

Respiratory syncytial virus infection among young children with acute respiratory tract infection in Iraq

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العدوى بالفيرس المخلوي التنفسي بين صغار الأطفال المصابين بعدوى تنفسية حادة في البصرة، العراق

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خلاصة: تم تقدير معدل وقوع العدوى بالفيرس المخلوي التنفسي بين 516 من الأطفال دون الخامسة من العمر، المصابين بعدوى تنفسية حادة، وبين مجموعة شاهدة مكونة من 57 طفلاً، لتحديد صلتها بالمتغيرات الربائية. وتم اكتشاف الفيرس المخلوي التنفسي في 188 (37.6%) من الأطفال المصابين بالعدوى التنفسية الحادة، بينما لم يكتشف بين المجموعة الشاهدة. ووجد أن العدوى كانت أكثر ما تكون في المصابين بعدوى تنفسية حادة وخيمة، وخصوصاً من يعانون التهاب القصبات والتهاب الرئة، وكانت من عوامل إحداث الربو القصبي الحاد في الأطفال بعد السنة الثانية من العمر. وكانت العدوى أكثر شيوعاً في الشهور الستة الأولى من العمر، وذلك بمعدلات متساوية بين الذكور والإناث. ولم يكن هناك دور ملحوظ للعوامل الاقتصادية الاجتماعية والازدحام في وقوع العدوى أو في انتشارها. كما أن الرضاعة من الثدي لم تكن ذات أثر وقائي واضح ضد هذه العدوى.

ABSTRACT The incidence of respiratory syncytial virus infection was assessed among 516 children under 5 years with acute respiratory infection and 57 control children free of respiratory infection to determine its relation to epidemiological variables. Respiratory syncytial virus was detected in 188 (37.6%) children with acute respiratory infection and in none of the control group. The infection was highest in those with severe acute respiratory infection, particularly severe bronchiolitis and pneumonia and it precipitated acute bronchial asthma in children over 2 years. The infection was most common in the first 6 months and both sexes were equally affected. Socioeconomic factors and crowding played no significant role in the incidence and spread of the infection. Breastfeeding had no clear protective effect against the infection.

L'infection par le virus respiratoire syncytial chez les jeunes enfants atteints d'infection aiguë des voies respiratoires à Bassora (Iraq)

RESUME L'incidence de l'infection par le virus respiratoire syncytial a été évaluée chez 516 enfants de moins de cinq ans atteints d'une infection aiguë des voies respiratoires et 57 enfants témoins sans infection respiratoire afin de déterminer sa relation avec les variables épidémiologiques. Le virus respiratoire a été décelé chez 188 (37,6%) des enfants ayant une infection respiratoire aiguë et chez aucun enfant du groupe témoin. L'infection était la plus forte chez ceux atteints d'une forme grave d'infection respiratoire aiguë, en particulier bronchiolite grave et pneumonie, et constituait un facteur précipitant courant de l'asthme bronchique aigu chez les enfants de plus de deux ans. L'infection était la plus fréquente durant les 6 premiers mois et touchait tout autant les deux sexes. Les facteurs socio-économiques et le surpeuplement ne jouaient pas de rôle important dans l'incidence et la propagation de l'infection. L'allaitement maternel n'avait pas d'effet protecteur manifeste contre l'infection.

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Introduction

Acute respiratory infections (ARI) are among the most important causes of morbidity and mortality in children around the world [1]. Much progress has been made in elucidating the microbial causes of ARI and the epidemiology of many of its etiologic agents. The problem, nevertheless, remains enormous and methods of diagnosis, treatment and prevention have been developed slowly [2].

Many viruses have been implicated in the etiology of ARI, but most severe illness is caused by relatively few viruses, which include respiratory syncytial virus (RSV), influenza virus, parainfluenza virus and adenovirus [3]. RSV is the only viral agent that produces severe disease in the first few weeks to months of life, when specific maternal antibody is uniformly present in infants' serum [4]. RSV has been identified as a cause of 50%–90% of cases of bronchiolitis and 5%–40% of cases of pneumonia in young children. RSV has also been associated with 10%–30% of cases of paediatric bronchitis. In contrast, less than 10% of croup cases have been associated with RSV. The virus is rarely isolated (less than 1%) from patients without respiratory disease [5–7].

The risk of severe, complicated or fatal RSV infection is correlated with a number of host characteristics, especially age and underlying disease, with some environmental factors such as poor socioeconomic status, and possibly also with variations in the virus itself [6–8]. One of the remarkable features of the epidemiology of RSV is its consistent pattern of infection and disease. RSV is the only respiratory pathogen that has produced a sizeable epidemic every year in large urban areas [9].

There is limited information available in our community about the epidemiology of

this virus. Thus, this study was carried out to explore the extent of RSV infection. The objectives of the study were:

- to estimate the incidence of RSV infection in children < 5 years of age with ARI and the role of RSV in various respiratory illnesses;
- to study RSV infection in relation to such variables as age, sex, socioeconomic factors, crowding and breast-feeding.

Subjects and methods

The study was a cross-sectional study conducted in the paediatric outpatient clinics of Basra General Hospital and Al-Tahreer Hospital. Children who came to the outpatient clinics with ARI were selected consecutively during the study period.

The study ran from 1 November 1992 to 15 April 1993. This period corresponds to relatively cold months in Basra when the incidence of ARI is known to be highest [10]. Accordingly, 516 children under 5 years of age were included in the study. In addition, 57 children free of respiratory illness were included in the last month of the study and served as a control group. These were healthy children under 5 years of age who were attending the health centres for routine immunizations and had not experienced an episode of ARI during the previous month. A special questionnaire was designed to collect information for each child with ARI. The mother or family member who brought the child to the outpatient clinic was the main source of information.

Sick children underwent a careful clinical examination to determine a specific diagnosis and the grade of severity of the respiratory illness. Two primary clinical signs, chest indrawing and fast breathing, were considered for the grading of severity

of ARI. However, the current terminology of ARI (cough or cold, pneumonia and severe pneumonia) was replaced by the old terminology (mild, moderate and severe) because this was more convenient and each of the old categories of ARI included several illnesses which served the objectives of our study [11].

After complete clinical diagnosis of ARI, nasopharyngeal secretions were obtained by suction with a disposable mucus extractor (Vycon, Ecouen, France) or nasogastric tube (Uno-Plast, Denmark) according to a method described McIntosh et al. [12]. Then the specimens were transported in standard packaging to the laboratory.

Phosphate-buffered saline (1.0–1.5 ml.) was usually added to the specimen to facilitate its transfer into a plastic test tube. The specimens were vortexed to obtain a homogeneous suspension, then frozen at -20°C and stored for later RSV antigen detection by an enzyme-linked immunosorbent assay (ELISA) procedure as recommended by the manufacturer (Abbott Laboratories Diagnostic Division, North Chicago, United States of America).

Results

Of the 516 children under 5 years included in the study, data were collected from 500. Of these 500, 312 (62.4%) were clinically diagnosed with pneumonia or bronchiolitis, whereas 188 (37.6%) were diagnosed with other respiratory illnesses, which included bronchitis, bronchial asthma, croup and upper respiratory tract infection (URTI). Lower respiratory tract infections (LRTI) were the most common cause for consultation at the outpatient clinics of the hospitals. There was a male predominance in different types of respiratory illnesses: 283 boys and 217 girls.

RSV antigen was detected by ELISA in 188 (37.6%) out of the 500 nasopharyngeal specimens collected (Table 1). whereas RSV antigen was not detected in any of the specimens from any of the control children who were free of respiratory illness. According to the clinical grading of severity, RSV infection was highest in children who presented with severe ARI (46.1%), then moderate ARI (34.7%) and then mild ARI (25.0%). The statistical difference of infection rates was highly significant ($\chi^2 = 13.34$, $P = 0.001$).

A higher incidence of RSV infection was seen in children with bronchiolitis, pneumonia and bronchial asthma: 45.7%, 41.2% and 41.9% respectively (Table 1). The lowest infection rate was observed in children with URTI (21.2%). The difference in the incidence of RSV infection in these respiratory illnesses was statistically significant ($\chi^2 = 20.09$, $P < 0.001$).

When the grades of severity for each ARI were considered, RSV was most frequently found in severe cases of acute bronchiolitis (53.1%), pneumonia (43.0%) and bronchitis (33.3%) (Table 1). In acute attacks of bronchial asthma and croup, cases of moderate severity were associated with high RSV infection rates (50.0% and 37.5% respectively) but RSV infection was more frequent in mild cases of acute URTI.

RSV infection was found to be relatively high during the first 6 months of life (43.7%) and decreased with increasing age. However, variation in the infection rates by age were not statistically significant ($\chi^2 = 3.51$, $P > 0.05$). Sex differences were also not statistically significant ($P > 0.05$) (Table 2).

Children clinically diagnosed with pneumonia showed a higher incidence of RSV infection in those over 2 years of age (58.0%). In bronchiolitis syndrome, the incidence of RSV infection was highest in the

Table 1 Incidence of RSV infection by grade of severity of acute respiratory illness

Acute respiratory illness	Grade of severity							Total tested ^a No. %
	Mild		Moderate		Severe			
	No. positive	%	No. positive	%	No. positive	%		
Pneumonia	0/0	0.0	5/16	31.3	37/86	43.0	42/102	41.2
Bronchiolitis	8/22	36.4	36/90	40.0	52/98	53.1	96/210	45.7
Bronchial asthma	0/0	0.0	8/16	50.0	5/15	33.3	13/31	41.9
Bronchitis	5/23	21.7	14/56	25.0	1/3	33.3	20/82	24.4
Croup	0/3	0.0	6/16	37.5	0/4	0.0	6/23	26.1
URTI	10/44	22.7	1/8	12.5	0/0	0.0	11/52	21.5
Total ^b	23/92	25.0	70/202	34.7	95/206	46.1	188/500	37.6

^a $\chi^2 = 20.09$, $P = 0.001$ ^b $\chi^2 = 13.34$, $P = 0.001$

RSV = respiratory syncytial virus

URTI = upper respiratory tract infection

Table 2 Incidence of RSV infection by age and sex

Age (months)	Sex ^a				Total ^b	
	Male		Female		No. positive	%
	No. positive	%	No. positive	%		
≤ 6	42/87	48.3	24/64	37.5	66/151	43.7
7–12	25/73	34.2	20/53	37.7	45/126	35.7
13–24	27/71	38.0	18/58	31.0	45/129	34.9
25–36	14/37	37.8	9/31	29.0	23/68	33.8
37–60	5/15	33.3	4/11	36.4	9/26	34.6
Total	113/283	39.9	75/217	34.6	188/500	37.6

^a $\chi_1 = 1.28$, $P > 0.05$ ^b $\chi_1 = 3.51$, $P > 0.05$

RSV = respiratory syncytial virus

first year of life (47.7%). In acute asthmatic attacks, RSV infection was higher among children over 2 years of age (46.4%), while no case occurred under that age. URTI was associated with a high incidence of RSV infection during the first 6 months of life (31.6%) (Table 3).

There was no significant difference in RSV infection in relation to various socio-economic factors (Table 4). Variations in RSV infection were not statistically significant with regards to feeding practices ($\chi^2 = 0.793$, $P > 0.05$). Of the 229 breastfed children, 88 (38.4%) were positive for RSV in-

Table 3 Incidence of RSV infection with age and type of acute respiratory illness

Age (months)	Acute respiratory illness									
	Pneumonia		Bronchiolitis		Bronchial asthma		Bronchitis		Croup	
	No.	%	No.	%	No.	%	No.	%	No.	%
	positive		positive		positive		positive		positive	
≤ 6	19/42	45.2	40/84	47.6	0/0	0.0	1/5	20.0	0/1	0.0
7-12	5/21	23.8	34/71	47.9	0/0	0.0	2/14	14.3	0/3	0.0
13-24	9/22	40.9	22/55	40.0	0/3	0.0	8/25	32.0	5/15	33.3
25-36	6/12	50.0	0/0	0.0	8/20	40.0	8/29	27.6	1/4	25.0
37-60	3/5	60.0	0/0	0.0	5/8	62.5	1/9	11.1	0/0	0.0

RSV = respiratory syncytial virus

URTI = upper respiratory tract infection

Table 4 Distribution of RSV infection according to socioeconomic factors and crowding

Variable	Total tested	No. positive	%
<i>Father's occupation^a</i>			
Employed	252	102	40.5
Self-employed	189	65	34.4
Unemployed	59	21	35.6
<i>Mother's occupation^b</i>			
Housewife	475	175	36.8
Employed outside the home	25	13	52.0
<i>Income^c</i>			
Low	301	113	37.5
Middle	124	50	40.3
High	75	25	33.3
<i>Crowding index^d</i>			
1	53	22	41.5
2	117	41	35.0
3	157	60	38.2
4	98	35	35.7
5	46	18	39.1
6+	29	12	29.7

^a $\chi^2 = 1.819$, $P > 0.05$ ^b $\chi^2 = 1.72$, $P > 0.05$ ^c $\chi^2 = 0.974$, $P > 0.05$ ^d $\chi^2 = 1.42$, $P > 0.05$

RSV = respiratory syncytial virus

fection. Of the 70 bottle-fed children, 28 (40.0%) were positive for RSV infection and of the 58 who were given mixed feeding, 26 (44.8%) were positive. This excluded 49 children who were not tested.

Discussion

RSV is considered the most important respiratory pathogen in infants and young children throughout the world [2,6,9]. The incidence of RSV infection in children under 5 years of age with ARI obtained from this study was 37.6%, indicating that RSV is a common respiratory

pathogen. However, a higher incidence has been recorded in the United Kingdom [8,13], while lower rates have been reported in the United States of America [5,7].

RSV was not detected in any of the control children free of respiratory illness. This finding is in agreement with most other studies [5,7]. RSV is almost never isolated from healthy infants, strongly supporting the view that RSV infection during infancy and early childhood usually results in respiratory illness [9,14].

RSV is the most common cause of LRTI in infants and young children [6,9]. In our study, RSV was detected more frequently among children with severe ARI, particularly severe cases of acute bronchiolitis and pneumonia, which appear to be the most common manifestations of LRTI. This trend has also been noted by others [13,15,16].

RSV was associated with different respiratory syndromes. It was most commonly detected among patients clinically diagnosed with bronchiolitis and pneumonia and patients with acute asthmatic attacks, but it was less frequently detected in children with croup and bronchitis and was least commonly detected in those with URTI. This finding is consistent with the finding that RSV is the major cause of pneumonia and bronchiolitis in infants and young children shown in a variety of inpatient and outpatient studies [5,7,13,17].

RSV was associated with 26% of croup cases; however, lower rates of RSV croup have been recorded by others [7,18]. This is probably due to the small number of croup cases in our study which may falsely indicate a high correlation.

RSV bronchitis in this study was within the estimated range of 10%–30% [6] but a higher incidence was reported in Newcastle in the United Kingdom [13]. In contrast, the rate of RSV URTI was higher than that re-

corded by others [7,13]. This might be because almost all children with URTI were seen in the first year of life when the risk of RSV infection is very high [6].

In young children, most attacks of obstructive airway diseases are caused by viral respiratory infection [19]. In our study, it was found that RSV was implicated in 46% of acute attacks of bronchial asthma among children over 2 years of age. This is consistent with other studies [19,20]. Thus, RSV is a common precipitant of acute attacks of bronchial asthma.

RSV infection was most common during infancy especially during the first 6 months of life; it then decreased with increasing age. A similar age pattern has been observed by others [4,15,21].

The peak incidence of RSV bronchiolitis was between the first 6 months and the first year of life, whereas the peak incidence of RSV pneumonia occurred at older ages. Thus, RSV appears to be more important as an etiologic agent in bronchiolitis than in pneumonia in early infancy. This finding agrees with other studies [6,7,17].

The sex of the child appears to play no role in the rate of RSV infection except during the first 6 months of life when it was relatively more common among males than females, but the difference was not statistically significant. This observation concurs with other studies [15,18,21].

Our study showed that the socioeconomic status of the family had no significant effect on the incidence of RSV infection in the children; this was also observed by Carlsen and Orstavik [17]. In contrast, some studies have found a positive correlation between poor socioeconomic conditions and increased numbers of RSV cases [4,8,21]. Regarding the parents' occupation, there was a nonsignificant relative increase of RSV infection in children with working parents compared to children

with unemployed parents. Working parents might leave their babies in the care of others or in nurseries with babysitters ignorant of child health regulations, which may increase their risk of infection. In addition, clustering of children increases the risk of infection in general [10]. As for socioeconomic factors, crowding seemed to have no important role in increasing the incidence of RSV infection in our study. In contrast, crowding has been reported to be an important factor in spreading RSV infection within families [6,22].

The observed high incidence of RSV infection among infants under 6 months of age suggests that the role of breastfeeding as protection from RSV infection is doubtful. There was no significant difference in infection rate between bottle-fed and mixed-fed children. Similar findings have been reported by others [23,24]. However, several adverse social and environmental factors are associated with RSV infection and these factors may affect the protective effect of breastfeeding [24].

Conclusions

The incidence of RSV infection in children under 5 years of age with ARI is high and the virus is a common respiratory pathogen. RSV infection is most commonly associated with severe ARI, particularly with severe LRTI. The most serious infection was seen in the first 6 months of life.

RSV infection was detected most frequently in children with acute bronchiolitis and pneumonia but less frequently in children with croup and bronchitis and even less often among patients with URTI. RSV infection was a common precipitant of acute attacks of bronchial asthma among children over 2 years of age.

Males and females seemed to be equally affected. Socioeconomic factors did not appear to play an important role in the incidence and spreading of RSV infection. Breastfeeding had no clear protective effect against RSV infection.

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