Epidemiology and Clinical Characteristics of Respiratory Syncytial Virus Infections in Jordan

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Summary

This study was carried out to determine the prevalence, seasonal distribution of RSV, the signs and symptoms associated with it in Jordan. A total of 200 nasopharyngeal aspirates were obtained from hospitalized children (below 2 years old). RSV was detected in 12.5% of patients using direct immunofluorescence technique. Most infections were associated with bronchilolitis, and higher rates of hypoxemia, retractions, tachypnea, hyperinflation and interstitial infiltrates in 1 to 3 months old children. RSV showed a clear temporal periodicity. The epidemic began in December and disappeared in March with a peak of incidence during February 2003 and January 2004. The seasonal distribution showed a significant correlation with temperature, rainfall and relative humidity. This study provides further information on RSV epidemiology which could help in planning of prevention and control programs in Jordan, distinguishing RSV infections on the basis of the clinical picture and considering RSV between December and March each year.

Key words: RSV, epidemiology, clinical characteristics, Jordan.

Introduction

Respiratory syncytial virus is the leading causative agent associated with respiratory tract infections among children [1]. RSV infections are usually symptomatic varying from a mild common cold to a life threatening that are characterized by worsening cough, tachypnea, dyspnoea, hyperinflation, atelectasis, and hypoxemia and increasing respiratory rate [2, 3]. Bronchiolitis and pneumonia are the most common clinical syndromes associated with RSV infections [3, 4].

The epidemiology and seasonal occurrence of RSV was reported for Western [5–8] and Asian countries [9–11] but such information is still limited in the Middle East [12–14]. In temperate regions of Europe and Asia RSV outbreaks usually occur during fall and winter of each year [5, 6]. In tropical countries, RSV causes outbreaks in the hot, rainy season from June to November [15, 16].

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There are no published reports on the prevalence, seasonality and clinical characteristics of RSV infection in Amman, the capital of Jordan. Previous studies in other regions of Jordan reported that the prevalence of RSV was 50% in Irbid (north of Jordan) [17] and 25.5% in Zarqa (north-east of Amman) [14]. None of these studies investigated the prevalence, seasonality and association between respiratory syndromes and RSV all together. Therefore, the aim of this study was to examine these parameters in infants under 2 years of age hospitalized with upper and lower respiratory tract illness. This study provides additional epidemiological information on RSV in Jordan which could help in planning of prevention and control programs in Jordan.

Methods

Patients

Two hundred patients under 2 years of age with the diagnosis of respiratory illness were examined by pediatricians and enrolled in the study. They were admitted to the pediatrics department of the Islamic hospital in Amman between September 2002 and March 2004. This hospital is one of the largest hospitals in Amman with about 29 000 admissions each year, of which about 4000 are admitted to pediatrics department.

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In Jordan, RSV detection is not routine in hospitals. Therefore, the study was approved by the hospital's ethics committee and the parents of patients who signed the consent form.

Clinical data
The clinical characteristics (Table 2) of enrolled patients were obtained from their files in the hospital.

Specimen collection and virus isolation
Nasopharyngeal aspirates ($n = 200$) were collected by the resident pediatricians from children within 24–48 hours of admission, processed and inoculated into fresh monolayer of Hep-2 cell as previously reported [14]. At the end of the incubation period, cells were scraped, pelleted, resuspended in one hundred microliters of PBS and deposited into a well (6 mm diameter) of eight-well Teflon-coated microscope slide (ICNI, USA) and fixed by acetone. Two slides of infected cells were prepared for the immunofluorescence technique. One slide was used for screening of respiratory viruses and the other for detecting RSV [14].

Immuuofluorescence analysis
The prepared screening slides were stained with the commercially available Imagen Respiratory Screen Kit (Dako, Denmark). The kit contains a screening reagent consisting of a pool of purified mouse monoclonal antibodies, each of which has individual specificity either for respiratory syncytial virus, parainfluenza virus 1, 2 or 3, adenovirus or influenza A or B virus. As previously reported [14], reagent was used in a two-step indirect immunofluorescence staining technique according to the manufacturer's recommendation. If either well in the screening slides was found to be positive, the corresponding well in the second slide was used to detect RSV by direct immunofluorescence [14], using the commercially available Imagen Respiratory Syncytial Virus kit (Dako, Denmark).

Weather data
Weather data were obtained from the metrological department of Jordan and included mean monthly temperature, mean monthly humidity, and total monthly rainfall in Amman during the study period.

Statistical analysis of data
The prevalence of RSV in the clinical specimens was determined by the true probability. Population proportions were estimated by using normal distribution tables. χ^2 test was used to determine the dependency of the clinical characteristics on the prevalence of RSV, and $P < 0.05$ was considered statistically significant. The relationship between the prevalence of RSV and the climatic conditions was tested by calculation of the correlation coefficient (r) [18].

Results

RSV

Prevalence of the respiratory viruses and RSV. The prevalence of the seven respiratory viruses and RSV is shown in Fig. 1. Respiratory screen test revealed that 54 (27%) of the total specimens was positive for the respiratory viruses including RSV. These viruses represented 23 (33.9%) of 68 cases in year 2002, 25 (25.8%) of 97 cases in year 2003, and 6 (17.2%) of 35 cases in year 2004. RSV accounted for 25 (46.3%) of the diagnosed respiratory viruses and 12.5% of all cases. In alternate years, RSV accounted for 5 (7.4%), 17 (17.5%) and 3 (8.6%) of the cases diagnosed in years 2002, 2003, and 2004, respectively. In addition to the detected viruses, other unidentified etiological agents that gave negative results with the respiratory viruses screening test accounted for 45 (66.1%), 72 (74.2%) and 29 (82.8%) of the total specimens screened in years 2002, 2003 and 2004, respectively.

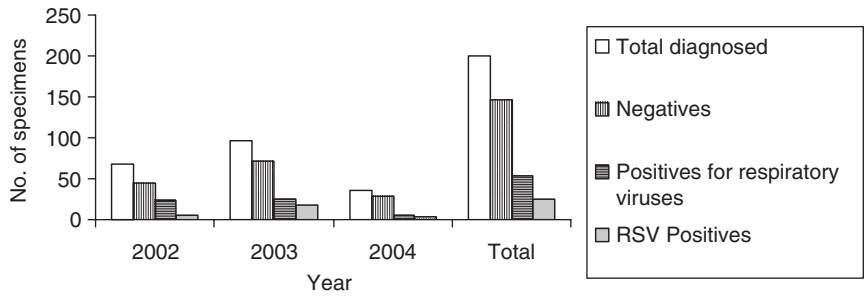

FIG. 1. Total specimens diagnosed, unidentified etiological agents (Negatives), and numbers positive for: respiratory viruses and RSV.

Seasonal distribution of RSV

The monthly distribution of the respiratory viruses and RSV isolates in relation to mean temperature, relative humidity and rain fall is shown in Fig. 2. The prevalence of RSV showed significant ($P<0.05$) negative correlation ($r=-0.66$) with temperature, and significant ($P<0.05$) positive correlation with relative humidity (RH) ($r=0.66$) and rainfall ($r=0.849$). There was a clear seasonal periodicity, RSV epidemics occurring in winter and disappearing in summer. The epidemics began in December 2002 and 2003 when the monthly mean temperature was 9.9°C and 9.4°C, respectively. However, total rainfall was 93.8 mm in December 2002 compared to 72 mm in December 2003. The mean monthly relative humidity was 84.9% in December 2002 and 79.6% in December 2003. RSV incidence peaked in February 2003 and January 2004 and the monthly mean temperature was 8°C and 8.6°C, respectively. However, the total rainfall was 140.1 mm in February 2003 compared with 59.5 mm in January 2004. The mean monthly relative humidity was 80.1% in February 2003, and 80% in January 2004. It was obvious that RSV was circulating in the coldest months of each year during the study period and the epidemics ended with the end of winter.

Patients

Age and sex of patients. The demographic characteristics of enrolled children and those infected with RSV are shown in Table 1. Males were more commonly affected than females ($P<0.05$), and the male to female ratio was 2.6:1. The occurrence of RSV infection in the first year of life 23 (92%) was higher than in the second year of life 2 (8%) with a median age of 8.5 months. Fifty two percent of RSV-infected patients were 1–3 months of age.

Clinical characteristics of RSV infection. Table 2 shows the syndromes and clinical characteristics of the enrolled patients on admission. RSV was associated with 84% of bronchiolitis and 16 % of bronchopneumonia. Forty-four percent of RSV-infected infants had fever and there was a negative significant difference ($P<0.05$) between them and negative patients (75%). RSV-infected

TABLE 1
The demographic characteristic of RSV-infected children

Characteristics	Total no. (%) of patients	No. (%) of RSV-infected patients
Males (M)	113 (56.6)	18 (72)
Females (F)	87 (43.5)	7 (28)
M:F ratio	1.3:1	2.6:1
Age groups (months)		
First year of age		
[1–3]	46 (23)	13 (52)
[4–6]	38 (19)	4 (16)
[7–9]	34 (17)	1 (4)
[10–12]	29 (14.5)	5 (20)
Total	147 (73.5)	23 (92)
Second year of age		
[13–18]	26 (13)	2 (8)
[19–24]	27 (13.5)	0 (0)
Total	53 (26.5)	2 (8)

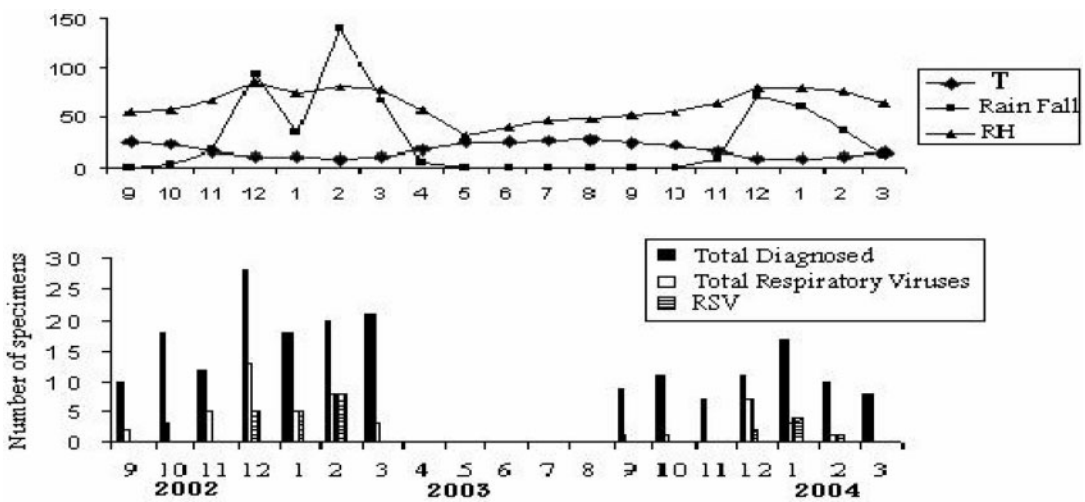

FIG. 2. Monthly total number of specimens tested, total detected respiratory viruses and RSV isolates, in relation to mean temperature (T) (°C), relative humidity (RH) (%) and monthly rainfall (mm).

TABLE 2
The syndromes and clinical characteristics of the enrolled patients on admission

Characteristic	RSV positive $n=25$ No. (%)	Negative* $n=146$ No. (%)	Totals $n=200$ No. (%)
Bronchiolitis	21 (84)	35 (36.5)	61 (30.5)
Bronchopneumonia	4 (16)	61 (41.9)	79 (39.5)
Croup	0 (0)	3 (10.9)	7 (3.5)
Pharyngitis	0 (0)	0 (0)	4 (2)
Tonsillitis	0 (0)	3 (10.9)	4 (2)
Fever ($\geq$38°C, axillary)	11 (44)	110 (75)	144 (72)
Infants aged $\leq$3 months	4 (36)	21 (19)	26 (18)
Infants aged >3 months	7 (64)	89 (81)	118 (82)
Hypoxemia O_2 sat <95%	17 (68)	38 (26)	63 (31.5)
Tachypnea ($\geq$50/min)	17 (68)	50 (34)	75 (37.5)
Retractions	17 (68)	40 (27)	65 (32.5)
Crackles	25 (100)	94 (64)	140 (70)
Chest X-ray findings			
Abnormal	24 (96)	114 (78)	155 (77.5)
Hyperinflation	9 (36)	26 (18)	39 (19.5)
Interstitial infiltrates	13 (52)	73 (50)	95 (47.5)
Consolidation	2 (8)	15 (10)	21 (10.5)
Received antibiotics	18 (72)	127 (87)	172 (86)

*Negative: specimens showed negative result in respiratory viruses screening test.

infants who are more than three months of age (64%) were more likely to be febrile than younger infants (36%).

Sixty eight percent of RSV infected patients had hypoxemia, tachypnea and retractions (Table 2) which is significantly ($P<0.05$) higher than in negative patients with hypoxemia (26%), tachypnea (34%) and retractions (27%). Crackles were observed in all RSV patients compared to 64% of negative patients.

Chest radiograph was abnormal in the majority of both RSV infected patients (96%) and negative patients (78%) (Table 2). Hyperinflation was found significantly ($P<0.05$) more frequent among infants with RSV infection (36%) than among the negative patients (18%). Interstitial infiltrates and consolidation were not significantly ($P>0.05$) different between the two groups (Table 2).

After admission, most infants (86%) with respiratory syndromes received antibiotics (Table 2). Antibiotics were administrated to 72% of the RSV infected infants and to 87% of negative infants (Table 2).

Discussion

Respiratory Syncytial Virus (RSV) is the most common causative agent associated with viral respiratory tract infections especially among children. In each community, the epidemiology of respiratory viruses has to be determined prior to the implementation of novel and costly therapies.

In the present study, the respiratory viruses were detected in 27% of hospitalized infants. Worldwide variation in the prevalence of respiratory viruses was reported to be between 2% and 78.6% [19, 20]. The reasons of this discrepancy are not clear but procedural differences probably played a large role [21].

RSV represented 12.5% of the total cases with a confidence interval of 0.07–0.17. This indicates that it is expected with 95% confidence, to find somewhere between 7% and 17% of hospitalized infants to have RSV infection. The highest prevalence of RSV (17.5%) was detected during year 2003 because sampling was conducted throughout the year. This prevalence in Amman was lower than that reported in Zarqa (25.5%) [14] and in Irbid (50%) [17]. The differences might be due to the differences in the geographical location and climatic conditions, social and economic conditions of the different cities in Jordan.

Our data demonstrated that RSV infections were found in the coldest months of the studied period peaking in February 2003 and January 2004. This result is consistent with other reports from temperate regions [8, 13, 15, 22, 23]. In Zarqa, which is located north-east of Amman, RSV epidemics occur during winter and spring and disappear in summer. The RSV peak incidence was reported in March 1998 and February 1999 [14]. It is difficult to formulate a single theory to explain the epidemiology of viral infections at different times of the year. The most appropriate theory may be that, by staying indoors in cold weather, families promote the spread of virus

infections which relay on the droplet transmission within confined spaces [1]. Susceptible children could acquire the virus from older children in whom manifestations of viral respiratory tract infections are mild [2].

Most RSV Jordanian infected children (92%) were in their first year of life (Table 1). The age incidence is similar to that reported in other parts of the world [10, 24–26]. RSV infections tended to be more common in younger children, because older children have developed immunity or might have bacterial infection [3, 4]. However, more males than females were affected, which agree with reports from Jordan and other countries [14, 26, 27].

The association between respiratory syndromes and RSV has been investigated. RSV was responsible for 84% and 16% of bronchiolitis and bronchopneumonia cases, respectively (Table 2). Similar findings were reported by other investigators [4, 5, 24, 26].

It is known that RSV replicate in the respiratory epithelium without evidence of systemic spread [1]. Therefore, fever is less commonly associated with RSV infection compared to other respiratory viruses and other etiological agents [26]. This fact is consistent with our findings, since 44% of RSV infected children experienced fever (Table 2).

RSV infection is characterized by virus-induced necrosis of bronchial epithelium, hypersecretion of mucus obstructing bronchioles, around cell infiltration and edema of the surrounding submucosa [2, 28]. This explains why clinical and radiological manifestations are marked in Jordanian RSV-infected infants, especially those under the age of three months, compared to negative patients (Table 2). Also, it explains the significant association ($P<0.05$) of RSV infection with hypoxemia, tachypnea, retractions, crackles, and radiological abnormalities. These findings are consistent with other studies [23, 27, 29].

Antibiotics were given excessively to 72% of RSV infected patients, and this exceeds the rates of prescribing antibiotics for similar conditions in Europe, USA, and Canada, which reaches to 40–45% [30, 31]. This can be attributed to two reasons: (i) the unavailability of the routine laboratory diagnosis of viral illnesses in Jordan which result in administration of antibiotics to all respiratory infected patients, (ii) the irrational prescribing of antibiotics, like in other developing countries [27].

In conclusion, this study has demonstrated the prevalence, seasonality of RSV, its associated illnesses, and clinical manifestations. This knowledge may help in: (i) the prediction of the beginning and end of epidemics, (ii) considering RSV in diagnosis and treating acute respiratory illnesses in children between December and March each year, (iii) Planning of prevention and control programs, (iv) distinguishing RSV infections depending on the clinical picture, especially because RSV detection is not routine in Jordan.

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