27.8)   | 12 (66.7) |
| RV              | 2 (11.2)   |         |
| PIV             | 1 (5.6)    |         |
| HCoV            | 1 (5.6)    |         |
| IV              | 1 (5.6)    |         |
| HMPV            | 1 (5.6)    |         |
| EV              | 1 (5.6)    |         |
| Bacteria        |            | 17 (94.4) |
| Streptococcus pneumonia | 1 (5.6) | 7 (38.9) |
| Blood culture   | 1 (5.6)    |         |
| Urine antigen   | 6 (33.3)   |         |
| Mycoplasma pneumonia | 1 (5.6) | 1 (5.6) |
| IgM             |            |         |
| IgG             | None       |         |
| PCR             | None       |         |
| Culture         | None       |         |
| Chlamyphila pneumonia | 1 (5.6) | 3 (16.7) |
| IgM             | 1 (5.6)    |         |
| IgG             | 2 (11.1)   |         |
| Indirect evidence | Procalcitonin (>0.5 ng/mL) | 6 (33.3%) |

In 8 LRTI episodes, evidence of bacterial–viral coinfection was detected.

Viruses were the commonest cause of ARI in this study, having been detected in 63.3% of episodes. This detection rate is comparable to the other studies that have used RT-PCR, and it varies from 45% to 79%.15-17 The detection rate of virus depends on the age, type of ARI (URT vs. LRTI), severity of the episodes and hospitalization requirement. Higher virus detection rate has been reported among serious disease and who required hospitalization.15-18

The type of viruses causing ARI varies in different geographical regions.9,15,12 In this study, RV was the commonest virus causing ARI throughout infancy, followed by RSV, PIV and CoV. Recent community-based studies in children from Sweden, Switzerland, Brazil and Madagascar also observed that RV is the commonest virus causing ARI.15,19,20 In studies from Kenya and Madagascar, RSV was detected as the commonest virus causing ARI in infants.21-22 A prospective study from China showed that IV is the commonest virus (19.4%) causing URTI, followed by PIV (10.8%) and RV (10.5%).19 A study by Chounmaitre et al20 from Galveston, TX had found that AV is the commonest virus for URTI in <3 years of age.

Recently, several novel viruses like HCoV, HMPV and HBoV have been reported in different studies in the etiology of ARI.15,20,21 In this study, HCoV, HMPV and HBoV were detected in 17.6%, 9.2% and 7.6% of ARI episodes, respectively. The role of EV as etiology of ARI is increasingly being recognized,15,22 in our cohort, EV was detected in 5.6% episodes.

There are several reports of viral coinfections in ARI ranging from 13% to 28%.15,16,23,34 We also observed viral coinfection in 18.3% ARI episodes as 2 viruses in 16.5% and 3 viruses in 1.8% episodes. A community-based birth cohort study from Switzerland by Regamey et al23 in 2008 also observed viral coinfection as 2 viruses in 15 (17%) cases and 3 viruses in 3 (3%) cases. RV was again the commonest virus associated with coinfections. We observed that rare respiratory viruses like AV, HBoV and PV were commonly associated as coinfection virus. The role of HBoV as a primary respiratory pathogen is debated since it was first discovered by Allander et al24 in 2005, and it has been commonly reported as coinfecting virus.35

RV was the commonest virus detected in all age groups except 9–12 months of age. A population-based study from Bangladesh had reported that RSV was common throughout the infancy followed by PIV especially in <3 months,13 while Lu et al36 from China had observed that RV was the commonest virus responsible for ARI followed by PIV and RSV in <6 months of age, which was similar to this study. Another study from Philippines done in serious respiratory infection in <90 days of age, EV was detected in 22%, RSV in 17% and RV in 10% of the cases.37

This study adds useful insight on the seasonal pattern of incidence of viral infections in infants in north India. India is a tropical country and has a diverse climate as we move from north to south and east to west.37 Some studies from tropical countries had reported that viral ARI occur round the year, while other studies had shown clear seasonal variation.15,24,26 In this study, we observed that there were 2 peaks of ARI: first peak in February–March and second peak in September–November. Seasonal variations have also been reported for various viruses.15,24,26

This study also gives important information regarding the clinical profile of ARI episodes in infants. Cold was the commonest symptom observed in ARI episodes followed by cough and fever. Although we did not observe a significant difference in mean duration of these symptoms among viruses, we documented that infection with RSV was responsible for more severe ARI episodes leading to LRTI. A study from Switzerland and Korea had also observed that children with RSV infection were more severely ill and had more severe symptoms,15,19 while other studies had observed that HMPV was associated with severe disease.9,40,41

In this study, RSV (27.8%) was the commonest virus causing LRTI. Other studies have also reported RSV to be the commonest virus involved in LRTI in infants.20,42-44 We observed evidence of bacterial infection in 94.4% of LRTI episodes, in which atypical bacteria were detected in 22.2% (M. pneumoniae in 5.5% and Chlamyphila pneumoniae in 16.7%) episodes. There is paucity of study investigating the bacterial etiology of ARI in infants. A study from Madagascar in children <5 years of age observed M. pneumoniae in 1.7% and C. pneumoniae in 0.7% of ARIs.35 Other researchers have documented that prevalence of atypical bacteria in ARI varies with age.45,46 In 8 (44.4%) of LRTI episodes, there were evidence of mixed bacterial and viral infections. Other studies also showed evidence of mixed viral and bacterial infection in different proportions.15,47 A study from Kenya documented mixed infection in 21.8% of ARIs.44

The clinical presentation among URTI and LRTI was almost similar except mean fever duration, which was more prolonged in the LRTI group (P < 0.001). Hoffmann et al25 also observed that incidence of fever was higher in LRTI group. Hospitalization was required in only 3.3% of ARI episodes of which 27.8% were LRTI. Regamey et al15 had observed 2% of hospitalization in their birth cohort study.

LIMITATIONS

One of the limitations of this study is that some of the ARIs may not have been reported by the parents. As there was no control group in this study, we cannot conclude whether all the viruses detected were causative agents or simply in the carrier state. This was a hospital-based study. We were able to test only 395 consecutive nasopharyngeal swabs for isolation of viruses because of limited funding.

Strengths of this study include the robust birth cohort design, large sample size, meticulous follow up and use of the sensitive multiplex RT-PCR assay.

CONCLUSION

In this prospective birth cohort study, we observed that ARI constituted a significant problem in infancy and the majority of the episodes were URTI. Viruses were the commonest cause of ARI, RV being the commonest etiology. RSV was the commonest virus detected in LRTI. Two seasonal peaks were seen with majority of the viruses.
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