

ACUTE RESPIRATORY INFECTIONS IN CHILDREN FROM A DEPRIVED URBAN POPULATION FROM URUGUAY

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SUMMARY

To obtain base line data on incidence, duration, clinical characteristics and etiology of acute respiratory infections (ARI), 276 children from deprived families living in Montevideo were followed during 32 months. The target population was divided into two groups for the analysis of the results: children aged less than 12 months and those older than this age.

During the follow-up period 1.056 ARI episodes were recorded. ARI incidence was 5.2 per child/year. It was 87% higher in infants than in the older group, as was the duration of the episodes. Most of the diseases were mild. Tachypnea and retractions were seldom observed, but 12 children were referred to the hospital, and 2 infants died.

Viral etiology was identified in 15.3% of the episodes. RSV was the predominant agent producing annual outbreaks. Moderate to heavy colonization of the upper respiratory tract by *Streptococcus pneumoniae* (32.3%) and *Hemophilus* sp. (18.9%) was recorded during ARI episodes.

This community-based study furnish original data on ARI in Uruguay. It enabled to asses the impact of these infections on childhood.

KEYWORDS: Respiratory tract infections; Respiratory syncytial viruses; *S. pneumoniae*; *Haemophilus* infections.

INTRODUCTION

In developing countries morbidity and mortality due to acute respiratory tract infections have remained major problems. As diarrheal disease mortality has been brought under control through the use of rehydration therapy, the need to address problems of acute respiratory infections (ARI) has become increasingly appreciated¹.

In Uruguay vaccine-preventable respiratory diseases have been largely controlled. However, ARI continues to contribute to most of the severe morbidity and mortality. As documented in a survey in 1982, ARI was considered by the mother-to-be the most frequent sig-

nificant childhood health problem¹⁴. Public health service monitoring shows that ARI management draws heavily upon health care service utilization, being either the first or the second most common cause for the seeking of care recorded every year.

The overall mortality rate due to ARI was 1.3 per 1.000 in 1988¹⁵, although rates are known to be far higher in subpopulations of children, especially young infants in low socioeconomic urban population¹⁷.

Despite the recognized prevalence of the problem, however, precise data required to understand and

control ARI, and to permit the rational diagnosis and management of cases, have been lacking. This paper describes a longitudinal, 32-month community-based study designed to monitor ARI in an index group of children followed from birth. The siblings of the index cases who were under five years of age were also followed ⁹.

The main characteristics of the index children population have been described in a previous publication which reported a provisional analysis of part of the study ⁹. This paper includes the whole study population, both index cases and siblings, as regards ARI incidence rates, duration of episodes, clinical signs and symptoms, severity of diseases, viral etiologies, bacterial colonization of the upper respiratory tract, and seasonal variation of the most frequent morbidities.

MATERIAL AND METHODS

A description of the target population has been published elsewhere ⁹. In summary, it included 166 index children followed from one month of age, and 110 of their siblings aged less than five years. For the purpose of the analysis, the study population was divided in two groups according to age: children under 12 months of age and an older group that included the index children that had passed their first year of life, and their siblings aged one year and older.

Enrollment was made when parents attended for the first time to control their newborn child at the Health Center of the 17th Section of Montevideo. This area was selected since it has higher infant and child (one to four years) mortality than the national rates, 52 and 30.3 deaths per 1.000 live births respectively. Families that accepted to participate in the study were visited for the first time when the child was one month old. At that moment the siblings aged less than five years, or any other child of that age, living in the same household, were also enrolled. Since that moment the children were checked regularly (every ten days) by pediatricians in their homes during the 32-month study (May 1985 - December 1987). Recall data on children's health and morbidities, were recorded on special precoded forms. Detailed results of physical examination obtained by the pediatricians at each visit and during ARI cases were also recorded. Specimens for microbiology studies were collected during the majority of ARI episodes.

DEFINITIONS

Upper and lower respiratory infections were based on BOSTID consensus criteria of June 1985, as follows. Upper respiratory infection was recorded when at least one of the following signs was present: purulent nasal discharge, sore throat, ear ache with or without discharge or uncomplicated cough. Lower respiratory infection was considered present if at least one of the following signs were observed during the episode: respiratory rate ≥ 50 breaths per minute, retractions, wheezes, rales, stridor or cyanosis.

Severity was assessed according to the presence of a respiratory rate ≥ 50 breaths per minute and/or retractions ²².

ARI incidence rates were calculated following Rothman ²¹, where new episodes comprise numerator, and each 10-day period comprises the denominator. Analysis were subsequently also corrected to express the number of episodes of ARI per child per year.

Microbiology studies:

Nasopharyngeal aspirates (NPA) were collected at every new ARI episode which was occurring at the time of the physician's visit. Thus the samples may have been taken between one and ten days after onset of symptoms ¹¹.

The samples were used for virus isolation in HEP-2, LLC-MK2 and MDCK cell cultures, and for specific antigen detection by indirect immunofluorescence (IIF) ⁶, for Influenza A, Influenza B, respiratory syncycial virus, parainfluenza viruses one and three, and adenovirus. Reagents for IIF were obtained from Burroughs-Wellcome Co., England, and quality controlled by Dr. M. Grandien from the National Bacteriological Laboratory in Sweden.

Bacterial colonization of the nasopharynx was determined in patients during ARI episodes by semiquantitative assessment of moderate or heavy growth performed by streaking samples on four quadrants of blood agar and enriched chocolate agar plates. At least five colonies in quadrant three, or any colony in quadrant four of *Streptococcus pneumoniae* or *Hemophilus* sp. growth was noted.

RESULTS

Incidence and duration of ARI episodes:

As the children aged during the study, the propor-

Table 1
Rate ratio for children risk factor of ARI and LRI

ARI						
Age in No. of new ARI episodes	No. Child-period* obs. & at risk	Incidence per child-year	Rate 95% conf. int.			
			Ratio	lower	upper	
< 6	267	6.624	2.11	1.80	2.49	
6-11	204	5.121				
> 12	358	2.992	1.71	1.44	2.03	
LRI						
< 6	126	2.984	2.35	1.85	2.97	
6-11	121	3.038				
> 12	152	1.271	2.39	1.88	3.04	

* period = 10 days

tion under one year of age decreased from 62% initially to 10% at the completion of the follow-up. As an average, 41% of the visits were made to children of less than one year of age.

During the 32-month of observation, 1.056 of ARI were clinically evaluated in 276 children. Of these, 399(37.8%) were lower respiratory tract episodes. Table 1 shows that the incidence of ARI varied with the age of the child. The rate for ARI was 87% higher in younger children for lower tract disease. The age associated difference became even more striking (131%) in children less than 12 months compared to older children.

Duration of ARI, both upper and lower tract disease were also affected by age. In the youngest group, 45% of episodes lasted more than 10 days (Table 2). In the older group episodes tended to be shorter.

Signs, symptoms and severity:

The most commonly recorded ARI signs and symptoms for both age groups and their distribution as upper and lower respiratory infections are shown in Table 3, cough, wheezing and rales were more frequently seen in the older child. Ear involvement requiring special management was present in 33.6% of young infants, and in 13% of those older than 12 months of age. Rhinitis was also a frequent finding. Moderate to severe cases were scarce at all ages. None of the children with upper respiratory tract infections had accelerated respiratory rate. Only 15 children had retractions and 13 had \geq 70 rpm (Table 4).

Only 22 children were referred to the Children's Hospital: 18 ARI(2.3% of all episodes) and four diarrheal diseases. Of those hospitalized, 12 had pneumonia, one bronchiolitis, five miscellaneous respiratory infections (measles: two, whooping cough:

Table 2
Duration of all ARI and LRI episodes by age

Duration (in days)	All ARI**		LRI ***	
	< 12 months n=471	\geq 12 months n=358	< 12 months n=247	\geq 12 months n=152
< 10	259 (55%)	233 (65.1%)	128 (51.8%)	90 (59.2%)
10-19	113 (24.0%)	71 (19.8%)	68 (27.5%)	35 (23.0%)
20-29	59 (11.9%)	25 (7.0%)	25 (10.1%)	13 (8.6%)
\geq 30	43 (9.1%)	29 (8.1%)	26 (10.5%)	14 (9.8%)

** p = 0.0015 (z test)

*** p = 0.0735 (z test)

Table 3
Percentage of signs and symptoms recorded in upper(URI) and lower(LRI) respiratory episodes by age.

Signs Symptoms	URI		LRI	
	< 12 months	≥12 months	< 12 months	≥ 12 months
Cough	51.8	55.0	82.6	91.9
Purulent rhinitis	24.2	36.3	32.7	23.0
Sore throat	16.6	19.4	10.3	16.2
Earache/discharge	33.6	13,0	27.1	5.1
Increased RR	-	-	22.5	16.2
Retractions	-	-	2.2	1.3
Wheezing	-	-	17.3	27.3
Rales	-	-	80.4	91.4
Stridor	-	-	0.5	0.4
Cyanosis	-	-	0.2	-
Total Episodes	300	113	409	234

Table 4
Age distribution of respiratory rates and retractions during lower respiratory tract episodes.

Age in months	No. child observed	No. w/RR*frequency of				R**(%)
		< 40 (%)	40-49 (%)	50-69 (%)	> 70 (%)	
0 - 11	418	131 (31.3)	195 (46.7)	84 (20.1)	8 (1.9)	9 (2.2)
12 - 59	345	140 (40.6)	167 (48.4)	33 (9.6)	5 (1.4)	6 (1.7)

* RR = respiratory rate **R= retractions
RR > 50 in 0-11 month group (92/418=22%)
RR > 50 in 12-59 month group (38/43=11%)
Z test difference in both groups: p < 0.001

one, tuberculosis: one, laryngitis: one) and four had severe diarrheal disease.

The second most frequent morbidity observed during the study was acute diarrheal disease (ADD). An increased occurrence of ADD was observed in the summer, as well as ARI increase during the colder months.

Considering the possibility that children at increased risk of ADD were also at increased risk of ARI, this relationship was analysed. A statistically significant association between ADD and ARI was found for children followed at least for one year (Table 5).

During the observation period, three fatal cases were recorded in children younger than 12 months. One infant died at home; the post-mortem history obtained by the pediatrician indicated sudden death, however the forensic report stated aspiration pneumonia. The other two babies were hospitalized, one with bronchopneumonia and the other with a protracted diarrhea asso-

ciated with severe under nourishment. None of the fatal cases had etiologic diagnosis.

Viral etiology:

Viral etiology was determined in 15.3% of the 856 specimens collected during ARI episodes (303 URI; 530 LRI). Some viruses were detected over longer periods of time, other sporadically. RSV isolates were recovered during 21 of the 32 months of observation. Influenza outbreaks were of short duration: influenza A was detected during five months, however none was seen except in 1986. Influenza B occurred in one month of 1987. Adenoviruses and parainfluenza viruses were occasionally isolated.

Table 6 describes the relative participation of the viral etiologies distributed among the children of the different age groups. RSV had a similar high frequency among both age groups. Of the total signs and symptoms recorded during ARI episodes, 14.3% of purulent rhinitis was present in RSV associated cases. Also the 87 RSV positive cases contributed to the increased respira-

Table 5
 Association of risk of ARI and ADD among study-children *

Illness	Total N° of children/ period at risk	Total N° of new episodes	Incidence per child/ period	Rate ratio	95% confid. interv.	
					lower	upper
Diarrhea	821	156	0.1900	1.34	(1.65	- 1.05)
No diarrhea	1539	218	0.14165			

* comprise only those children observed at least one year.

Table 6
 Viral positive results in NPA of ARI cases by age groups.

Virus	N° identified in age group	
	< 12 months	(> 12 months)
Resp. Syncytial virus	51 (10.6)	36 (10.3)
Influenza A	3 (0.62)	3 (0.86)
Influenza B	0	1 (0.29)
Parainfluenza 1	3 (0.41)	1 (0.29)
Parainfluenza 3	3 (0.62)	5 (1.4)
Adenovirus	5 (1.0)	5 (1.4)
Enterovirus	5 (1.0)	0
Others	1 (0.2)	6 (1.7)
Negatives	413 (85.5)	293 (83.7)
Total	483	350

elsewhere on the different sectors of the respiratory tract^{2, 5, 7, 25}.

Although the majority of ARI cases were mild, and lacked the usually monitored severity markers¹⁰, about 50% involved the lower respiratory tract, and 45 percent lasted more than ten days. Therefore ARI represented an important challenge for the child's development and a major burden for the community because of the cost to both families and health services. Two fatalities occurred in twelve of the ARI hospitalized children. Although the frequency of ARI hospitalizations was within the range of that found by GLEZEN et al.⁸, both deaths reflected the persistence of severe diseases despite the overall low specific mortality rates recorded in Uruguay^{12, 13}.

tory rate in 17.7%, to retractions 16.7% and to wheezing in 11.8% of cases.

Bacterial colonization:

Moderate to heavy colonization by *Streptococcus pneumoniae* was detected in 32.3% of 833 ARI episodes. *Hemophilus* sp. had a frequency of 18.9 percent. A B hemolytic *Streptococcus* was recovered in only one case of all the studied ARI cases.

DISCUSSION

This community-based study on ARI is the first to be performed in the southern part of South America. It furnishes information about the occurrence of ARI in a cohort of children from a deprived urban population living in a mid-developed temperate climate country.

The children under 12 months of age had an annual incidence rate of 5.8 episodes of ARI, similar to that found in other countries. This finding underlines an increased ARI risk related to age^{3, 23}. Repeated or lengthy infections due to ARI and the 251 episodes that included ear compromise in this population, emphasize the potential for long-term deleterious effects noted

Viral etiology was defined for 67 of the 303 cases of upper respiratory tract disease and 64 of 530 of the LRI cases. RSV was identified in a sufficient number of cases to assess signs and symptoms associated with the community disease. The mild nature of the disease seen in most of the cases was striking. The lower percentage of positive results obtained either for RSV and for the other respiratory virus (15.3%), might be explained by the lower viral shedding in such mild infections^{16, 19, 24}. It could also be affected by the timing of the specimen collection due to the periodicity of the pediatrician's visits or exceptionally to delays in the cell culture inoculation of the specimens. As rhinoviruses were not investigated, its participation is another possibility that cannot be excluded (ARRUDA et al.¹).

In a community-based study in a tropical area found that rhinoviruses were the most important etiologic agent of ARI.

The relative distribution of viruses as well as the importance of RSV, related to all ages covered by the longitudinal study, were similar to those found in many studies carried out in industrialized and in developing

countries¹⁸. The viruses involved in diarrheal disease were not investigated, but the increase of ADD cases during the periods when ARI episodes were mostly undiagnosed enables us to propose some shared etiology²⁰.

This emphasizes the continuous high incidence of ARI. As further information was required before specific measures to prevent the occurrence of severe disease could be undertaken¹⁶, a hospital-based study was subsequently started.

RESUMO

Infecções respiratórias agudas em crianças de famílias pobres de Montevidéu

Para obter informação básica sobre a incidência, duração, características clínicas e etiologia das infecções respiratórias agudas (IRA), foram observadas 276 crianças de famílias pobres que moram em Montevidéu durante 32 meses. A população alvo foi dividida em dois grupos para análise dos resultados:

Crianças com menos de 12 meses e acima dessa idade. Durante o período de seguimento foram registrados 1056 episódios de IRA. A incidência de IRA foi 5.2 por criança/ano. Foi 87% mais alta nos lactentes do que nos grupos de mais idade, com duração maior dos episódios. A maioria das infecções foi pouco grave. Observaram-se poucos casos com taquipnéia e retrações, mas 12 crianças foram hospitalizadas e dois lactentes morreram. Etiologia viral foi identificada em 15.3% dos episódios. RSV foi o agente predominante, produzindo epidemias anuais.

Registrou-se durante os episódios de IRA a colonização moderada até alta no trato respiratório superior de *S. pneumoniae* (32.3%) e *Hemophilus* sp. (18.9%).

Este estudo de comunidade forneceu informações originais sobre IRA no Uruguai. Permitiu avaliar o impacto destas infecções nas crianças.

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